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Contents

ABSTRACTS

The tables and figures attached at the time of submission have been deleted due to space limitations.

PLENARY SESSION

Plenary Session 1

Hematopoietic Stem Cell Expansion: Present and Future

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Self-renewing multipotent hematopoietic stem cells (HSCs) are a rare population of cells that support life-long hematopoiesis and the reconstitution of the hematopoietic system after HSC transplantation. HSCs can also be collected from umbilical cord blood but often contains too few HSCs for successful engraftment. Ex vivo expansion of human HSCs, particularly cord-blood-derived HSCs, is therefore a key goal in hematology and one that remains a considerable obstacle to the wider and safer therapeutic use of HSCs.

Although various reagents have been tested in attempts to stimulate the expansion of human HSCs, cytokines have long been thought to be essential for supporting HSCs ex vivo. Recently, we reported the establishment of a culture system that allows the long-term ex vivo expansion of human HSCs, achieved through the complete replacement of exogenous cytokines and albumin with chemical agonists and a caprolactam-based polymer. A phosphoinositide 3-kinase activator, in combination with a thrombopoietin-receptor agonist and the pyrimidoindole derivative UM171, were sufficient to stimulate the expansion of umbilical cord blood HSCs that are capable of serial engraftment in xenotransplantation assays.

Other researchers have also been actively working on advancing the expansion techniques of HSCs, with some already conducting clinical trials. In April 2023, the FDA approved omidubicel, a modified form of allogeneic hematopoietic progenitor cell therapy derived from cord blood and enhanced with nicotinamide. In a phase III trial, omidubicel demonstrated a shorter neutrophil recovery period and reduced infection rates.

This presentation will provide an overview of the current state and future prospects of rapidly advancing cord blood ex vivo expansion technology.

Plenary Session 2

Cellular Therapy for Acute Leukemia

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The world-wide usage of CD19 CAR-T therapies increases the response rate of patients with refractory or relapsed B-cell acute lymphoblastic leukemia. Clinical practices become much more safe with the help of immunotherapy-related toxicity management guidelines such as ASTCT consensus grading system. Tocilizumab and steroids are major interventions to control CRS and ICANS. However, some severe adverse events can not be well controlled. New drugs and interventions are investigated and can be considered such as JAK1/2 inhibitors. Runxolitinib and steroids combination is effective for controlling severe CRS without impeding CAR-T cell expansion. Refractory CNS3 status and CNS mass are excluded from clinical trials because of high risk of severe ICANS. Intracranial injection with steroids and Ommaya capsule implantation can be effective. For some heavily treated patients, difficulties in CAR-T manufacturing and expansion may be resolved by blinatumomab combination. Relapse is major concern after CAR-T therapies, combination interventions are investigated in many centers, such as allogeneic stem cell transplantation, dual target CAR T cell therapies, and sequential CD19/22 CAR-T infusion. For T-lineage target CAR-T therapies, CAR-T cell fratricide can be overcome by many techniques. The efficacy and safety of CD7 CAR-T cell therapies are widely reported these years. The autologous and allogenic T cell resources are widely used for CAR-T cell manufacture. High response rate can be achieved while immune reconstitution is prolonged. Infections especially virus re-activation should be carefully monitored. Relapsed is another question. Switching target and eliminating residual CD7 CAR-T cells in blood are key points for patients relapsed after CD7 CAR-T cell therapy. CAR-T cell therapies for AML are no investigated in large-scale cohort except CD19-positive AML with AML1-ETO fusion gene.

Plenary Session 3

The role of eHealth in the management of BMT patients

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The invention of the Internet and innovation in electronics in the second half of the 20th century have altered the way human interact with each other. This in turn has accelerated the progress in many scientific fields including Healthcare/Medicine. One such development is the focus of this presentation, eHealth. Wikipedia describes eHealth as healthcare services which are supported by digital processes, communication or technology, although its definition is contested in the literature. Besides audio-virtual communication among individuals, the capability of delivering of images of diagnostic radiology and histopathology in real-time across the Globe were demonstrated in the late 1990's leading to the development of telehealth which is the distribution of health-related services and information via electronic information and telecommunication technologies. Literature on Telehealth in Asian Pacific region appeared in the late 1990's demonstrating the feasibility of supervision of chemotherapy to oncology patients in remote clinics in Australia. In the area of blood and marrow Transplantation (BMT), telehealth aids the management of transplant patients living in rural regions and its usage expanded during the recent pandemic. The Internet has also provided an invaluable platform for members of the APBMT to mentor the establishment of new transplant centres in our region. A major obstacle of eHealth is the inability to delivery treatments such as drugs. Successful delivery of non-pharmaceutical treatments via the Internet such as psychotherapy has recently been demonstrated in the HCT. The convenience and ease of the technology allows the flourish of Telehealth, however, Telehealth also carries certain disadvantages and risks. These will be detailed during my presentation.

SESSION 01 – PRESIDENTIAL SYMPOSIUM FOSTERING THE NEXT GENERATION TRANSPLANT PHYSICIANS

Session 1 – Presidential symposium

Fostering next generation transplant physicians

– APBMT perspectives –

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Hematopoietic cell transplantation (HCT) and cellular therapy (CT) exploit the therapeutic potential of hematopoietic cells to treat a variety of hematological disorders. While initially dedicated to the treatment of hematological malignancies and disorders, the use of these therapies currently continues to expand in non-hematological disorders. However, the expansion also highlights the global shortage of transplant physicians and cellular therapists adequately trained in this field of high expertise. This shortage can significantly impact patients' access to those therapies and its quality. A critical number of qualified transplant physicians are definitely needed to ensure continuing expansion of accessibility to HCT/CT, provide a standardized curriculum, training experience to attract young hematologists and promote expertise and quality care to meet the needs of both patients and society. Hematopoietic cell transplantation (HCT) is a highly complex procedure that requires a dedicated multidisciplinary team to optimize its safety and efficacy. Workforce shortages are also being reported for other multidisciplinary HCT/CT team members team members such as nurses, pharmacists and medical technologists. Regarding projected shortage of HCT health professionals, work-related distress and work-life balance were noted to be potential barriers to recruitment/retention.

To address this unmet need and attract aspiring hematologists to the field of HCT/CT, national task force aiming to develop a structured academic program in HCT/CT should be created. APBMT address the specific needs of trainees working in a variety of aspects in HCT/CT, and provide advice and support them at all levels. APBMT will also consider to create the group composed of trainees and young investigators in all field of HCT/CT with a broad range of experience and interests and serves to provide a platform for trainees to engage with a variety of activity in APBMT. Encourage medical students and young hematologists to consider a career in

HCT/CT, and provide a platform for trainees to establish themselves within the APBMT community and encourage them to communicate available positions. Transplant physicians must be actively engaged in the medical education process to show young medical students and residents, who are not committed to another subspecialty career, the excitement and challenges of a career in HCT/CT, so that our field will have providers for the future.

Session 1 – Presidential symposium

Fostering next generation transplant physicians – ASTCT perspectives –

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The field of hematopoietic cell transplantation (HCT) and cellular therapy has been rapidly evolving over the past few decades. These therapies have been shown to be curative for patients with hematologic malignancies as well as non-malignant hematologic disorders. Significant progress has been made in patient selection, donor selection, conditioning regimens, graft-versus-host disease (GVHD) prevention and treatment, and other supportive care measures, which have resulted in overall improved outcomes. In 2023, we are able provide transplant options to older patients and patients with co-morbidities. In addition, we are in an era where we can guarantee a donor for all patients, in large part due to the use of alternative donors, including haploidentical donors, mismatched unrelated donors, and cord blood. We have also seen the advent and rapid development of other cell therapies, including immune effector cells such as CAR T cells. CAR T cells are now routinely used in patients with non-Hodgkin lymphoma, multiple myeloma and acute lymphoblastic leukemia. In the next few years, we expect to see expansion of these therapies to other hematologic malignancies, as well as potentially to solid tumors.

In this context, it is critical to train the next generation of transplant and cell therapy physicians, who will not only take care of patients but also perform the basic, translational and clinical research that will ensure that we continue advancing the field. Furthermore, we must continue to foster collaborations both nationally and internationally. In this presentation, we will review studies performed at Memorial Sloan Kettering Cancer Center in New York over the past 20 years with a particular focus on studies led by junior investigators both in transplant and in CAR T cells. We will also highlight initiatives of the American Society for Transplantation and Cellular Therapy in helping to develop the next generation.

Fostering The Next Generation Transplant Physician – The LABMT perspective –

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In Latin America, transplants have increased in the last years; however, there is still a low transplant rate of just 77 procedures for every ten million inhabitants and a low density of team of 1.6 for 10 million, almost six times less than in Europe or North America. One of the goals of LABMT is to increase the number of transplants and the number of teams doing transplants. One of the aspects necessary to improve is the number of hematologists trained in this complex procedure. Our group has done two surveys to know the current stage of training in our region and to understand the most critical barriers to doing that. The last one was presented in the previous EBMT meeting (1), in summary; there are 31 training programs in 10 countries; 71% of them are formal programs with structured learning curriculums and durations of 6 to 12 months, and the majority are in the public health system, only 50% of program offers a salary and 22.6% of them charge a fee to the trainee. In most programs, hematologists acquire expertise in autologous and allogeneic transplants, including haplo and non-related donors. Only one has an active program in Car T cell therapy. The main barriers identified in the survey were lack of funding (48.4%), lack of support for the teaching staff (25.8%), and lack of recognition by local authorities (9,7%).
It is necessary to work on increasing the number of training programs, but most importantly, in funding them with the goal that more Latin American hematologists can access the training. It is also essential to be creative and take advantage of the online possibilities for education and partnership. Finally, it is crucial to adapt the teaching curriculum to the reality of our region.

(1)Gomez A- EBMT meeting 2023

SESSION 02 –
EARLY COMPLICATIONS AFTER HCT

Graft Failure

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Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT) is a potentially curative treatment for various hematological malignancies and bone marrow disorders. However, graft failure remains a challenging and devastating complication that can compromise the therapeutic success of the transplant. We will provide a detailed examination of the underlying mechanisms, risk factors, clinical manifestations, and management strategies associated with graft failure in allogeneic HSCT. We will start with an overview of graft failure, which occurs when the transplanted donor stem cells fail to engraft and reconstitute the recipient's hematopoietic system adequately. The different types of graft failure, including primary and secondary, are discussed, along with their distinct pathophysiological processes. To identify and understand the risk factors associated with graft failure, the class examines recipient-related factors, such as age, comorbidities, and disease stage, as well as donor-related factors, such as human leukocyte antigen (HLA) mismatch and graft source. Additionally, the impact of conditioning regimens and graft-versus-host disease (GVHD) prophylaxis on graft failure incidence is explored. The clinical manifestations and diagnostic approaches for graft failure are then elucidated, emphasizing the importance of vigilant monitoring of blood counts and chimerism analysis to detect engraftment failure at an early stage. The class also discusses the differentiation between graft failure and rejection, along with their distinct management implications. Management strategies form a critical part of the prsentation, covering interventions such as donor lymphocyte infusions (DLI), stem cell boost, and alternative donor sources for salvaging graft failure cases. Furthermore, the role of immune-suppressive agents and the balance between promoting engraftment and preventing GVHD are carefully addressed. We conclude with insights into ongoing research and future directions for preventing and managing graft failure in allo-HSCT, highlighting the importance of individualized patient care and multidisciplinary collaboration. In conclusion, graft failure in allo-HSCT represents a formidable clinical challenge. Through comprehensive risk assessment, early detection, and tailored therapeutic approaches, healthcare professionals can optimize engraftment success and improve patient outcomes in the context of allo-HSCT. Continued research and advancements in transplant technology hold the promise of reducing graft failure rates and enhancing the overall efficacy of this life-saving therapeutic modality.

Harmonizing Definitions for Diagnostic Criteria and Prognostic Assessment of Transplant Associated Thrombotic Microangiopathy: A report on behalf of the European Society for Blood and Marrow Transplantation (EBMT), American Society for Transplantation and Cellular Therapy (ASTCT), Asia-Pacific Blood and Marrow Transplantation Group (APBMT) and the Center for International Blood and Marrow Transplant Research (CIBMTR)

Schoettler M, Carreras E, Cho B, Dandoy C, Ho VT, Jodele S, Moissev I, Sanchez-Ortega I, Srivastava A, Atsuta Y, Carpenter P, Koreth J, Kroger N, Ljungman P, Okamoto S, Popat U, Shaw BE, Soiffer R, Williams A, Vasu S

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BACKGROUND: Transplant associated thrombotic microangiopathy (TA-TMA) is an increasingly recognized complication of hematopoietic cell transplant (HCT) associated with significant morbidity and mortality. However, TA-TMA is a clinical diagnosis, and multiple criteria exist without universal application. Lack of harmonization of diagnostic and prognostic features have precluded large multi-institutional studies to understand incidence and outcomes. To address this unmet need, ASTCT, CIBMTR, APBMT, and EBMT-nominated representatives, formed an expert panel to generate consensus diagnostic and prognostic criteria.

METHODS: The expert panel reviewed literature, generated consensus statements using the Delphi Method regarding diagnostic and prognostic features of TA-TMA and identified future directions of investigation.

RESULTS: Consensus was reached on four key concepts. 1) TA-TMA can be diagnosed using *either* clinical and laboratory criteria *or* tissue biopsy of kidney or gastrointestinal tissue. 2) Consensus diagnostic criteria are proposed using modified Jodele criteria (Figure 1). TA-TMA is diagnosed when ≥ 4/7 following features occur twice within 14 days: anemia, defined as failure to achieve transfusion independence despite neutrophil engraftment, thrombocytopenia defined as failure to achieve transfusion independence, elevated lactate

dehydrogenase (LDH), schistocytes, hypertension, elevated sC5b-9 (>ULN) and proteinuria (≥ 1mg/mg random urine protein:creatinine ratio, rUPCR). 3) Patients with any of the following should be classified as high-risk TA-TMA given known association with non-relapse mortality: elevated sC5b-9, LDH ≥2X ULN, rUPCR ≥1 mg/mg, multiorgan dysfunction, concurrent grade II-IV acute GVHD, or infection (bacterial or viral). 4) All allogeneic and pediatric autologous HCT recipients with neuroblastoma should be screened weekly (complete blood count, schistocytes, LDH, blood pressure, rUPCR) for TA-TMA during the first 100 days post HCT. If diagnosed with TA-TMA, patients should be risk stratified and those with high-risk disease should be offered participation in a clinical trial for TA-TMA directed therapy if available.

FUTURE DIRECTIONS: We propose these criteria and risk stratification features be used in data registries, prospective studies, and clinical practice across international settings. This harmonization will facilitate the investigation of TA-TMA across populations diverse in race, ethnicity, age, disease indication and transplant characteristics. We expect continued refinement of these criteria as needed and continued efforts to identify more specific diagnostic and prognostic biomarkers. Lastly, investigation of the impact of TA-TMA directed treatment, particularly in the setting of concurrent highly morbid complications such as steroid refractory GVHD and infection, is critically needed.

SESSION 03 –
PEDIATRIC SESSION 1

Novel Cell and Gene Therapies in Children

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The era of regenerative medicine (cell therapy, gene therapy, and tissue engineering) as the future of medication is upon us. Thousands of ideas to market have demonstrated profound, durable, and potentially curative effects that are already improving human quality of life for patients with no other available therapeutic options.
From the past four decades until 2017, the approval promptness of CGT (cell, gene and tissue) products was deliberate; nevertheless, after two CGT products were approved (Kymriah and Yescarta), incredible numerous CGT products succeeded in receiving approval from the Food and Drug Administration of different countries. The gene therapy and cell-based immuno-therapy developers raised a vast investment, generating $10.2B and $10.1B in 2021, respectively. However, investment in cell-based immuno-therapy companies is growing faster than gene therapy financing. There is no reason except breakthrough treatment for cancer patients and their promising results. According to the latest reports, several clinical trials in different phases have achieved unprecedented bench-to-bedside clinical success. So, related market-authorized products are increasing subsequently.
By 2023, several new products for incurable and lethal children's disorders entered the medical market. Currently, the diseases such as Spinal Muscular Atrophy, Thalassemia Major, Hemophilia, and Duchenne Dystrophy can be treated with gene therapy. It seems that the speed of advancement of science and technology of genome editing will be such that in recent years, it will completely change the future face of the world by converging with Artificial Intelligence technology.

Using Homologous Recombination based Gene Editing (HDR-Editing) of Hematopoietic Stem Cells to Create Therapies for Rare and Common Diseases

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Gene editing is a method to modify the DNA sequence of a cell in a precise location of the genome. By harnessing the homologous recombination repair pathway, we can engineer the genome not only at a precise location but with precise sequences ranging from the changing of a single nucleotide to the insertion of a large gene cassette (HDR-editing). This versatility is unique among all of the gene editing platforms. We have developed a high efficiency HDR-editing system in which the frequency of HDR exceeds the frequency of INDELs by 5-fold or more. We have applied this system to a wide variety of cell types but most notably in hematopoietic stem cells. In my talk I will describe how we have engineered hematopoietic stem cells to correct the underlying genetic defects in hemoglobinopathies, to give the progeny of hematopoietic stem cells a safe and selective advantage, and to insert new genes to create resistance to HIV in a variety of novel ways.

SESSION 04 –
LATE COMPLICATIONS FOR LONG TERM SURVIVORS

Fertility after Hematopoietic Stem Cell Transplantation

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Issues related to quality of life (QOL) have been recognized with the increasing number of long-term survivors after hematopoietic cell transplantation (HCT). Among these, post-transplant infertility is an important issue affecting QOL in patients of reproductive age.

Although most standard chemotherapy treatments for leukemia and lymphoma are considered low-risk for gonadotoxicity, preparative regimens for autologous and allogeneic HCT are extremely high-risk treatments for infertility in both men and women. Several previous studies, including many cases have reported very low birth rates after HCT. Therefore, HCT recipients who wish to have children after HCT are recommended to undergo fertility preservation (FP).

Oocyte or embryo cryopreservation in women is available for FP in clinical practice. Ovarian tissue cryopreservation (OTC) has been an option in available institutes, although it remains in the research stage. Ovarian shielding has recently been reported for female patients receiving preparative regimens, including TBI. Sperm cryopreservation in men is established as a standard FP and is considered early after diagnosis. Testicular sperm extraction may be an option for patients with azoospermia after treatment. Testicular tissue cryopreservation is the only option for prepubertal boys, but it is still experimental.

While various FP approaches are being established, successful FP in patients with hematological diseases is frequently difficult, especially in female patients with insufficient time to undergo FP therapy. Therefore, the transplant physician should inform the patients of the possibility of infertility and the consideration of FP timing in collaboration with a reproductive specialist from treatment initiation. Here, I overview infertility and FP for patients with hematological diseases. Furthermore, I

review the reports of spontaneous pregnancies after HCT and pregnancies with assisted reproductive technologies and discuss the current situation regarding FP.

Bronchiolitis obliterans syndrome (BoS) after allo-HSCT; a therapeutic role for mesenchymal stem cells (MSCs)?

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While allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a curative approach against a wide range of malignant and non-malignant disorders, graft-versus-host disease (GVHD), as its major complication, compromises the survival and quality of life of patients. By potentially affecting almost all human body organs, chronic GVHD (cGVHD) exerts significant inverse impacts on the quality of life of affected individuals. Despite the rarity, lungs can be involved in cGVHD in various forms. BoS is a common yet lethal manifestation of lung cGVHD. BoS is estimated to affect 2-3% of all allo-HSCT cases and about 6% of individuals with cGVHD and is characterized by the accumulation of inflammatory fibrosis, smooth muscle cell hyperplasia, intraluminal mucosal accumulation, and luminal narrowing of small airway tracts. Unfortunately, despite the application of steroids and extracorporeal photopheresis, no approved therapies for refractory BoS have been introduced yet.
Mesenchymal stem/stromal cells (MSCs) are multipotent adult stem cells that have the potential to exert anti-inflammatory, anti-aging, and tissue reconstructive impacts. Applied systematically, these cells can reside in injured tissues and secrete a wide variety of anti-inflammatory, anti-apoptotic, pro-angiogenic, and growth factor molecules and through these, can robustly enhance tissue regeneration and reconstruction and alleviate exaggerated inflammation and fibrosis. In particular, MSCs, and especially adipose tissue-derived (AT)-MSCs suppress TNF-α, IFN-γ, IL-1, and IL-6 pro-inflammatory signaling and promote anti-inflammatory IL-10 signaling and regulatory T-cell activities. These cells have been successfully used against several inflammatory disorders, as well as aGVHD and cGVHD. Notably, the negligible expression of HLA-1 and HLA-2, especially by AT-MSCs, makes them feasible to transplant them from healthy donors to patient candidates. Given the fact that BoS probably establishes in a chronic inflammatory milieu, and considering the observations of the safety and probable efficacy of MSC therapy against BoS, the application of allogeneic MSCs can be an intriguing approach to intervene with the initiation and progression of refractory BoS.

SECOND PRIMARY MALIGNANCY AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION -- Single Institute Experience

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Background: Hematopoietic stem cell transplantation is a curative treatment for various hematologic malignancies and some benign hematologic diseases. Besides chronic GVHD, the second primary malignancy is also a long-term adverse effect.
Aims: We analyze the incidence and types of second malignancies in a single institute in 20 years and their outcome.
Methods: We retrospectively searched our post-transplant patients' long-term follow-up data between 2001 and 2021 and analyzed our cohort's incidence and pattern of the second primary malignancy.
Results: Twelve patients of second primary malignancy, including 5 of head and neck squamous cell carcinoma, 3 of MDS/AML, 1 of ALL, 1 of esophageal squamous cell carcinoma, 1 of breast cancer, and 1 of papillary thyroid cancer in 380 patients of our cohort (autologous in 184 and allogeneic in 196 patients). Eight patients who underwent allogeneic hematopoietic stem cell transplants had five head and neck, one esophageal, one breast, and one papillary thyroid cancer. Four who underwent autologous transplants were three MDS/AML and one ALL. All five patients with head and neck cancer and one esophageal cancer patients had extensive chronic GVHD. Of these six squamous cell carcinoma patients, four had persistent disease-free after surgery, but one died after the vaccination for COVID-19. Two died of second cancer in progression. In four of the MDS/AML and ALL patients, two in persistent leukemia-free after intensive chemotherapy and salvage allogeneic hematopoietic stem cell transplantation, one low-risk MDS on

watchful observation without treatment, and one AML patient died of leukemia relapse even after allogeneic transplant. The other two patients of breast cancer and papillary thyroid cancer were persistent disease-free after surgery and adjuvant therapy. Nine of our patients were disease-free or progression-free, and three died of second cancers (hypo-pharyngeal, esophageal cancer, and AML).

Conclusion: The cumulative incidence of second malignancy was 6% in 10 years and 16% in 19 years, and post-autologous and post-allogeneic transplants were 5% vs. 7% and 15% vs. 17% in 10 years and 19 years, respectively. Extensive chronic GVHD is a risk factor for upper aerodigestive tract squamous cell carcinoma. Most patients can be salvaged after local or systemic treatment.

SESSION 05 –
PEDIATRIC SESSION 2

HSCT for Inherited Bone Marrow Failure Syndrome's

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Bone marrow failure (BMF) refers to the decreased production of one or more major hematopoietic lineages, which leads to diminished or absent lineage specific hematopoietic precursors in the bone marrow resulting in respective cytopenias. BMF can be classified based on aetiology into acquired and inherited types (IBMFS). The IBMFS can be further classified into lineage specific such as diamond blackfan anemia, congenital neutropenia or congenital amegakaryocytic thrombocytopenia, alternatively they can have multilineage involvement such as in fanconi anemia or dyskeratosis congenita. Although conventional diagnostic tests such as chromosomal breakage analysis aid in the diagnosis but in recent times, NGS based genomic analysis provides a lot information about the molecular diagnosis which in-turn helps in planning therapeutic intervention in a much better way. Awaiting gene therapy, allogenic HSCT is the only curative modality for haematological manifestations of IBMFS (BMF/clonal evolution). From a clinical and therapeutic stand-point the inherited BMFS can be classified into Fanconi and non-fanconi phenotype. As most of these syndromes have a multisystem involvement, the therapeutic objectives of HSCT should be very clearly defined/stated and disease specific strategies need to be planned in a way to minimize early and long-term complications of HSCT. Over the years the donor options have also expanded, thus adding new dimensions to anticipated and un-anticipated toxicities. Although HSCT can cure the BMF/clonal evolution but other disease specific complications need to monitored over an extended period of time. Having said that, it is equally imperative to distinguish HSCT-related late effect from per-se disease specific late manifestations of various IBMFS, which might be independent of the HSCT, to offer appropriate counselling, surveillance, and treatment.

One-stop no-edited allogenic CAR-T therapy bridging HSCT to treat children with relapse and refractory acute lymphoblastic leukemia: a prospective clinical study from a single center

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Key words: allogeneic CAR-T, hematopoietic stem cell transplant, children, B-cell acute lymphoblastic leukemia

Object: Chimeric Antigen Receptor T-Cell (CAR-T) therapy has been developed to be the most effective treatment for relapse and refractory(R/R) B-cell acute lymphoblastic leukemia (B-ALL). However, in some patients prolonged chemotherapy and previous autologous-CAR-T(auto-CAR-T) therapy severely impaired lymphocyte function leading to inability in vitro expansion for effective CAR-T therapy. To address this challenge, we designed this clinical trail to use one-stop no-edited allogenic CAR-T（allo-CART）bridging to same donor conditioning free HSCT to treat children with R/R B-ALL.

Methods: Myeloablative conditioning was given to reducing the leukemia burden and clearing lymphatic function for these active ALL. After that allo-CART was used to regain the immune killing effect and clear leukemia cells. Same donor seamless conditioning free HSCT were performed to rapid reconstruction of hematopoietic cells to overcome Immune effector cell associated hematologic toxicity post CAR-T therapy. Ex vivo TCRαβ+ T-cell depleted hematopoietic stem cell were transplanted for haplo-identical donor (HID) to minimize allogeneic reactivation and only macophenolate mofetil (MMF) were given for GHVD prophylaxis and to avoid more immunosuppressive to injury CART effect.

Results: From October 2020 to April 2023, 16 extremely R/R B-ALL children with the median age of 10y (1.5-17) were recruited in this study, all patients relapsed 2-5 times and failure of 1-3 times auto-CART therapy with mean blast 70.6%±28.8%. Myeloablative conditioning with total body irradiation (12GY，-7d to -5d),Flu (160mg/m2, -5 to -2d) and CTX (120mg/kg，-4d to -3d) were given.

After conditioning all patients received no-edited family donor allo-CAR-T therapy with the average cart (5.29±2.92)×10^6/kg, 3 from matched sibling donor (MSD) and 13 from haplo identical donor(HID). 6 patients received CD22-targeted CAR-T therapy due to loss of CD19 after previous auto-CART and another 10 received bispecific CD19/CD22-targeted CAR-T therapy. Immediately after the peak of cytokine release syndrome (CRS), median 11 days (range: 8-34 days), same allo-CART donor hematopoietic stem cell were transplanted with the median CD34+(6.88±2.77)×10^6 /kg and TCRαβ+T cells (8.65±16.10)×10^4 /kg for TCRαβ+depleted HSCT. After median follow-up of 8 (range 3 to 34) months for the surviving patients. Out of the 16 patients, 6 (37.5%) achieved CR after conditioning, 13 (81.3%) achieved CR after CAR-T therapy and 15 (93.8%) got CR at one month post HSCT. Among the 16 patients, 15 experienced CRS (above grade 1) and one accompanied by immune effector cell-associated neurotoxicity syndrome (ICANS), but no one died of CRS. 13(81.2%) patients developed acute graft-versus-host disease (aGvHD) before transplant mainly presented with skin GVHD except 3(18.9%) had a grade III GVHD which easily be resolved. Before HSCT, all patients achieved complete chimerism with donor T-cells. Almost every one experienced several episodes infection during these therapy. Until the last follow-up, 2 cases relapsed and 5 died (2 died of infections, 1 died of relapse and 2 died of GvHD combined thrombotic microangiopathy and infection). Despite being a cohort of R/R patients with non-CR, the estimated overall survival (OS) at 1 year is 58.7%±16.0%, event-free survival (EFS) was 44.4%±14.2%.

Conclusion: For children with repeated relapsed B-ALL failure of previous auto-CART, Allo-CART treat can be considered as long as CART targets still presented. One-stop no-edited same donor allo-CART bridging to conditioning free HSCT provides a chance of survival for these extremely refractory/relapsed B-ALL with manageable CRS and GVHD, but more serious infection.

Session 5 – Pediatric Session 1

HSCT for Primary Immunodeficiency Diseases

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Primary immunodeficiency diseases (PID) are a heterogeneous group of genetic disorders involved in immune host defense and immunoregulation. The group manifests various combinations of recurrent infections, autoimmunity, lymphoproliferation, inflammatory manifestations, atopy, and malignancy. Since long ago, hematopoietic stem cell transplantation (HSCT) has been a promising treatment approach for many PIDs. Myeloablative conditioning regimens have been used for decades with short- and long-term complications and transplant-related mortality. The widespread experience has been gained with several different modifications with less toxicity, improving HSCT outcomes over the years. Today, most physicians recommend using a reduced-intensity conditioning regimen in PID patients, especially those with preexisting comorbidities, to reduce the risk of complications and transplant-related mortality. Although matched-related donor is the gold standard concerning donor selection, today the results of HSCT from matched unrelated donors are almost equivalent to the matched-related donors due to the HSCT organizations increasing experience over the years. The haploidentical transplant in-vitro selective depletion of T lymphocytes is the only valid alternative available when no compatible related and unrelated donors exist. Despite the improved outcomes after HSCT, PID patients with pre-HSCT recurrent infections history, still face significant challenges. Therefore, choosing new HSCT strategies to improve survival and long-term quality of life is essential. Howsoever, it seems that gene therapy will replace HSCT in many PIDs within the next few years due to the significant progress in the gene therapy of various genetic diseases and the approval of new products by the Food and Drug Organization of different countries every few months.

SESSION 06 – AUTOLOGOUS STEM CELL THERAPY FOR MALIGNANT AND NON-MALIGNANT DISEASE

Autologous Stem Cell Transplantation for Lymphoma in the Era of CART Cells

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In the ever-evolving landscape of cancer treatment, the role of autologous stem cell transplantation (ASCT) for non-Hodgkin lymphoma (NHL) has undergone significant shifts, particularly with the emergence of Chimeric Antigen Receptor T-cell (CAR-T) therapy. ASCT, a procedure where a patient's own stem cells are collected and then reintroduced into their body after intensive chemotherapy, has long been a crucial treatment option for aggressive NHL. It aims to destroy cancerous cells and rejuvenate the bone marrow, which is often damaged during the aggressive treatment.

However, the introduction of CAR-T therapy has revolutionized the treatment paradigm for certain NHL cases, particularly relapsed or refractory B-cell lymphomas. CAR-T therapy involves engineering a patient's T-cells to express chimeric antigen receptors on their surface, enabling them to target and eliminate cancer cells more effectively. This personalized approach has shown remarkable success in patients who have exhausted conventional treatment options, offering high response rates and even potential for long-term remission.

As a result, the role of ASCT in NHL treatment has become more nuanced. For patients who achieve durable remission after CAR-T therapy, the need for ASCT as a consolidation treatment has diminished. CAR-T therapy, with its precise targeting and potential for long-lasting response, may obviate the need for the intensive ASCT procedure and associated complications. However, ASCT still retains its significance for patients who do not respond optimally to CAR-T therapy or experience relapse after an initial response.

In conclusion, the landscape of non-Hodgkin lymphoma treatment has evolved dramatically with the advent of CAR-T therapy. While autologous stem cell transplantation remains a valuable option, its role has evolved. CAR-T therapy has shown impressive efficacy, particularly in refractory cases, potentially reducing the reliance on ASCT as a front-line treatment. The precise interplay between these treatments is an active area of research, as clinicians strive to tailor therapeutic strategies to individual patients' needs, aiming for improved outcomes and enhanced quality of life.

Stem cell transplantation for multiple myeloma

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Treatment advances have significantly improved outcomes for multiple myeloma patients. These novel agents include newer generation proteosome inhibitors and novel immunotherapeutic agents targeting CD38 and BCMA. Upfront use of these novel agents in induction has also allowed for deeper responses that are translated into better survival outcomes. This has led to a paradigm shift in the treatment for myeloma, with a move away from cytotoxics towards an immunotherapy-based approach. As such, the role of high-dose chemotherapy and autologous stem cell transplant for the treatment of multiple myeloma is increasing being challenged. Several studies have investigated the role of stem cell transplant for myeloma. In this session, the following will be discussed: i) the relevance of autologous stem cell transplantation in the current era of novel agents ii) deriving optimal benefits from stem cell transplants (upfront vs delayed transplant and single vs tandem transplant) iii) role allogeneic stem cell transplant in myeloma. These will provide evidence-based frameworks to guide management of transplant-eligible myeloma patients.

CAR-T Therapy for Autoimmune Disease

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Chimeric antigen receptor (CAR)-based cellular therapies have achieved great progress in the treatment of relapsed/refractory hematological malignancies and some solid tumors. CAR-T cells can also target and eliminate autoreactive cells in autoimmune and immune-mediated diseases such as systemic lupus erythematosus (SLE), Sjogren's syndrome, and systemic sclerosis etc.. More and more clinical trials about CAR-T therapy for autoimmune disease have been developed. They can contribute to an effective efficacy and relatively safety. On the other hand, CAR-Treg interventions may have a highly effective and durable immunomodulatory effect via a direct or bystander effect, which may have a positive impact on the course and prognosis of autoimmune diseases. CAR-based cellular techniques have a complex theoretical foundation and are difficult to implement in practice, but they have a remarkable capacity to suppress the destructive functions of the immune system in clinical trials. This topic provides an overview of the numerous CAR-based therapeutic options developed for the treatment of autoimmune diseases. We believe that well-designed, rigorously tested cellular therapies could provide a promising novel personalized treatment strategy for a significant number of patients with autoimmune diseases.

SESSION 07 –
MANAGEMENT OF INFECTION

Fungal Infection

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Fungal infections remain important causes of transplant-related morbidity in recipients of hematopoietic stem cell transplant. However, there have been notable changes in the epidemiology and outcomes of invasive fungal infections, induced by changes in the transplant procedures as well as supportive care. This talk discusses invasive fungal infections in hematopoietic stem cell transplant recipients, with a focus on South and Southeast Asian settings. I will discuss:

1. Epidemiology of fungal infections in our setting
2. Novel agents causing invasive infections post BMT
3. Newer diagnostic approaches for these infections
4. Current and emerging treatment approaches, relevant to our setting.

Conditioning regimens: TBI and non-TBI regimens

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Total body irradiation (TBI), used as part of the conditioning regimen prior to allogeneic and autologous hematopoietic cell transplantation (HCT), is the delivery of a relatively homogeneous dose of radiation to the entire body. TBI has a dual role, being cytotoxic and immunosuppressive. This allows it to eliminate disease and create "space" in the marrow while also impairing the immune system from rejecting the foreign donor cells being transplanted. Advantages that TBI may have over chemotherapy alone are that it may achieve greater tumor cytotoxicity and better tissue penetration than chemotherapy as its delivery is independent of vascular supply and physiologic barriers such as renal and hepatic function. Therefore, the so-called "sanctuary" sites such as the central nervous system (CNS), testes, and orbits or other sites with limited blood supply are not off-limits to radiation. Nevertheless, TBI is hampered by challenging logistics of administration, coordination between hematology and radiation oncology departments, increased rates of acute treatment-related morbidity and mortality along with late toxicity to other tissues.

In the two decades there has been a consistent improvement in the clinical outcomes of patients diagnosed with acute leukemia undergoing allogenic HCT. These improvements have been made possible by advancements in supportive care practices, more precise risk stratification of leukemia patients by genetic testing at diagnosis, accurate disease assessment by measurable residual disease (MRD) in pretransplant marrow and attempts to clear residual disease clones prior to transplant. Availability of targeted therapies and immunotherapies such as blinatumomab, inotuzumab ozogamicin and venetoclax has also improved remission rates for patients who are undergoing HCT. For patients who are unable to achieve a morphologic or MRD-negative remission prior to transplant, the risk of relapse post-HCT remains high. TBI-based intensification of transplant conditioning may be able to overcome risk of increased relapse rate in this clinical setting by improving clearance of leukemic clones. However, increased non-relapse mortality (NRM) due to higher incidence of Graft-versus-Host disease (GVHD) and infectious complications offset the benefit of reducing relapse rate resulting in no significant improvement in overall survival.

In this session, we are going to review several recent comparative data between TBI-based vs. non-TBI based regimens in acute leukemias and discuss of possible incorporation of new radiation strategies including total marrow irradiation (TMI), total lymphoid irradiation (TLI), and combined total marrow and lymphoid irradiation (TMLI).

Late Infection and Immunization after Hematopoietic Stem Cell Transplant

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Infections can occur throughout the post-hematopoietic stem cell transplant (HSCT) period. A late infection is defined as an infection occurring one year after engraftment. During this period, almost all host immune responses have returned to normal if graft-versus-host disease (GvHD) does not occur or if high-dose immunosuppressive therapy is not required. Patients are vulnerable to community-acquired infections similar to normal hosts. Focused infections during this period include viral respiratory tract and gastrointestinal infections, community-acquired bacterial infections, and viral reactivation. The incidence of infection in this period is still higher than in the normal population. Bacterial, fungal, and viral infections seem to be more common in these patients, however, the magnitude is less for viral infections. The presence of chronic GvHD or a history of relapse are the main factors contributing to an increased risk of infections. With the advent of COVID-19, these patients are also more vulnerable to this disease and have a higher mortality rate. Since immune reconstitution has almost completed during this period, vaccination is a good strategy to prevent infection in these patients. Generally, antibody titers after diphtheria, tetanus, rubella, hepatitis B, and influenza seem to be excellent in these patients. Those for mumps, measles, and pneumococcus are moderate, and that for pertussis seems to be poor. mRNA vaccination for COVID-19 has a lower, but highly variable, in vitro immune response in HSCT recipients than in normal hosts. Many factors can affect the immune response to these vaccines, for example, low T- or B-cell numbers, presence of GvHD, or immunosuppressive drugs during vaccination. Vaccination in post-HSCT patients is an active field for research as strategies, for example boosting or vaccine combination, are still being searched for better vaccine immune response in these patients.

SESSION 08 –
ORAL PRESENTATION 1

The Dose Impacts of Post-transplant Cyclophosphamide on Outcomes After HLA-haploidentical Allogeneic Hematopoietic Cell Transplantation

by Hirohisa Nakamae | Yasuhiro Nakashima | Mitsutaka Nishimoto | Hiroshi Okamura | Teruhito Takakuwa | Masatomo Kuno | Yosuke Makuuchi | Kentaro Ido | Kazuki Sakatoku | Mirei Horiuchi | Mika Nakamae | Masayuki Hino | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Department of Laboratory Medicine and Medical Informatics, Osaka Metropolitan University, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Department of Clinical Laboratory, Osaka Metropolitan University Hospital, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Department of Clinical Laboratory, Osaka Metropolitan University Hospital, Department of Laboratory Medicine and Medical Informatics, Osaka Metropolitan University, Osaka, Japan | Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Department of Clinical Laboratory, Osaka Metropolitan University Hospital, Department of Laboratory Medicine and Medical Informatics, Osaka Metropolitan University, Osaka, Japan

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Keywords: HLA- haploidentical allogeneic hematopoietic cell transplantation, dose Impacts of PTCy., post-transplant cyclophosphamide (PTCy)

Aims

Performance of allogeneic hematopoietic cell transplantation (HCT) with post-transplant cyclophosphamide (PTCy) from a human leukocyte antigen (HLA)-haploidentical hematopoietic donor (PTCy-haplo) has recently spread internationally due to its simplicity and safety, and PTCy-haplo has become a platform for HLA-haploidentical HCT. However, several recent reports have shown that the risk of disease relapse is higher after PTCy-haplo than after HCT from HLA-matched unrelated donors. Recent experimental studies in a major histocompatibility complex-haploidentical murine HCT model have also suggested that PTCy may decrease graft-versus-leukemia effects. Currently, PTCy is administered at a standard dose of 50 mg/kg on Days 3 and 4 post-transplant. However, the optimal dose of PTCy has not been clinically established based on sufficient investigation. In addition, the optimal dose of PTCy may differ depending on whether PTCy-haplo is conducted with peripheral blood stem cells (PBSCs) or bone marrow as the stem cell source. We performed a retrospective clinical study at our institution to determine the effects of PTCy dose

reduction on outcomes after PTCy-haplo.

Methods

Patients with hematological malignancies who underwent PTCy-haplo from December 2011 to April 2023 in our institute were analyzed.

Results

One hundred and forty-two patients were included in the analysis. PTCy-haplo was analyzed in three groups: i) standard dose of 50 mg/kg on Days 3 and 4, ii) 50 mg/kg on Day 3 and 25 mg/kg on Day 4, and iii) 25 mg/kg on Days 3 and 4. Mobilized PBSCs was used as the stem cell source and the most frequent conditioning was reduced-intensity conditioning (95%) in all groups.

Neutrophil engraftment did not significantly differ among the three groups, but platelet engraftment was significantly better in the 50 mg/kg on Day 3 and 25 mg/kg on Day 4 group. Despite no significant differences, there was a trend toward a higher cumulative incidence of grade III–IV acute graft-versus-host disease in the 25 mg/kg on Days 3 and 4 group. In addition, there was a trend toward worse overall survival in the 25 mg/kg on Days 3 and 4 group (3-year overall survival was 64%, 61%, and 33% in the 50 mg/kg on Days 3 and 4, 50 mg/kg on Day 3 and 25 mg/kg on Day 4, and 25 mg/kg on Days 3 and 4 groups, respectively). The cumulative incidences of relapse/progression did not significantly differ among the three groups.

In multivariate analysis, the double dose of 25 mg/kg PTCy was a significant poor prognostic factor for overall survival (HR 2.05, 95% CI: 1.08–3.91, P=0.028) in addition to non-remission disease status, history of transplant, and high/very high refined Disease Risk Index.

Conclusions

The results of the present analysis showed that reduction of the standard dose of PTCy to 50 mg/kg on Day 3 and 25 mg/kg on Day 4 was feasible even using PBSCs; however, PTCy dose reduction did not obviously suppress disease relapse/progression. Further studies are required to establish strategies for improving outcomes after PTCy-haplo.

Conflict of Interest Statement

No conflict of interest to disclose.

Allogeneic Stem Cell Transplantation with 3-days Busulfan plus Fludarabine as Conditioning Regimen for patients with Relapsed or Refractory T- and NK/T-cell lymphomas

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Topic: Conditioning Regimens
Keywords: Relapsed and refractory T- and NK/T-cell lymphoma, allogeneic stem cell transplantation, and fludarabine, busulfan, conditioning

Aims

Peripheral T-cell lymphomas (PTCL) and NK/T-cell lymphoma (NKTCL) share common characteristics of high chemotherapy resistance with frequent relapses and rapid disease progression. Efforts to improve outcome have incorporated autologous (auto-SCT) and allogeneic stem-cell transplantation (Allo-SCT). Allo-SCT has been to show a plateau of survival in responding patients. Although attempts to apply Allo-SCT in adult PTCL and NKTCL are steadily increasing, cases are still scarce so that there are very few prospective trials. Even though Allo-SCT could improve survival in relapsed and refractory patients who would otherwise have grave prognosis, there are several unsolved problems.

Subject and Method

This is a prospective phase II trial which plans to enroll 34 patients. Histologically confirmed relapsed and refractory T- and NK/T cell lymphomas who relapsed after or were refractory to one or more of previous chemotherapy including auto-SCT and had achieved partial response (PR) or complete response (CR) after salvage chemotherapy were enrolled. Patients who had HLA full-match (8/8 in HLA) or one-locus mismatch (7/8) sibling, or unrelated bone marrow (BM) or peripheral blood (PB) or cord blood (CB) stem cell donors

were enrolled. Conditioning therapy was started on day -8. Busulfan was given 3.2 mg/kg intravenously once daily for 3 days and fludarabine 30 mg/m^2 was infused once daily for 6 days . Primary endpoint of this study is 2-year progression-free survival (PFS). This is the preliminary result of 18 patients enrolled to the study.

Result

Eighteen patients received Allo-SCT with Bu3Flu6 conditioning regimen for relapsed and refractory T- and NK/T cell lymphomas. Median age was 54 years and median previous lines of therapies was 2. 50% of the patients had received auto-SCT. Stem cell source were PB and CB in 16 patients and 2 patients, respectively; stem cell donor type were full-matched sibling and unrelated donor in 39% and 33% of the patients, respectively, and mismatched related and unrelated donor in 6% and 11% of the patients, respectively. After a median 3 cycles of salvage chemotherapies 61 % and 39% were in CR and PR, respectively, before enrollment to the study, and for 7 patients who were in PR before Allo-SCT, 4 patients further achieved CR after Allo-SCT with Bu3Flu6. After a median follow-up duration of 20.82 months, 2-year PFS and OS were 81.1% , and 58.7% , respectively. Poor graft function occurred in 2 patients. Patients who were engrafted recovered neutrophils and platelets rapidly with a median of 12 and 12 days, respectively. There were no unexpected regimen-related toxicities. Sinusoidal obstruction syndrome had occurred in 2 patients, and 3 patients died of fungal combined with bacterial pneumonia after Allo-SCT. Grade 3-4 acute graft -versus-host disease and moderate-to-severe chronic GVHD occurred in 17% and 44% patients, of which chronic GVHD combined with infection lead to death in 2 patients.

Conclusion

3-days Busulfan and 6-days Fludarabine combination as a conditioning regimen is effective with no unexpected adverse event profile for relapsed or refractory T- and NK/T-cell lymphoma patients who are undergoing allogeneic stem cell transplantation. (NCT02859402)

Long-term Survival Rates of Post-Haematopoietic Stem Cell Transplantation Thalassemia Patients: A Systematic Review and Meta-Analysis

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Topic: Hemoglobinopathies, primary immune deficiency disease and metabolic disorders
Keywords: Haematopoietic Stem Cell Transplantation, Survival Rates, Thalassemia

Aims: Since first being done in 1981, hematopoietic stem cell transplantation (HSCT) is the only curative option for thalassemia. However, HSCT poses some risks of complications that could have life-threatening impacts on its recipients and reduced long-term survival rates. This review intends to summarize the current knowledge regarding the long survival rate of thalassemia patients that undergo hematopoietic stem cell transplantation.

Methods: Detail searches were done in several databases including PubMed, Cochrane Controlled Register of Trials (CENTRAL), Europe PMC (medRxiv and bioRxiv), EBSCOHost (Medline), and ProQuest (gray literatures) from inception to 10 July 2023 using keywords such as “Haematopoietic Stem Cell Transplantation”, “Thalassemia”, “Survival Rates”, and other relevant synonyms. Inclusion criteria were (1) thalassemia patients of all ages, investigating (2) haematopoietic stem cell transplantations, and (3) long term survival rates ≥ 10 years. There was no restriction in time and settings. Studies were excluded if the following criteria were met: (1) case reports, letter to editors, reviews, (2) non-English articles, (3) irretrievable full-text articles. The study selection was done by two authors independently, and disagreement was resolved by the third author. To assess the risk of bias, all authors independently assessed methodological quality of the included studies using the Quality in Prognosis Studies tool. Heterogeneity among the studies we employed I-squared statistics. Pooled estimates were calculated using the DerSimonian Laird’s inverse-variance random effect model with $p<0.05$ was regarded as statistically significant. Sensitivity analysis was done by leave-one-out analysis.

Results: From a total of 690 articles, four studies culminating a total of 616 transplanted thalassemia patients were included in this study. The median follow-up years were 11-30 years. 522 patients received HSCT from HLA-matched relatives, and the other 96 patients acquired HSCT from unrelated donors. The survival rates were 86.8% (95% CI, 80.1%-

92.3%) in 15 years, 89.2% (95% CI 82.2%–96.2%) in 20 years, 82.6% (95% CI 79.9%-85.3%) in 30 years, and 81.4% (95% CI 74.5%–88.9%) in 39 years. The pooled survival rate was 85% (95% CI 82%-94%; I^2=40%). Risk of bias assessment found that three studies had a low risk of bias, and one study had a moderate risk of bias. The pooled survival rate showed no significant differences when each study was individually removed in leave-one-out sensitivity analysis.

Conclusions: The present meta-analysis showed relatively high long-term overall survival rates in patients with thalassemia after HSCT.

Maintenance Therapy with Trametinib after Allogeneic Hematopoietic Stem Cell Transplantation in Patients with RAS Mutated Hematologic Malignancies

by Zhihui Li | Teng Xu | Xianxuan Wang | Xiaopei Wen | Lei Wang | Jingjing Wang | Tong Wu | Beijing Gaobo Boren Hospital | Beijing Gaobo Boren Hospital | Beijing Gaobo Boren Hospital | Beijing Gaobo Boren Hospital | Beijing Gaobo Boren Hospital | Beijing Gaobo Boren Hospital | Beijing Gaobo Boren Hospital

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Event: 28th Annual Meeting of APBMT
Topic: Leukemia
Keywords: RAS Mutation, allogeneic hematopoietic stem cell transplantation, hematologic malignancy, maintenance therapy, trametinib

Aim: The abnormal activation of RAS-RAF-MEK-MAPK signaling pathway plays an important role in the occurrence of leukemia. MEK inhibitor may be a potential agent to treat RAS mutated hematologic malignancies. In present study, the efficacy and safety of trametinib maintenance therapy after allogeneic hematopoietic stem cell transplantation (allo-HSCT) in patients with RAS mutated hematologic malignancies are analyzed retrospectively.

Methods: Between January 2018 and January 2023, 61 patients with RAS mutated hematologic malignancies who underwent allo-HSCT in our hospital were included. The diagnosis included AML (23, 37.7%), B-ALL (33, 54.1%), T-ALL (3, 5.0%) and the others (2, 3.3%). The median age was 15 (1-68) years old. Before transplant, 5 patients (8.2%) had extramedullary diseases and 16 patients (26.2%) had chromosomal abnormalities. Fifty-three patients (86.9%) received second-line treatment. Fifteen cases (24.6%) underwent secondary transplants. The disease status pre-transplant was in CR (42, 68.9%) or in NR (19, 31.1%). Donor type included identical sibling (5, 8.2%), unrelated (11, 18.0%) and haploidential (45, 73.8%). Myeloablative conditioning regimen with TBI/fludarabine (33, 54.1%) based or busulfan/fludarabine (28, 45.9%) based was applied. Twenty-five patients (41.0%) received maintenance therapy with trametinib post-HSCT (trametinib group), and 36 patients (59.0%) did not receive any maintenance therapy after transplant (control group). No significant differences in clinical features were found between two groups. Trametinib treatment was initiated at a median of 94 (63-178) days at a median dose of 1 (0.5-2) mg daily.

Results: With a median follow-up 16.5 (16.8-24.8) months, overall survival (OS) and progress-free survival (PFS) were 81.2 (68.6-89.1) % and 73.0 (59.7-82.5) %. For trametinib group, OS and PFS were 91.5 (70.0-97.8) % and 88.0 (67.3-96.0) %. For control group, OS and PFS were 73.9 (55.9-85.6) % and 65.8 (47.7-78.9) %. Maintenance therapy with trametinib significantly improved OS and PFS (P=0.044; P=0.041). Relapse rate was significantly lower in trametinib group than that in control group (12.0% vs. 28.0%,

p=0.031). The median duration of trametinib maintenance therapy was 270 (30-630) days. Trametinib was temporarily discontinued in 9 patients (14.8%) and dose modified in 12 patients (19.7%) due to side effects. Grade 2 side effects occurred during trametinib treatment, and no ≥ grade 3 side effects were observed. The most common adverse events were neutropenia, anemia, thrombocytopenia, epistaxis, neutropenic fever and fatigue, and all of them were tolerable and reversible. No organ toxicities or drug-related deaths were observed.

Conclusions: Our study has shown that maintenance therapy by trametinib post-transplant in the patients with RAS mutated hematologic malignancies is safe and effective, and can significantly decrease relapse rate and improve OS and PFS in this setting. A prospective, randomized, controlled clinical trial with larger sample size are needed for further research.

Lymphocyte subset analysis of stem cell graft and peripheral blood of patient following allogenic stem cell transplant – a single centre study

by Digambar Panchal | Trainee physician

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Topic: GVHD
Keywords: GVHD, Infections, allogenic HSCT, lymphocyte subset analysis, relapse

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Abstract Text

- **Aims –** To study the lymphocyte subset analysis of stem cell graft and patient following allogeneic stem cell transplant, and its correlation with infection, GVHD and relapse.
- **Methods –** We retrospectively analyzed lymphocyte subsets performed on stem cell grafts of 26 patients with hematological disorders who underwent allogeneic peripheral blood stem cell transplant (Haploidentical + Matched related) at our centre from 2020 to 2022. We compared the subset analysis parameters with the incidence of GVHD, infections and relapse in these patients. We also compared the subset analysis in peripheral blood of patients at 3, 6 and 12 months post transplant with the risk of GVHD, infections and relapse.
- **Results-** We found out that 42% patients with low T Helper cell count (<350cells/kg) in stem cell graft developed grade II-IV of acute GVHD. This is also confirmed by low CD4/CD8 in these patients (2 out of 3 patients with Grade IV GVHD had CD4/CD8 ratio <1). B cell count <250 cells/kg in the graft has a direct correlation with incidence of bacterial infection (5/10 patients). There is no correlation of regulatory T cell and NK cell levels in the graft and risk of acute GVHD. The lymphocyte subsets of the graft have no correlation with day of engraftment and chronic GVHD. Analysis of lymphocyte subset analysis of patient (3 months post transplant) shows that NK cell count <20/uL is associated with increased risk of disease relapse. (50% patients relapsed). Patients with low T cell count, Helper T cells and Cytotoxic T cells counts at 3 months post transplant have an increased risk of BK virus reactivation and bacterial infection and sepsis (P value <0.05). Low Regulatory T cell counts have an increased

risk of bacterial infection in first 3 months. (Mean-4.667/uL, P value-0.057) B cell absolute counts <50/uL has a direct correlation with risk of bacterial and fungal infection and severe sepsis in first 3 months post transplant (50% patients). These findings are in correlation with a previous study done in our institute by Balar and Apte et al which showed a higher absolute T cell count, Helper and Cytotoxic T cell count is associated with higher grade of acute GVHD. A correlation between peripheral blood subsets at 6 and 12 months and the risk of chronic GVHD or relapse could not be established.

- **Conclusions-** Study of lymphocyte subsets of stem cell grafts might give a significant information in predicting the risk of aGvHD and infection. Monitoring lymphocyte analysis of patient post transplant can help in prediction of risk of infection and relapse.

Conflict of Interest Statement - No conflict of interest to disclose

TCR alpha beta haploidentical hematopoietic stem cell transplantation in inborn errors of immunity and the role of CD34 boost in improving immune reconstitution and survival

by VENKATESWARAN V S | SATISH KUMAR MEENA | KAVITHA GANESAN | SURESH RD | ANUPAMA NAIR | VIJAYSHREE M | RAMYA UPPULURI | REVATHI RAJ | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI

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Topic: Pediatric Transplantation
Keywords: CD 34 BOOST, IEI, IMMUNE RECONSTITUTION, TCR ALPHA BETA DEPLETION

BACKGROUND
TCR alpha beta depleted hematopoietic stem cell transplantation (HSCT) in inborn error of immunity (IEI) is an available curative option; however, can be associated with viral reactivation and delayed immune reconstitution. We present outcome data and variables associated with immune reconstitution.

PATIENTS AND MATERIALS
This retrospective study includes children with IEI who underwent TCR alpha beta depleted haploidentical HSCT from January 2013 to December 2022.

RESULTS
A total of 47 children aged 8 weeks to 14 years were included. The diagnosis was SCID 17, CGD 9, familial HLH 8; MSMD, LAD, IL10R defect, hyper IgE syndrome 2 each and 1 each of DOCK8 deficiency, XLA, XLP, hyper IgM syndrome and severe congenital neutropenia. 89% received conditioning chemotherapy and 57% received GVHD prophylaxis with calcineurin inhibitors. The median TCR gamma delta dose was 11.5 x 10 6 /kg and the median
CD34 dose was 10 x 10 6 /kg. 87.2% of the children engrafted with median duration for neutrophil engraftment being 11 days. Acute GVHD was documented in 27% children and viral reactivation in 68%. The median absolute lymphocyte count on day 30 was 364. The overall survival was 63.8% with a median follow up of 36 months, with infections being the most common cause of death. Children with <500 ALC on day 30 had higher risk of viralreactivation (67% vs 32%) as compared to those with ALC > 500 (p = 0.098). Eleven children received CD34 boost around day+45 with documented rise in absolute levels of T B and NK cells.

CONCLUSION
Although TCR alpha beta depleted HSCT has lower rates of GVHD, it has shown to have delayed immune reconstitution and early viral reactivation. Absolute lymphocyte count can

be a valuable tool to predict immune reconstitution. Stem cell boost based on ALC count on day 30 can help reduce viral reactivation and mortality in these children.

TCR-αβ depleted haploidentical HSCT with CD45RO Memory T-cell addback in Inborn Errors of Immunity: the way forward!

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Topic: Pediatric Transplantation
Keywords: Immune reconstitution, Inborn Error of Immunity, TCR-αβ, haploidentical

Introduction/Aims: Advances in the field of haploidentical HSCT like TCR-αβ depletion techniques present with their own challenges like delayed immune reconstitution, viral reactivations, graft failure and graft versus host disease (GVHD). In this regard, post-transplant infusion of memory (CD45RO) T-cells could potentially ameliorate immune reconstitution without increasing the risk of acute GVHD, which is mainly induced by naïve (CD45RA) T-cells. Our aim is to describe the profile of children with Inborn Error of Immunity (IEI) who received CD45RO-T-cell-add-back at regular intervals after stem cell infusion.

Methods: This is a prospective observational study, conducted in the Department of Pediatric Hemato-Oncology, in two tertiary care multi-speciality hospitals in Chennai. Eight children with IEI who underwent haploidentical HSCT were included in this study. Pre-transplant lymphocyte profile wherever relevant, and infections if at all, were recorded. Myeloablative conditioning regimen (Thiotepa/Treosulphan/Fludarabine/Rabbit-ATG) was employed in all children. Single dose of rituximab, was administered on day(-1) for B-cell depletion and to prevent Ebstein-Barr-virus associated post-transplant lymphoproliferative disease (EBV-PTLD). TCR-αβ depleted hematopoietic stem cells were infused on the following day. On post-transplant day +1 and then at regular intervals, escalating doses of CD45RO memory T-cells, were infused, as tolerated. Children were monitored for viral reactivations with weekly viral PCRs and for GVHD. Lymphocyte subset analysis and donor chimerism levels were monitored at monthly intervals. Recovery of each lymphocyte subset (CD3+CD4+, CD3+CD8+ and CD19+) was defined as absolute counts ≥200/microL and ≥150/microL for CD16+CD56+ NK cells. Data was analysed and inferences were drawn.

Results: Our cohort had two children with SCID, two with Chronic-Granulomatous-Disease, one each with Wiskott-Aldrich-Syndrome, Hyper-IgM syndrome, Primary HLH and Leukocyte-Adhesion-Defect. Median age of HSCT was 11 months (range 5.75-17.25 months). Three(37.5%) children had disseminated CMV infection, one had influenza and one had disseminated BCGiosis prior to HSCT. Two children with SCID had near zero lymphocytes

and one with CGD had low normal lymphocyte profile. A higher dose of TCR-alpha-beta-depleted stem cells were infused (median 17 million/kg; range 15-19.25). On day+1, six (75%) children received CD45RA negative CD45RO rich T-cell add-back (median 1 million/kg; range1-1.2). Subsequently, four children(50%) received add-back on day +15, one on day +30 and one on day +60. Four children (50%) showed NK-cell recovery with median time of 112.5 days (41-180) for recovery; three(37.5%) showed CD4+ and CD8+ cell recovery (median 180 days, range60-180); one(12.5%) showed B-cell recovery(day +180). Three(37.5%) children attained 100% donor chimerism with no evidence of GVHD; two (25%) had donor chimerism of 98.27% to 99.6%. Two children are currently entering into post-transplant phase. Two children(25%) had CMV viremia and one(12.5%) had CMV viremia and norovirus gastroenteritis. One (12.5%) child had stage-1 gut GVHD (grade-II). One (12.5%) succumbed within one month of HSCT due to bacterial sepsis.

Conclusion:CD45RA-negative/CD45RO-memory-T-cell add-back led to quicker immune reconstitution, enhancing the anti-viral immunity during the immediate post-transplant period, without increasing the incidence of acute GVHD. Hence, periodic memory-T-cell boost could be an attractive and promising tool in low-middle income countries in TCR-αβ-depleted-HSCT. Large scale prospective studies are needed to consolidate our results further.

No conflicts of Interest

A Single-Center Retrospective Analysis of Allogeneic Hematopoietic Cell Transplantation in Patients with Aggressive Adult T-Cell Leukemia-Lymphoma in a Non-Endemic Metropolitan City in Japan

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Abstract ID: 91
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: HTLV-1, adult T-cell leukemia-lymphoma, mogamulizumab

(Background) Aggressive adult T-cell leukemia-lymphoma (ATL) is a rare hematological malignancy caused by HTLV-1 infection. Although Osaka is not an endemic area for HTLV-1 infection, an increase in ATL cases has been observed in the region. The clinical outcome of aggressive ATL is generally poor, but allogeneic hematopoietic cell transplantation (allo-HCT) has the potential to significantly improve outcomes for this population. However, our previous report found that allo-HCT was not associated with improved survival in the Osaka cancer registry. We hypothesized that recent improvements in treatment strategies for aggressive ATL, such as up-front allo-HCT in chemosensitive disease status and an interval of more than 50 days between the last mogamulizumab (Mog) treatment and allo-HCT when Mog is used in chemorefractory disease, could improve clinical outcomes after allo-HCT. In this study, we assessed the clinical outcome of ATL patients who underwent allo-HCT at our institute.

(Patient and methods) We included patients who underwent allo-HCT for aggressive ATL at our institute between April 2017 and May 2023. We assessed the impact of stem cell source and Mog use on clinical outcomes after allo-HCT. The primary endpoint was overall survival (OS) after allo-HCT, while secondary endpoints included relapse/progression, non-relapse mortality, and GVHD.

(Results) A total of 30 patients were included in the analysis. The median age at allo-HCT was 58.5 years (range: 33-70). The clinical subtype of ATL was acute-type (n=18), lymphoma-type (n=7), chronic-type (n=4), and smoldering (n=1, primary cutaneous tumor

type). Disease status at allo-HCT was chemo-responsive in 26 patients and chemo-refractory in 4 patients. Seven patients received Mog before allo-HCT for relapsed/refractory ATL, with a median interval of 100 days between the last Mog treatment and allo-HCT. All patients received a reduced-intensity conditioning regimen incorporating fludarabine plus melphalan in combination with low-dose TBI or busulfan. The stem cell source was an unrelated volunteer donor (n=13), cord blood (n=11), HLA-matched related donor (n=3), or haploidentical related donor (n=3). The median follow-up for surviving patients was 854 days after allo-HCT. The probability of 2-year OS for this population was 50.2% (95% CI: 29.9-67.5, Figure A). The cumulative incidences of relapse/progression and non-relapse mortality at 2 years were 34.4% (95% CI: 16.8-52.9, Figure B) and 23.4% (95% CI: 9.1-41.5, Figure C), respectively. There was no statistically significant impact of stem cell source on OS. In the seven patients who received Mog before allo-HCT, the probability of 2-year OS was 68.6% (95% CI: 21.3-91.2), while the cumulative incidences of relapse/progression and non-relapse mortality at 2 years were 0.0% and 31.4% (95% CI: 3.0-68.3), respectively. The cumulative incidence of grade III-IV acute GVHD was 14.3% (95% CI: 5.0-49.1).

(Conclusion) The clinical outcome of allo-HCT using various stem cell sources was favorable in this cohort of patients with aggressive ATL. In patients who received Mog before allo-HCT, non-relapse mortality remained a major concern, but overall clinical outcomes were favorable with an acceptable risk of severe acute GVHD.

The impact of low dose ATG on haploidentical hematopoietic stem cell transplantation with post-transplant cyclophosphamide in children with non-malignant disorders - Balancing graft failure, graft versus host disease and infections

by VENKATESWARAN V S | SATISH KUMAR MEENA | KAVITHA GANESAN | SURESH RD | VIJAYSHREE M | ANUPAMA NAIR | RAMYA UPPULURI | REVATHI RAJ | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE,CHENNAI | APOLLO CANCER CENTRE, CHENNAI | APOLLO CANCER CENTRE, CHENNAI | APOLLO CANCER CENTRE, CHENNAI | APOLLO CANCER CENTRE, CHENNAI | APOLLO CANCER CENTRE, CHENNAI | APOLLO CANCER CENTRE, CHENNAI

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Event: 28th Annual Meeting of APBMT
Topic: Pediatric Transplantation
Keywords: Immune cytopenia, graft rejection, graft versus host disease, low dose ATG, ptcy

Background

There is an increasing trend in the number of haploidentical hematopoietic stem cell transplantation (HSCT) for children with non-malignant disorders. The risk of graft rejection and graft versus host disease and infections secondary to delayed immune reconstitution remain significant challenges in this modality. We present our data on the use of low-dose ATG and post-transplant cyclophosphamide (PTCY) in children with non-malignant conditions.

Patients and Methods

We conducted a retrospective study in the Department of Blood and marrow transplantation and included children with blood disorders including bone marrow failure and thalassemia major who underwent haploidentical HSCT with PTCY from January 2015 to January 2023.Children with Fanconi anemia received conditioning with fludarabine and cyclophosphamide along with 2GY TBI with post-transplant cyclophosphamide(PTCY) 25mg/kg/day on day +3 and day+4. In 2019, we added low dose Rabbit ATG at 1.5 mg/ kg/ day for three days to this conditioning in view of high incidence of graft versus host disease.All children with thalassemia major received two cycles of pre-transplant immunosuppression with fludarabine and dexamethasone (PTIS).
Conditioning included low dose Rabbit ATG at 1.5 mg/kg/day for three days, 2Gy total body radiotherapy, Fludarabine, Thiotepa and Cyclophosphamide and PTCY
at the dose of 50mg/kg/day on day+3 and day+4.

In 2019, we replaced
Cyclophosphamide (RIC – reduced intensity) with Treosulfan (Myeloablative)in our

conditioning. We collected data on engraftment,graft versus host disease,graft rejection, infections post HSCT including CMV, EBV, adenovirus and BK virus and survival.

Results

A total of 93 children – 35 with Fanconi anemia and 58 with Thalassemia major underwent haploidentical HSCT. We documented the use of low dose ATG and PTCY in combination in 71 children with a male: female ratio of 1.1:1.

In children with Fanconi anemia, the addition of ATG, reduced the acute GVHD rates dramatically from 73% down to 7% and chronic GVHD from 36% to 13% and we documented
viral reactivation in 31%. The overall survival improved from 63% to 71%.

In children with thalassemia major, MAC conditioning with low dose ATG and PTCY reduced the graft rejection from 23% down to 8%.The incidence of graft versus host disease was extremely low at 7 %. However, life threatening immune cytopenia especially autoimmune hemolytic anemia occurred in 40% children requiring prolonged immunosuppression. Viral reactivation was also high with the prolonged immune suppression and delayed immune reconstitution at 66% in the thalassemia cohort. The overall survival was 86% .

Conclusion

Low-dose ATG and PTCY in combination helps improving survival by reducing the incidence of GVHD in children with Fanconi anemia and graft rejection in children with Thalassemia Major with an overall survival of 71% and 86% respectively. The addition of the PTIS to the ATG backbone in children with Thalassemia Major significantly increases the risk of immune cytopenia due to profound B cell aplasia in the first 100 days and regular monitoring of immune recovery and warrants intravenous immunoglobulin -IVIG replacement post-HSCT helps prevent immune cytopenia. The morbidity and mortality from the high rates of viral reactivation remains high and we hope to address this issue in our future trials.

Long term follow-up of children with Fanconi anaemia undergoing hematopoietic stem cell transplantation: a twenty year follow up study from India

by Aiswarya Thriumal | Jerlin Robin | Thilagavathi Govindan | Sankavi Nagamuthu | Viveka Veeramani | Department of Paediatric Hematoncology, Blood and marrow transplantation unit, Apollo hospitals, Chennai, India | Department of Paediatric Hematoncology, Blood and marrow transplantation unit, Apollo hospitals, Chennai, India | Department of Paediatric Hematoncology, Blood and marrow transplantation unit, Apollo hospitals, Chennai, India | Department of Paediatric Hematoncology, Blood and marrow transplantation unit, Apollo hospitals, Chennai, India | Department of Paediatric Hematoncology, Blood and marrow transplantation unit, Apollo hospitals, Chennai, India

Abstract ID: 111
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: , DNA repair, Fanconi, HSCT, Karnofsky score

BACKGROUND:

Hematopoietic stem cell transplantation (HSCT) is the curative option for children with Fanconi anemia and severe aplasia. These children have significant late effects as they have DNA repair defect and there is paucity of data from our country. Long-term follow-up is essential to detect complications related to the disease or treatment in this setting.

PATIENTS AND METHODS

We collected data from our follow up clinic charts of children who underwent HSCT between 2002 to 2022 and have completed atleast one year at our center. We performed a telephonic interview with the families to collect data collect on endocrine dysfunction, growth failure, organ dysfunction, current Karnofsky score and FA-associated malignancy.

RESULTS:

A total of 63 children with Fanconi anemia underwent transplantation of which 32 of them are alive.The male female ratio was 19/13 and the median age was 10 .The time from HSCT to data collection ranged from 14 months to 20 years with a median of 10.The Karnofsky score in 18 was 100%, 11 was 90% and 3 was80%. We documented a malignancy in 5patients, AML in two patients, squamous cell carcinoma of the head and neck region in two patients and Hodgkins lymphoma in one patient, all of whom succumbed to their illness despite therapy. We observed hypothyroidism in four children who are on thyroxine replacement and three children on growth hormone replacement. All children had optimal pubertal changes. Chronic oral and eye graft versus host disease over five years duration occurred in four children. One child had hearing loss, one with mild renal dysfunction, two with avascular necrosis of the femoral head and one patient with significant learning disability.

CONCLUSION:

This is the first long term data on patients with Fanconi anemia from India and the patients have significant late side effects including endocrine, renal and hearing loss and dedicated follow up is essential. We documented cancer in 15.6% with an increasing incidence with the passage of time. Cancer prevention with HPV vaccination and screening for head and malignancy must be explained at the time of HSCT.

SESSION 09 –
ORAL PRESENTATION 2

Chemo-mobilization, Conditioning Regimens, Toxicities and Clinical Outcomes of Autologous Stem Cell Transplantation in Lymphoma and Multiple Myeloma Patients at National Kidney and Transplant Institute

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Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: Autologous Stem Cell Transplant, Chemo- mobilization, Clinical Outcomes, Conditioning Regimens, Lymphoma, Multiple Myeloma, Toxicities

AIM

The study aimed to discuss and analyze the chemo-mobilization, conditioning regimens, toxicities and clinical outcomes of Lymphoma and MM ASCT adult patients from January 1, 2019 to December 31, 2022 in a unit where expenses were subsidized by the government.

METHODS

A single center retrospective cohort study.

RESULTS

A total of 42 patients, 18 MM and 24 Lymphoma patients were included. Nine were DLBCL while 15 were HL.

The average age of MM patients was 49 years old (SD=9.0), predominantly ISS stage II (50%); seventeen (94%) patients underwent ASCT after first line therapy. Among lymphoma patients, average age was 28 years old, gender split was equal, Ann Arbor stage III-IV and 62.5% refractory. [Table 1]

For MM and Lymphoma patients, chemo-mobilizing regimens were Cyclophosphomide (CY) + GCSF (77.8%) and Cyclophosphomide + Plerixafor + GCSF (22.2); Cyclophosphomide + GCSF (79.2%) and ICE + GCSF (8.3%) respectively. There was no difference on mean number of peripheral blood CD34+ count and number of harvest with the different chemo-mobilizing agents used on both groups.

For the both MM and Lymphoma, higher peripheral blood CD34+ count resulted to higher values of CD34+ cells/kg body weight collected (p=0.0058, Myeloma; p=0.00001 Lymphoma).

Conditioning regimen was melphalan in all MM while BeEAM+/-R was used for Lymphoma

patients. All of the source of stem cells is peripheral blood.

The most common toxicities in both MM and Lymphoma groups were Grade 2 Mucositis; Grade 2-3 Diarrhea; Infection complications (94%, MM, 100%, Lymphoma) and Febrile Neutropenia. [Table 2] Two lymphoma patients died, one from Neutropenic Enterocolitis and one from Hospital Acquired Pneumonia.

The average day of neutrophil engraftment was 16 days (16 ± 3.3) for MM, and 13 days for Lymphoma (13.7± 4). No documented engraftment syndrome was reported. No correlation between total CD34+ count infused and the day of engraftment and no significant difference between giving of GCSF at day 1 to 3 versus ≥day 4 with the onset of engraftment.

Upon discharge, all MM patients were alive and the average hospital day is 22. Among lymphoma patients, 22 (91.75%) were alive. The average hospital day is 23.

After 100 days, all discharged MM and lymphoma patients were alive. For MM, the remaining 38.9% who had VGPR pre-transplant achieved CR. Among lymphoma patients, 35% achieved CR from PR, one patient (5%) was still refractory. For MM, 1-3 year-Relapse Free Survival (RFS) is 93%, and 4 year-RFS is at 70%; 1-3-year Progression Free Survival (PFS) is at 93% and 4-year PFS is at 70%. On the other hand, for lymphoma, 1 year-RFS is 90%, 2-year is 77% and year 3 to 4 RFS is 51%; the 1 year-PFS is 82%, 2 year-PFS at 71% and 47% at year 3 and year 4.

CONCLUSION

Over the course of four years, ASCT in MM and R/R Lymphoma was successfully performed in this government subsidized institution, from chemo-mobilization phase to post transplant care. Immediate and long-term outcomes showed durable response and prolonged survival.

“No conflict of interest to disclose”

Significance Of Clostridioides Difficile detection In Hematopoietic Stem Cell Transplant (HSCT) Recipients

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Event: 28th Annual Meeting of APBMT
Topic: Infections
Keywords: C. difficile, Diarrhoea, Hematopoeitic stem cell transplant

Diarrhoea is almost universally observed after stem cell transplantation. *C. difficile* has been recognized as a cause of diarrhoea in hematopoietic stem cell transplantation (HSCT) recipients for many years. No studies are available from India in HSCT patients regarding the magnitude of problems caused by C. *difficile.*

Aim: To find out the significance of *C. difficile* infection in HSCT recipients.

Methods: It was a prospective longitudinal study, performed at a BMT centre at a tertiary care teaching Institute in North India. All consenting patients, irrespective of age, sex or diagnosis, were included. Stool samples were collected (irrespective of the presence or absence of diarrhoea) at the time of hospitalization (baseline) and every week starting from the first day of conditioning for four weeks and thereafter every two weeks if the patient's stay was prolonged beyond this period till discharge or two months whichever was earlier. All stool samples were subjected to the detection of Glutamate dehydrogenase (GDH), toxin A, and toxin B (CDTA) using a commercially available FDA-approved immunoassay kit (Minividas). All stool samples were cultured on chrome agar plates and blood agar plates. Phenotypic identification of *C. difficile* was done by using Bruker Daltonik MALDI Biotyper. The DNA was extracted by a DNA stool extraction kit by Qiagen. PCR was performed for the gene *tcdab* (toxin A and toxin B) for all positive and negative cultures and adequate DNA could be isolated in 102/212 samples.

Results: 212 stool samples were collected from 58 HSCT recipients (Allogeneic = 28, Autologous =30) with a median age of 30 (8-64)years and M: F ratio was 39:19.Total diarrhoeal episodes were 63 and the average duration of diarrhoea was 10 days. Overall, GDH, CDTA, C.*difficile* culture and PCR were positive in 29 (13.6%),15(7.1%) and 14 (6.6%) samples, respectively. PCR was positive in 14/102(13.7%) of stool samples. Table-1 shows the result of these tests in those with or without diarrhoea.

69/ 115 (60%)sample from 15 cases with diarrhoea were positive for either C. difficile by culture or by GDH with toxin or by PCR suggesting the incidence of C DI in 15/58 (25.8%) whereas 12/90 (13.3%) samples from 8 patients without diarrhoea were positive for either C. difficile by culture or by GDH with toxin or PCR resulting in an 8/58 (13.8%)carrier rate.

Conclusions:

To the best of our knowledge, this is the first prospective longitudinal single institutional study providing the incidence of C. difficile infection and carriage rate in HSCT recipients in India. Incidence of C.*difficile* was 25.8% in cases with diarrhoea whereas 13.8% of cases had asymptomatic C. *difficile* carriage which may be an important source for the spread of CDI. It was also observed that some GDH and culture-negative samples had tested positive by PCR suggestingthat molecular biology technique is more sensitive than the normal methods for detecting *C. difficile.*

This work was funded by the Indian Council of Medical Research. It had no role in analysing the data or preparing the abstract.

An increasing trend in adenoviral infections in children undergoing alternate donor hematopoietic stem cell transplantation

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Abstract ID: 124
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Topic: Infections
Keywords: nothing

Background

Adenoviral infection can occur due to reactivation or from the graft in children undergoing hematopoietic stem cell transplantation (HSCT). The clinical spectrum ranges from pneumonia, colitis, hemorrhagic cystitis to disseminated disease with multiorgan failure. We report our experience with an increasing trend of adenoviral infection in our alternate donor HSCT cohort over the last five years.

Patients and methods

We performed a retrospective study between March 2018 to February 2023 and analyzed data from medical records on all children up to 18 years of age undergoing alternative donor HSCT at our center. We included all children who had engrafted and survived till Day 30 post-HSCT. We recorded the demographic data, the underlying disorder – malignant versus non-malignant, type of HSCT - if matched unrelated or haploidentical donor, adenoviral PCR values, organ affected, and survival outcomes. We tapered immunosuppression and offered cidofovir at 5mg/kg/dose weekly to children with one log increase till a negative blood PCR. The Institutional Ethics Committee approved the study.

Results

We transplanted 317 children aged two months to 18 years with 242 haploidentical (76%) and 75 matched unrelated donor HSCT (23%). The underlying diagnosis was hemoglobinopathy in 91, inborn errors of immunity in 76, bone marrow failure syndromes in 38, and malignant disorders in 81children. The rate of adenoviral reactivation was 32/317 (10%). The annual incidence showed an increasing trend with 3/52(5.7%) in 2018, 8/81 (9.8%) in 2019, 4/42 (9.5%) in 2020, 7/68(10.2%) in 2021 and 10/74 (13.5%) in 2022.

In non-malignant conditions, the adenoviral reactivation rate was 14.5% in the haploidentical cohort and 6.7% in the MUD cohort. The incidence was 19% (18/91) in children with hemoglobinopathy, 10.5% (4/38) in bone marrow failure syndromes and 8% (6/76) in inborn errors of immunity. The adenoviral reactivation was higher at 72% following haploidentical HSCT for hemoglobinopathy in contrast to MUD HSCT at 27%.

In the malignant disorders, the adenoviral reactivation rate was low at 4.7% in the haploidentical cohort and nil in the MUD cohort. The adenoviral reactivation occurred between 2 to 3 months post HSCT. Adenovirus affected the gastrointestinal tract in 6 children, genitourinary system in 2, lung in 1, was disseminated with multi organ involvement in 3 children. Twenty-two (68%) children received cidofovir, with an average of four doses required to achieve negative copies. The copies documented ranged from 1000 to 935,656 copies. Cidofovir was well-tolerated in all children with no documented nephrotoxicity. Mortality directly due to disseminated adenoviral infection was 8% and occurred in 3/32 children.

CONCLUSION

The study reports adenoviral reactivation in 10% of children undergoing alternative donor HSCT with an increasing annual trend from 5.7% in 2018 to 13.5% in 2022. The children at highest risk are those undergoing haploidentical HSCT for hemoglobinopathy. Treatment with reduction in immunosuppression and cidofovir is effective 68% of children and 31% recovered without cidofovir with low copies. Based on this study we plan to analyze the impact of adenoviral vector based covid vaccination in multiple transfused children with thalassemia major and alter our protocol to help rapid immune reconstitution.

Clinical diagnosis of liver dysfunction and correlated histopathological findings of liver biopsy in patients treated with allogeneic hematopoietic cell transplantation

by Jae-Ho Yoon | Ka Young Kim | Gi June Min | Sung-Soo Park | Silvia Park | Sung-Eun Lee | Byung-Sik Cho | Ki-Seong Eom | Yoo-Jin Kim | Hee-Je Kim | Seok Lee | Chang-Ki Min | Seok-Goo Cho | Jong Wook Lee | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea | Department of Hematology, Catholic Hematology Hospital and Leukemia Research Institute, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

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Event: 28th Annual Meeting of APBMT

Topic: GVHD

Keywords: Allogeneic hematopoietic stem cell transplantation, Graft-versus-host disease, Liver biopsy

Aims: Liver dysfunction is one of the dismal complications after allogeneic hematopoietic cell transplantation (Allo-HCT). Although hepatic graft-versus-host disease (GVHD) and toxic hepatitis are frequently suspected complications, it is still difficult to find out the diagnosis exactly. For the accurate diagnosis of hepatic dysfunction after allo-HCT, we sometimes conduct liver biopsy. However, pathologic findings are also complicated due to overlapping features among the hepatic complications. We tried to review the pathologic findings of liver biopsies obtained from patients whose liver enzymes elevated after allo-HCT.

Methods: We obtained 92 liver biopsy samples from 88 patients who underwent allo-HCT in Catholic Hematology Hospital from 2008 to 2023. All patients showed elevated liver enzymes presenting with either cholestatic pattern (hyperbilirubinemia and/or high alkaline phosphatase [ALP] or gamma glutamyl-transferase [GGT]) or hepatocellular pattern (elevating AST/ALT levels). Clinical course, laboratory and pathological findings were obtained on the date of liver biopsy. Acute hepatic GVHD was assessed by the original Glucksberg criteria and chronic hepatic GVHD was assessed by the National Institutes of Health criteria 2014. Hepatic GVHD was clinically diagnosed in patients showing elevated ALP or GGT with hyperbilirubinemia (typical cholestatic) or elevated aminotransferase (hepatic variant).

Results: Median duration to the date of biopsy was 6.3 months (range, 0.8 to 61.3). Hepatic GVHD was divided into typical cholestatic pattern (n=30) and hepatic variant (n=28). Other clinical features were isolated isolated hyperbilirubinemia (n=17), elevation of aminotransferase (n=8), HBV reactivation (n=5), toxic hepatitis (n=2), liver cirrhosis (n=1), PTLD (n=1). Among the 30 cholestatic hepatic GVHD, 20 biopsies revealed early pathologic features including bile duct damage and portal lymphocytic infiltration, 9 showed late features including loss of bile duct and fibrosis, and 1 showed non-specific findings. For 28 hepatic-variant GVHD, 22 biopsies revealed early pathologic features, and 5 showed late features including loss of bile duct and fibrosis, and 1 showed non-specific findings. For 8 isolated aminotransferase elevation, all showed typical GVHD findings (early feature 6, late feature 2), while for 17 isolated hyperbilirubinemia showed 8 hepatitis pathology, 5 GVHD, 3 VOD, 1 hemochromatosis.

Among our final 36 hepatic variant GVHD, 35 (97.2%) patients showed GVHD improvement after treatment, while among final 35 cholestatic GVHD, 15 (42.8%) showed response ($p<0.001$).

Conclusions: Our clinical diagnosis for hepatic GVHD was well correlated with pathologic findings. Clinical outcome of hepatic GVHD with cholestatic pattern was very poor than hepatic variant GVHD. Isolated aminotransferase elevation strongly correlated with GVHD pathology. As isolated hyperbilirubinemia was related with various etiologies in pathologic findings, we recommend liver biopsy in this group of patients.

Ten-year follow up study of children with thalassaemia major post transplantation using treosulfan, thiotepa, fludarabine based conditioning regimen and its impact on growth and puberty

by Suresh R Duraisamy,Kavitha Ganesan, Satishkumar Meena,Anupama,Vijayashree, Venkateswaran VS, Ramya Uppuluri, Indira Jayakumar, Vidya, Revathi Raj | APOLLO CANCER CENTRE,CHENNAI

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Topic: Conditioning Regimens
Keywords: nothing

Introduction

We present a uniform cohort of children with thalassaemia major who underwent treosulfan conditioning based HSCT and its impact on growth and puberty.

Methods

Our study is a retrospective analysis on children who underwent allogeneic HSCT for transfusion dependent thalassaemia major between 2010 to 2020 with a minimum follow up period of two years. All children were classified as per Lucarelli Class 1, 2 and 3 based on the iron overload status and received conditioning chemotherapy with treosulfan, thiotepa and fludarabine with ATG for MUD And ATG and 2 Gy total body radiotherapy for haploidentical HSCT. Data collection focussed on the presence of graft versus host disease and the need for steroid use for over 4 weeks. We documented the height and weight and Tanner stage if applicable at the time of HSCT and the current height, weight and Tanner stage and the need for growth hormone replacement.

Results

Of 202 children in our study 59% were males and 41% females and 110/202 (54%) had a matched family donor (MFD), 62/202 (31%) haploidentical and 30/202 (15%) matched unrelated donor (MUD). 73 (36%) were in <5 years of age at HSCT, 90 (45%) between 5 to 10 years and 39 (19%) over 10 years of age. The mean height SDS at HSCT was -0.574 and at current assessment the mean height SDS was -0.669 (p=0.391). There was no major reduction in growth potential. 29 (14.4%) were short at the time of HSCT (height SDS <-2) and at current assessment only 6 (20.7%) were still short and 23 (79.3%) had catch up growth and moved to height SDS >=-2. The mean height SDS during HSCT in Class1 thalassemia was -0.216, -0.478 in Class 2 and -0.898 in Class 3 respectively (p=0.026). The current height SDS in these classes are -0.115, -0.710 and -0.929 respectively, confirming that children in Class 1 and 2 are able to catch up on their growth but the Class 3 patients failed to catch up growth after HSCT (p=0.010). In children with acute GVHD there was no

difference in contrast to a statistically significant difference in mean current height SDS in chronic GVHD group (-0.468 against -0.920, p=0.020).

In the children currently above 10 years group, 17 (43.6%) were in Tanner stage 5. Of the 83 female children, 45 (54.2%) attained spontaneous menarche and their mean age during HSCT was 8 years and their current mean age is 14.8 years. 14 (6.9%) children requiring growth hormone GH.

Conclusion

In treosulfan based conditioning followup on growth and puberty in children with thalassaemia major,there was no significant reduction in height SDS from the time of HSCT to the current assessment and only 6.9 % children required growth hormone supplementation. There was no impact on puberty in both boys and girls and over half the girls have attained menarche at a median age of 14.8 years. Despite the higher cost of treosulfan the reduced late side effects and intact survival justifies its use in all children undergoing HSCT for thalassaemia major.

Long Term Outcome of Haploidentical Transplantation: A Single Center Experience from India

by Jhansi Jayachandran | Ashish Dixit | Mallikarjun Kalashetty | Amit Rauthan | Poonam Patil | Santosh Subramanian | Manipal Hospitals, Bangalore | Manipal Hospitals, Bangalore | Manipal Hospitals, Bangalore | Manipal Hospitals, Bangalore | Manipal Hospitals, Bangalore | Manipal Hospitals, Bangalore

Abstract ID: 155
Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: GVHD, Haploidentical transplantation, India, Pediatric transplantations

AIMS:

Haploidentical stem cell transplantation (SCT) is emerging to be an excellent alternative for patients who do not have a matched donor. This study aims to estimate complication outcomes like transplantation-related mortality (TRM), infections, and graft-versus-host disease (GVHD), survival outcomes like overall survival (OS) and event-free survival (EFS) in patients undergoing haploidentical SCT for various indications, and to compare the outcome of pediatric population with that of adults.

METHODS:

A single center retrospective study was performed using the hospital registry. We included patients who underwent haploidentical SCT for various indications between May 2013 and May 2023 and followed up till date. Data on baseline patient and disease characteristics, ABO mismatch, Cytomegalovirus(CMV) status, various conditioning regimens used, and post-transplant follow-up were collected. Post-transplantation cyclophosphamide (PTCy), along with mycofenolate mofetil (MMF) and tacrolimus, was used for GVHD prophylaxis. Chi-square tests were used to compare the proportions of categorical variables in various subgroups. Survival curves like OS and EFS, wherein the event was either death, relapse or need for a second transplant, were assessed using the Kaplan-Meier method, and survival amongst subgroups were compared with the log-rank test. Median follow-up duration was 6 months (0 to 127 months), post-HSCT

RESULTS:

59 patients underwent 65 haploidentical transplantations. Pediatric patients (Age<18 years) comprised 51% cases. Median age of the group was 16 years (Range:2 months-59 years). 58% cases were males. Indications were both malignant(81%) and benign(19%). Amongst the malignant causes, Acute Lymphoblastic Leukemia(ALL) was the most common disease. CMV status of the recipient was positive in 90% cases.

Major ABO mismatch was seen in 15% and minor ABO mismatch, in 17% of transplants.

Conditioning regimens used were both myeloablative(51%) and non-myeloablative(49%). Most common myeloablative regimen used was Flu/TBI. G-CSF mobilized peripheral blood stem cells were used in most cases(65%). Primary graft failure was observed in 5% cases. 15% cases died before engraftment. Amongst those who got engrafted, the median day of neutrophil engraftment was 14 days (range:11-36 days). Day-100 TRM was seen in 24% transplants. Acute GVHD(aGVHD) was seen in 32% transplants, most of who presented with skin GVHD of grade I/II. Only 7 transplants had grade III/IV aGVHD. There was significant increase in occurrence of aGVHD in myeloablative transplants (p=0.005). Chronic GVHD was seen in 15% cases and most were limited skin GVHD that got resolved with topical steroids.

Infective complications were observed in 61% transplants, Klebsiella pneumonia being the most common bacterial infection and CMV, the most common viral infection.

On follow-up, 47% cases had died (including 16 TRM). Of the 52 transplants done for malignant conditions, 16 (30%) had relapsed. Median OS of the patients post-haploidentical SCT was 27 months, which was significantly higher in pediatric cases (p=0.38). 2-years OS of the group was 53.5%. Median EFS post-haploidentical SCT was 10 months, which did not differ between the two age groups.

CONCLUSIONS:

Although haploidentical SCT has emerged as a curative option for patients who otherwise didn’t have a suitable matched donor, strategies to reduce aGVHD and infection-related mortality must be explored further.

“No conflict of interest to disclose”

Generation, Expansion, and Characterization of Cytomegalovirus (CMV), Adenovirus (AdV), Epstein-Barr Virus (EBV) and Multi-Virus Specific T cells (M-VST) using In-house Designed Peptides Restricted to Common HLA Alleles in the Indian Population

by Omkar Bhosale | Bhanu Kota | Nishant Jindal | Akanksha Chichra | Selma D\'silva | Cloris Gonsalves | Sachin Punatar | Anant Gokarn | Sumeet Mirgh | Lingaraj Nayak | Navin Khattry | Meenakshi Singh | Transplant Immunology and Immunogenetics Lab; Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Transplant Immunology and Immunogenetics Lab; Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Transplant Immunology and Immunogenetics Lab; Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Bone Marrow Transplant Unit, Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India | Transplant Immunology and Immunogenetics Lab; Advanced Centre for Treatment, Research and Education in Cancer, Tata Memorial Centre, India

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Topic: Cell and Gene Therapy
Keywords: Adeno Virus, Bone Marrow Transplant, Cytomegalo Virus, Epstein-Barr virus, In-house Peptides, Post transplant Viral reactivation, Virus Specific T cells

Aim: Allogeneic hematopoetic stem cell transplant remains the most curative therapy for several hematological malignancies. Post-transplant viral reactivations contribute to significant morbidity and mortality. Available anti-viral drugs are associated with significant toxicities and are not effective in all patients. Third part donor-derived Virus-Specific T cell (VST) therapy is an alternative and has been shown to be effective in several studies. In this study, we aimed to generate third party donor derived CMV, AdV, EBV and M-VSTs restricted to common HLA alleles found in the Indian population. This was done by identifying the highly immunogenic In-house Peptides (IP) from corresponding viral antigens and specifically selecting them to generate VSTs. We compared the results with VST generated using Commercial Peptivators (CP).

Methods: For generation of VST, 0.5-1 x 10^9 mononuclear cells (PBMC) were isolated from the apheresis product of healthy donors using Ficoll gradient centrifugation. From these, 1 x

10^8 PBMC were used for Monocyte-derived Dendritic Cell (MoDC) generation using 3% AB serum + RPMI (cRPMI) and a cocktail of cytokines (IL-4, GM-CSF, and TNF α). On day 6, the MoDCs were pulsed for 2 hours with IP for CMV, AdV, EBV, and the complete peptide pool for M-VST. Parallelly, CP were used to stimulate the MODCs. Post-stimulation, the MoDCs were cocultured with the donor PBMCs for 7 days. On day 13, the cultures underwent a secondary stimulation with corresponding CP/IP in addition to IL-2. The generated VSTs were expanded till day 28, with the addition of IL-2 and cRMPI every 2-3 days. The immune cell profile analysis was performed using flow cytometry. IFN γ secretion assay was performed for functional characterization of VSTs. Cytotoxicity assay for EBV and CMV VSTs was performed against auto or HLA-matched EBV Lymphoblastoid Cell Lines (LCL) and pp65 antigen-pulsed auto-PHA blasts respectively.

Results: 8 healthy donors were used to generate 45 VST products (9 CMV,12 EBV,13 AdV and 11 MSV). The immunophenotype (n=29, 16 CP/13 IP) confirmed these to be predominantly CD3+ T cells (86.5% +/- 11%). CD8+ T cells were higher compared to CD4+ cells for products with single virus specificity and the opposite was noticed for M-VST (Table 1). The T cell subset analysis showed that the majority of cells belong to the effector memory and central memory subset (Table 2.). The IFN γ secretion assay was performed for 32 VSTs (16 CP/16 IP) and showed comparable results for CP and IP-generated VSTs (Figure 1). Cytotoxicity assay was performed on 3 EBV (1 CP/2 IP) and 2 CMV (1 CP/1 IP) VSTs and was found to be >15% at 20:1 (Effector:Target) ratio, suggestive of efficacy.

Conclusion: The preliminary data suggests that the VSTs generated using IP are functionally and phenotypically comparable to VSTs generated using CP, and the mentioned protocol can be used for generating clinical-grade VSTs to provide a treatment alternative for the Indian population cohort at a fraction of the cost.

Conflict of Interest Statement: This research was supported by BIRAC (INDIA), ‘PACE’. The company had no role in analysing the data or preparing the abstract.

Unrelated Donor Hematopoietic Stem Cell Donation in Asia; Report from World Marrow Donor Association

by Monique Jöris | Lydia Foeken | World Marrow Donor Association (WMDA), Leiden, the Netherlands | World Marrow Donor Association (WMDA), Leiden, the Netherlands

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Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: , Unrelated donor, cord blood bank, donor registry, hematopoietic stem cell donation

Aim

Treatment of hematologic diseases with unrelated donor (UD) hematopoietic stem cell transplantation (HSCT) has become the standard of care for many patients. However, it is a costly and specialized therapy requiring significant economic investment, infrastructure, and training which prohibit it from being widely adopted in many parts of the world.

World Marrow Donor Association (WMDA) strives for access to life-saving UD HSCT for all patients and operates the global database (WSMS) to facilitate search and selection of the most suitable UD hematopoietic stem cell (HSC) product.

Another key project of WMDA is the Global Trends Report (GTR) which has become an established instrument to describe the global status of UD HSC donations.

By analysing data from these 2 projects we investigate the current status of UD HSC donation in Asian countries represented in Asian Pacific Bone Marrow Transplant (APBMT) group to determine the need for development of Asian national UD registries/CBBs.

Methods

Number of available UD and cord blood units (CBUs) and UD HSC donation numbers from WMDA GTR and number of searches performed in WSMS in 2022 were collected for 19 Asian countries represented in APBMT. Additionally, demographics were collected from worldometer website and incidence statistics of disease indications for UD HSCT were collected from the Global Cancer Observatory (Globocan) website.

Results

In 2022, almost 6 million UD and 200 thousand CBUs were registered and available for UD HSCT in 10 countries (Table 1). Considering the combined population, only 13.86 UDs and 0.47 CBUs per 10 thousand inhabitants are available, compared to 53.51 UDs and 1.04 CBUs per 10 thousand inhabitants worldwide (Figure 1).

In 2022, a total of 5,646 UD HSC products (marrow, apheresis and cord) were donated for national patients, 124 products exported for international patients and 150 products

imported from international donors (Figure 2). A total of 2,723 unique searches were performed in WSMS (Figure 2).

By 2040, the combined population size will increase by an estimated 2.58%, compared to 17.18% globally. However, median age will increase at a higher rate than globally (22.47% vs 14.48%) and fertility rate will decrease at a higher rate than globally (-7.98% vs -5.96%). Additionally, incidence of the 4 major disease indication for UD HSCT will increase by an estimated 40.4% (Table 2).

Conclusions

With UD registries/CBBs in 10 countries and significant UD HSC donation in 9 of them, it is likely there are many patients who do not have access to live-saving UD HSCT. Most UD HSC donations are done for national patients and only 6% of international searches in WSMS resulted in a donation from an international donor, highlighting the importance of establishing local UD registries and/or CBBs in the other 9 countries. Furthermore, connecting to WSMS will increase the number of potential UD/CBUs for Asian patients living in the diaspora.

The need for UD will likely increase with growing, aging populations and increased disease incidences. Furthermore, fertility rates are estimated to decrease, meaning smaller families and therefore decreased availability of family donors.

Conflict of interest

The authors have nothing to declare.

Myeloma- A Hope for Setting Up a New Transplant Centre in Tier-2 City in India

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Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: Myeloma, New Transplant centre, Tier-2 city

Aim

Most of the haemopoietic stem cell transplant (HSCT) centres are established in tier-1 cities (population of 1 million and above). Establishing a HSCT centre in a tier-2 city (0.5 to less than 1 million population) remains a challenge for a new transplant physician especially in a private sector health centre. Here we share our experience in establishing a new and the first HSCT in Tiruchirapalli (a tier-2 city in Tamil Nadu, South India). As usual Myeloma, remained the first disorder and continued to be the leading disorder to be transplanted here, bringing hope for the physician, new HSCT team as well as patients in this part of the country.

Methods

We have established a 2 bedded HSCT unit with HEPA filter (high efficiency particulate air filter) at the top most floor of Kauvery hospitals, Tiruchirapalli, India in 2020. Patients with myeloma were managed with standard regimens. First line regimen was VRD (Bortezomib, Lenalidomide, Dexamethasone), CyBorD (Cyclophosphamide, Bortezomib, Dexamethasone) or Thalidomide Dexamathasone. Second line regimens (VDT PACE or KPD) were used if the first line regimen (minimum 4 cycles) failed to show at least a partial response as per IMWG criteria. Patients with at least a partial response and up to 65 years with a good physical performance were counselled for an autologous stem cell transplantation. Stem cell mobilization was done with G-CSF and Plerixafor. Peripheral blood stem cell harvest was done using haemonetics MCS+ or Spectra optia apheresis systems through a Jugular venous HD catheter. Conditioning regimen used was Melphalan (200mg/sq.m if normal renal function, 140mg/sq.m if renal failure or age > 65 years). Supportive care (antibiotics, mucositis care, irradiated blood products) was given until engraftment and recovery of mucositis or defervescence.

Results

Amongst 40 stem cell transplants done in last 3 years, 18 (12 males, 6 females) myeloma patients have undergone autologous BMT procedure. Median age is 55.5 years (range 25-65 years). Anaemia was present in 14/18 patients, bone lesions were present in 13/18, renal failure in 9/18 and 3/18 had hypercalcemia at diagnosis. Five had diabetes mellitus, 6 had hypertension and 3 had peripheral neuropathy. Very good partial response was achieved in 7, complete response in 8 and 3 had only a partial response. Mean CD34 cell dose infused was 8 x 10^6/Kg (ranged from 3.3 x 10^6/Kg to 17.6 x 10^6/Kg). 17 patients engrafted neutrophils and platelets successfully (94%). Two patients grew microbes in blood culture (Pseudomonas aeruginosa and Acinetobacter baumanii). One patient expired on day +18 before engraftment in view of Acinetobacter sepsis.

Two amongst above 18 patients also underwent a tandem transplant subsequently

Conclusion

The mission of the IMWG is to conduct collaborative basic, clinical, and translational research to improve outcomes for myeloma patients while providing scientifically validated, critically appraised consensus guidelines for the myeloma community globally.
Myeloma still remains the most common disorder where a haematologist starting transplantation services at a new centre begins with. It brings hope for both the patient as well as the new stem cell transplantation team.

“No conflict of interest to disclose”.

Early Prediction of Platelet Recovery with Immature Platelet Fraction in Patients Receiving Hematopoietic Stem Cell Transplantation

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Topic: Leukemia
Keywords: hematopoietic stem cell transplantation, immature platelet fraction, platelets, thrombopoiesis, transfusion

Aims

Hematopoietic stem cell transplantation (HSCT) is a significant therapeutic approach for various hematologic disorders, wherein patients undergo a period of pancytopenia. To mitigate the risks associated with this condition, prophylactic transfusions are often administered. Identifying an effective marker to monitor patients' hematopoietic function and anticipate the recovery of hematopoiesis in advance could reduce unnecessary prophylactic transfusions. Previous studies have suggested that immature platelets may serve as an early predictor of platelet recovery. Therefore, this study aims to investigate whether the immature platelets fraction (IPF) can early predict platelet hematopoietic recovery in patients undergoing stem cell transplantation and determine the optimal cut-off value.

Methods

This is a prospective study that included 53 patients who underwent hematopoietic stem cell transplantation at Taipei Veterans General Hospital. Comprehensive parameters of peripheral blood cells were measured using the Sysmex XN analyzer. Successful recovery of neutrophils and platelets was defined as a consecutive three-day absolute neutrophil count greater than 0.5×10^9/L and a consecutive seven-day platelet count greater than 20×10^9/L, respectively. From the receiver operating characteristic (ROC) curve analysis, Youden index derivation was able to determine an optimal IPF cut-off value.

Results

Neutrophil and platelet recovery were observed 10 (median; range 10-12) and 15 (median; range 15-18) days after HSCT, respectively. There were 38 patients (71.7%) who presented with an increase in the immature platelet fraction (IPF) of more than 2% occurred prior to platelet recovery. The optimal cut-off IPF was found to be 2.15% for platelet recovery within

5 days (specificity 0.89, sensitivity 0.63, positive predictive value 0.85). On average, patients received 3.89 units of platelet transfusions following transplantation. However, if a patient's IPF reached the cut-off value of 2.15%, refraining from platelet transfusions could potentially reduce the need for 0.59 units of platelet transfusions.

Conclusion

The results show that IPF can serve as a predictor of platelet engraftment, and its peak value occurs before the rise in platelet count. We identified an optimal IPF cut-off value of 2.15%, which can be utilized to predict post-HSCT platelet recovery. Implementing this cut-off value in transfusion strategies may potentially reduce the need for prophylactic platelet transfusions. Therefore, IPF can be considered a novel tool for assessing post-transplant hematopoietic function and predicting recovery.

SESSION 10 –
HSCT FOR LEUKEMIA

HSCT for Ph(+) ALL/CML in The Era of TKI

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The introduction of Tyrosine Kinase Inhibitors (TKIs) transformed clinical practice with regards to Philadelphia chromosome positive (Ph+) leukemias. In chronic phase Chronic Myeloid Leukaemia (CP-CML), the majority of TKI treated patients can expect long term survival similar to their age-matched peers.

Despite substantial improvements in outcomes, significant challenges remain. In CP-CML, up to 30-40% of patients may discontinue their frontline TKI treatment because of either toxicity or treatment resistance. Even though increasingly potent TKIs (including second & third-generation TKIs, as well as the allosteric inhibitor asciminib) are now clinically available, some patients may still need consideration for allogenic stem cell transplantation (alloSCT), including those with resistance against all currently available TKIs, or patients with profound and prolonged cytopenias. Additionally, outcomes remain poor in patients either presenting as, or progressing to, blastic phase CML, and alloSCT remains to the only path to cure.

In Ph+ Acute Lymphoblastic Leukaemia (ALL), TKIs have made an equally significant contribution to clinical practice, dramatically increasing remission rates and survival when combined with chemotherapy, and when used as post-transplant maintenance therapy. As with other subtypes of ALL, immunotherapy such as blinatumomab and inotuzumab, as well as Chimeric Antigen Receptor T-Cell (CAR-T) therapy, are now all recognised as effective salvaged treatments for relapsed Ph+ ALL, either alone or combined with TKIs. New evidence suggests their frontline use may lead to deep responses in a high proportion of patients, without chemotherapy associated toxicity. It is increasingly speculated that patients with negative Minimum Residual Disease may achieve long term leukaemia free survival without alloSCT in first remission, especially where highly effectivesalvage is available as a bridge to transplant in the event of relapse. This presentation will serve as an overview of alloSCT considerations for Ph+ ALL/CML in 2023.

Ex Vivo Lymphoid Cell Selection for Haplo HCT in Hematological Malignancies

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Depletion of T cells in the stem cell graft is one approach to enable haplo-HSCT. This approach has been refined over the years from CD34 positive selection or pan-T cell depletion in the 1990s, to a more selective depletion of T cell subsets in the past decade. Basic research shows that the TCRab+ T cells and CD45RA+ T cells mediate GVHD. Therefore, their selective depletion while preserving CD45RO+ memory T cells as well as innate cells such as gamma delta T cells, NK cells overcome the problem of GVHD while preserving anti-pathogen and graft-vs tumour activity, such that problems associated with T cell depletion such as high rejection risk and poor immune-reconstitution are overcome. This approach has been used in both adults and paediatrics with outcome comparable to historical data on matched donor transplant.

In Singapore, under guidance of Prof Wing Leung, a shared protocol amongst National University Hospital, Singapore General Hospital and KK Women's and Children's hospital started the "Haplo-17" protocol since 2017 with the above method. Stem cell graft is divided into a larger fraction for TCRab depletion aiming for a target CD34 cells of at least 4million/kg, and a smaller fraction for CD45RA depletion giving a target CD45RO cells of 1 million/kg as T cell add-back. Conditioning regimen included thiotepa, fludarabine, melphalan and 6Gy TNI in 3 fractions or a single fraction TBI of 2Gy. GVHD prophylaxis was single agent tacrolimus to be tapered at 1 month and stopped by 2 months. To date we have transplanted more than 100 patients with various haematological malignancies using this protocol, with a 2y OS of 70% and EFS of 58.7%, as well as GRFS of 57.3%. Details of stem cell processing and clinical data will be presented.

SESSION 11 – IMMUNOLOGY IN AND AFTER HSCT

Reactive granulopoiesis depends on T-cell production of IL-17A and neutropenia-associated alteration of gut microbiota

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Disruption of the intestinal microbiota (dysbiosis) after allogeneic hematopoietic cell transplantation (allo-SCT) plays a critical role in the pathophysiology of acute graft-versus-host disease and has been well recognized as a prognostic biomarker for worse transplant outcomes. Recently, it has been shown that composition of the gut microbiota is associated with neutrophil recovery after allo-SCT (Schluter J Nature 2020). Severe bacterial infection induces “emergency granulopoiesis” that can increase granulocytes several-fold above steady-state level to eliminate infectious agents. The term “reactive granulopoiesis” refers enhanced granulopoiesis in the absence of active microbial infection that could be induced by neutropenia after SCT, whereas the mechanism by which neutropenia induces granulopoiesis remains to be clarified. Recent studies demonstrated that intestinal microbiota plays a critical role in the development of granulopoiesis in infants after birth (Deshmukh, Nat Med 2014). Thus, we studied the mechanism by which neutropenia induces granulopoiesis after SCT or chemotherapy focusing on the role of intestinal microbiota. First, we found that plasma levels of IL-17A and G-CSF were elevated after SCT. When IL-17A deficient (IL-17A-KO) mice were used as recipients, elevation of plasma levels of IL-17A and G-CSF were abrogated, and neutrophil recovery was significantly delayed, indicating that IL-17A plays a critical role in reactive granulopoiesis after SCT. Next, we explore the role of gut microbiota in granulopoiesis after SCT. Gut decontamination using antibiotics abrogated elevation

of plasma levels of IL-17A and G-CSF and significantly delayed neutrophil recovery. 16S rRNA sequencing revealed that composition of gut microbiota was significantly altered after prolonged neutropenia after SCT. Finally, transplantation of fecal microbiota collected from neutropenic, but not naive, mice promoted neutrophil recovery in these gut-decontaminated SCT recipients, suggesting that neutropenia-associated microbiota had a potential to stimulate reactive granulopoiesis. Our study uncovered a novel cross talk between gut microbiota and neutropenia after SCT and chemotherapy.

Advances in Chronic GVHD Treatment

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Chronic graft-versus-host disease (cGVHD) is the most common late complication following allogeneic stem cell transplantation. This disease has variable features resembling autoimmune disorders such as scleroderma, primary biliary cirrhosis, bronchiolitis obliterans (BO), and chronic immunodeficiency, and so on. Thus, cGVHD can lead to debilitating complications, such as joint contractures, blindness, and end-stage lung disease, which have major impacts on both survival and quality of life. Steroid-refractory cGVHD is associated with high morbidity and to date, there is no standard therapy for patients who fail to respond to steroids. Recently, promising medications such as ruxolitinib, ibrutinib and belumosudil had been introduced in the clinical practice for the treatment of cGVHD. But refractory cGVHD such as BO is an area of unmet need in spite of the new drugs that need development of novel treatment.

Strategies for Augmenting Graft vs Tumor Effect after Transplant

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Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT) stands as a cornerstone in the curative treatment of patients battling hematologic malignancies. At the heart of this life-saving procedure lies the potent and promising graft-versus-leukemia (GVL) effect. The GVL effect is a remarkable phenomenon wherein the transplanted immune system not only engrafts itself but also discerns and diligently attacks cancerous cells, thereby offering the tantalizing potential of long-term remission and, ultimately, a cure. However, while the GVL effect holds great promise, realizing its full potential has proven to be an intricate and multifaceted challenge. In this 30-minute presentation, we embark on a journey to explore strategies meticulously crafted to augment the GVL effect, skillfully navigating the intricate landscape of immune responses following transplantation. Our expedition begins with a introduction to the GVL effect. Moving forward, we delve into the often perplexing and disheartening issue of relapse after allo-HSCT, dissecting the intricate mechanisms at play that undermine initial treatment success. The crux of our discussion revolves around an in-depth exploration of the methods employed to enhance and redirect the GVL response squarely towards malignant cells. We unravel the intricacies of immune reconstitution, illuminating how it can be accelerated and optimized to fortify the body's defenses. Additionally, we venture into the fascinating realm of reversing T cell exhaustion, showcasing the potential to reawaken and mobilize exhausted T cells to engage robustly in the relentless fight against leukemia. Our journey culminates with the unveiling of innovative approaches aimed at refocusing the GVL response with precision, pinpointing cancer cells while minimizing collateral damage to healthy tissues. By meticulously examining these strategies and their potential applications, we strive to bring newfound clarity to the landscape of curative intent treatment for hematologic malignancies.

SESSION 12 – TRANSPLANT AND DONOR REGISTRIES IN HCT

Cord blood banking

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Umbilical cord blood is one of the major stem cell sources in the transplantation for patients with various hematological diseases as well as congenital disorders. In Japan, the number of unrelated cord blood transplantation (CBT) from 1997 to 2022 is 23377and it was 1360 in 2022. It is one third of total allogeneic stem cell transplantation and higher than that of bone marrow or peripheral blood stem cell transplantation in unrelated setting. In Japan, six cord blood banks (CBBs) are now working and all are approved by the government for providing CB unit (CBU) to the transplantation centers.

The number of collection center in Japan was 97 in 2020 and 12654 of CBU was transported to CBBs. After selection, 8212 of CBU was prepared and 2582 was cryopreserved. The testing includes the number of nucleated cells, CD34 positive cells, and CFU-GM, as well as infection marker and allelic typing of HLA-A, B, C, and DRB1. The criteria of preparation of CBU are more than 11.4x10^8 nucleated cells and 3x10^6 CD34 positive cells in Central Japan Cord Blood Bank, Seto Japan.

In 2022, 9689 CBUs are open for search by doctors and 4307 (44.5%) is over 12x10^8 nucleated cells and 3069 (31.7%) is over 3x10^6 CD34 positive cells appropriate for patients with 60kg body weight in the Japanese guideline. In 1392 CBUs transferred to transplant centers, 1119 (80.4%) was over 12x10^8 nucleated

cells and 1241 (89.2%) was over 3x10^6 CD34 positive cells.

Since the number of CD34 positive cells is the most significant prognostic factor for engraftment and survival, CBBs in Japan is now working for revision of consensus guideline for collection and transplantation of CBU to improve the nationwide transplant outcomes.

Protecting Donors (focus on donor safety) Donor Issues WBMT Standing Committee

Nina Worel

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The contribution of related donors to the globally rising number of allogeneic haematopoietic stem cell transplantations (HSCT) remains increasingly important, particularly because of the growing use of haploidentical HSCT and also growing numbers of HSCT in regions with currently very low transplant activity.
Compared with the strict recommendations on the suitability for unrelated donors, criteria for related donors allow for more discretion and vary between centres. Pretransplant donor assessment and testing are very important processes affecting the quality and safety of donation including definition of risk for harm for donors but also recipients. In situations where a family donor does not meet the suitability criteria for unrelated donors, involved physicians often struggle with the decision whether the matched relative is suitable for donation or not. On behalf of WBMT Standing Committee on Donor Issues, consensus documents with recommendations for donor workup and final clearance of family donors who would not be able to serve as unrelated donors due to their age or pre-existing diseases have been published to support decision making with the goal of minimizing the medical risk to the donor.
Regarding safety of stem cell donation, current data predominantly from unrelated donors, give reliable information on the frequent early events associated with donation-most of them of mild-to-moderate intensity. Information on the type and relative risk of serious adverse reactions is more limited and only few data exist on long-term donor outcome. Based on this need, the recommendations for a minimum data set for prospective donor follow-up have been developed by the WBMT. Establishment of a standardized global follow-up for both, related and unrelated, donors will enable monitoring of the short- and long-term safety profiles of hematopoietic cell donation and form a solid basis for future donor selection and counseling.

Unrelated marrow donor program – Raising interest in society, increasing donor registration, and increasing donor retention

Patrick Paul

DKMS BMST Foundation India, DKMS Life Science Laboratory India Private Limited Company

Non-Caucasian donors are underrepresented in the worldwide database. For India, as per World Marrow Donor Association, globally, over 40 million people have registered as potential blood stem cell donors, of which only 0.04% are Indians. The unrelated marrow donor program is still nascent in low and middle-income countries due to a lack of funds, government support programs, internationalization and awareness, and myths & misconceptions about blood stem cell donation.

Raising Interest in Society: DKMS addresses the issue by generating awareness through extensive coverage in prominent publications, social media, press releases, engaging events, and conferences with donors or patient-donor meetings and renowned transplant physicians.

Donor Registration: Donor registration in low and middle-income countries faces hurdles due to low education, motivation, and awareness, resulting in challenges in offline and online registrations and a lower availability rate. Drives conducted at Colleges, Corporates & Patient related community drives add to the donor pool. Website & Social media are promising but need unique strategies to develop into sustainable channels of donor registration.

Donor Retention: Engagement via social media, critical updates on emailers, and celebrating donors on World Marrow Donor Day goes a long way in donor retention. The family plays a significant role in the decision-making for a donor to go ahead with the donation. Another critical challenge is contacting registered donors, especially when they change their email addresses or phone numbers. Offering counseling services, sharing video content, and interacting with Donor support groups significantly help overcome these challenges.

Making people aware, increasing Donor Database, retaining it, and, most important, addressing prevailing myths and employing tailored strategies are the key to success.

SESSION 13 –
ORAL PRESENTATION 3

OPTIMISING OUTCOMES FOR CHILDREN UNDERGOING HAPLOIDENTICAL HSCT FOR THALASSEMIA MAJOR WITH HLA ANTIBODIES

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Abstract ID: 126
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Topic: Hemoglobinopathies, primary immune deficiency disease and metabolic disorders
Keywords: nothing

INTRODUCTION

Haploidentical hematopoietic stem cell transplantation (HSCT) provides an alternate donor source for children with thalassemia major without a HLA matched sibling, family or unrelated donor. The major challenge is an increased incidence of graft rejection especially in developing children where HLA alloimmunization is common as there is no universal leukodepletion. Recent advances in desensitization strategies have resulted in improved thalassemia free survival (TFS).

AIM OF THE STUDY

To compare TFS between children undergoing haploidentical HSCT with HLA with and without panel reactive antibodies.

PATIENTS AND METHODS

We performed a retrospective study at our center between January 2016 and December 2022 and included all children who underwent T cell repleted haploidentical HSCT for transfusion dependent thalassemia major. Panel reactive antibodies were tested using the single antigen bead assay (SABA) test and they were considered donor specific and significant if they were above 1500 MFI as per EBMT guidelines. All children had two cycles of pre transfusion immunosuppression (PTIS) with fludarabine and dexamethasone with intensive chelation with deferoxamine for six weeks. All patients received conditioning with Rabbit antithymocyte globulin (r-ATG), thiotepa, treosulfan, fludarabine and 2 Gy total body radiotherapy and peripheral blood stem cells (PBSC) from the donor and post-transplant cyclophosphamide (PTCY) at 50mg/kg on day 3 and 4. Children who had HLA antibodies received double volume plasma exchange and one dose of rituximab at the start of conditioning therapy. We collected data on patient demographics, engraftment, chimerism, viral reactivation, graft versus host disease, mortality and thalassemia free survival.

RESULTS

A total of 60 children underwent haploidentical HSCT with PTCY and the comparative

outcomes are depicted on Table 1

PARAMETER	PRA POSITIVE	PRA NEGATIVE
TOTAL NUMBER	27	33
DONOR SPECIFIC ANIBOIDES	3/27 (11%)	NA
MFI RANGE	1200 TO 19000	NA
MALE: FEMALE	1:1.7	1:1.2
MEDIAN AGE AT HSCT	10 YEARS	8 YEARS
ENGRAFTMENT	24 (88%)	30 (90%)
GRAFT REJECTION	3 (11%)	8 (24%)
MIXED CHIMERISM	5 (20%)	4 (18%)
ACUTE GVHD	4 (16%)	7 (23%)
CHRONIC GVHD	9 (37%)	4 (13%)
VIRAL REACTIVATION	18 (66%)	21 (13%)
MORTALITY	3 (11%)	3 (9%)
TFS	21 (77%)	22 (66%)

CONCLUSION

Our data confirms that HLA antibodies in children with transfusion dependent beta thalassemia are common and this is no longer a barrier to haploidentical HSCT. Effective desensitization combination strategy with plasma exchange and rituximab results in 77% thalassemia free survival with no graft rejection even in the three children with donor specific antibodies. Our day 100 mortality stands at 10% due to regimen related toxicity and we need to augment our supportive care strategies. This study offers renewed hope to this high risk cohort with no access to other curative options.

Efficacy and Safety of Total Body Irradiation-based versus Busulfan-based Myeloablative Conditioining (TBI-MAC vs BU-MAC) for Hematopoietic Stem Cell Transplantation in Acute Leukemia Patients – A Systematic Review and Meta-Analysis

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Event: 28th Annual Meeting of APBMT
Topic: Conditioning Regimens
Keywords: acute leukemia, busulfan, conditioning regimens, hematopoietic stem cell, total body irradiation

Acute leukemia, the most prevalent form of blood cancer, necessitates comprehensive treatment strategies to enhance survival outcomes. Despite advancements in hematopoietic stem cell transplantation (HSCT), concerns persist regarding nonrelapse mortality and relapse incidence. To optimize disease control and promote engraftment, myeloablative conditioning (MAC) is employed. However, the optimal MAC for acute leukemia patients undergoing HSCT remains uncertain. Therefore, this meta-analysis aims to critically compare the efficacy and safety of total body irradiation (TBI)-based and busulfan (BU)-based conditioning regimens (TBI-MAC vs BU-MAC) before HSCT in acute leukemia patients. A systematic search was conducted through MEDLINE, EMBASE, Web of Science, ScienceDirect, and Scopus using appropriate keywords and Boolean operators up to June 2023. The primary outcomes assessed were overall survival (OS) and leukemia-free survival (LFS), while secondary endpoints included nonrelapse mortality (NRM), relapse incidence (RI), and graft versus host disease (GVHD) incidence to assess its safety. Relative risk ratios (RR) with 95% confidence interval (CI) were calculated for each outcome using Review Manager 5.4 in a dichotomous Mantel-Haenszel analysis. This study was registered in PROSPERO and adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 guidelines. Out of 4298 potential studies, eight studies involving 3603 patients with acute leukemia were ultimately included in the analysis. The result showed that overall survival and leukemia-free survival outcome between BU-MAC and TBI-MAC did not differ significantly (RR=0.99 [0.95-1.03] P=0.51 and RR=1.07 [0.97-1.18] P=0.17), respectively. However, nonrelapse mortality was significantly higher in TBI-MAC intervention (RR=1.44 [1.18-1.77] P=0.0004), while the use of BU-MAC trended to a significantly higher relapse incidence (RR=0.68 [0.54-0.87] P=0.002). Additionally, acute GVHD grade II-IV and III-IV and chronic GVHD incidence did not differ significantly between the two groups (RR=0.99 (0.81-1.20) p=0.89). To our knowledge, this study is the first meta-analysis comparing the efficacy and safety of TBI-MAC and BU-MAC in acute leukemia patients undergoing HSCT in CR1 and CR2. Although both regimens are comparable in overall- and leukemia-free survival, the choice between the two should be

based on the patient’s age, disease stage, previous treatments, overall health status, survival benefit, and the availability of donors. TBI-based conditioning is more favorable for younger patients and higher-risk diseases, while busulfan-based conditioning is more suitable for patients with pre-existing comorbidities and extensive prior chemotherapy and radiation. Further prospective trials are required to validate these findings and optimize the selection of myeloablative conditioning for specific patient populations.

Inferior outcomes with Melphalan based conditioning compared to Busulfan with Fludarabine in children undergoing HSCT

by Suresh R Duraisamy,Kavitha Ganesan, Satishkumar Meena,Anupama,Vijayashree, Venkateswaran VS, Ramya Uppuluri, Indira Jayakumar, Vidya, Revathi Raj | APOLLO CANCER CENTRE,CHENNAI

Abstract ID: 127
Event: 28th Annual Meeting of APBMT
Topic: Conditioning Regimens
Keywords: nothing

Introduction

The efficacy of a reduced toxicity regimen (RTC) with Fludarabine and Melphalan compared to a Myeloablative regimen (MAC) with Fludarabine and Busulfan has not been studied extensively in children. We performed a retrospective analysis of the outcomes of the first transplantation in patients who had underwent an allogeneic HSCT after RTC or MAC at our centre over the last ten years with specific emphasis on chimerism after HSCT.

Methods

Our study analysed the outcome of children under 18 years between December 2015 to December 2021 who underwent allogeneic HSCT following a RTC with Fluadarabine 40 mg /m2 for 4 days and Melphalan 140 mg/m2 for 1 day or a MAC regimen with Fluadarabine 40 mg/m2 for 4 days with intravenous Busulphan at a dose of 4.8 mg/kg/day in above two years and 3.2 mg/kg/day in children less than 2 years old. We did not perform Busulfan pharmacokinetics. Data collected included demographics and the indications for HSCT. We documented mixed chimerism or graft rejection as an event at Day 100 and 1 year and complete chimerism as event free survival. We also recorded data on overall survival and the cause of mortality. The study was approved by Institutional Ethics Committee.

Results. We analysed data on 85 children aged between 2 months and 17 years with 59 (69%) male and 26 (31%) females. The indication for HSCT was a malignancy in 50 (58%) and a non- malignant disorder in 35(42%) children. We used Melphalan based RTC in 31 (36%) and Busulfan based MAC in 54 (64%). The EFS and OS did not differ based on malignant or non- malignant indication, age less than 3 years or over 3 years or the sex of the child. The EFS on Day 100 was 48.4% in the RTC group versus 72.2% in the MAC group and this was statistically significant (p 0.025). The EFS at one year was also superior in the MAC group at 77.8% versus 45.2% in the RTC group (p 0.003). The overall survival was similar in both groups at 45.2% in the RTC group and 37% in the MAC group and this was not statistically significant (p 0.30). Relapse or rejection was the main cause of mortality 10/34 (31%) in the RTC group and 11/54 (20%) in the MAC group.

Conclusions. The results suggest that the Melphalan based RTC regimen is an inferior conditioning strategy for children as the there is a higher incidence of mixed chimerism and the need for donor lymphocyte infusions and post-transplant graft manipulation. Our cohort did not receive targeted busulfan with fludarabine and hence the reduced EFS in this group. Busulfan with pharmacokinetics with fludarabine is the most effective option for children undergoing MAC conditioning HSCT.

Conditioning Regimen Predicts Survival Outcome in Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Acute Myeloid Leukaemia (AML): Fludarabine- Melphalan is the Right Choice

by Rajat Pincha | Arijit Nag | Debranjani Chattopadhyay | Dibakar Podder | Rizwan Javed | Amrita Gope | Reena Nair | Mammen Chandy | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Dept of Clinical Hematology and Cellular therapies, Tata Medical Center, Kolkata | Former Director,Tata Medical Center, Kolkata

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Event: 28th Annual Meeting of APBMT
Topic: Conditioning Regimens
Keywords: AML, CONDITIONING REGIMEN, FLUDARABINE-MELPHALAN, HSCT, RELAPSE

AIM: To assess the outcomes of Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) in Acute Myeloid Leukaemia (AML) patients using different condition regimen. The objective was to determine the survival outcomes including relapse free survival (RFS), overall survival (OS), cumulative incidence of relapse (CIR) and factors influencing RFS and OS.

Methods: Total 366 allogeneic Stem cell transplants were performed between January 2011 to July 2022 at our centre. Of these 117 allogeneic HSCT for AML were analysed in the present study. Categorical and continuous variables were presented as counts (with respective percentages) and median (with range) values, respectively. Kaplan-Meier product-limit-estimate was used to calculate OS and RFS. Logistic regression model was used to predict the prognostic significance of the conditioning regimen. A multivariate analysis using cox regression method was done using the following variables to predict impact on RFS and OS. The variables included in the multivariate analysis were- age (as continuous variable), disease risk Index (DRI), remission status, conditioning regimen, transplant type: matched vs haploidentical, CD 34 cell dose (as continuous variable), grade 2-4 acute GVHD. For the statistical analyses $p < 0.05$ was considered significant.

Results:

A total of 117 transplants were performed whose baseline characteristics are presented in Table 1A. All patients received peripheral blood stem cell as graft source. 25 patients received Fludarabine-Treosulfan (Flu-Treo) based conditioning regimen, 18 received Fludarabine-Melphalan (Flu-Mel) conditioning, while 57 patients received Fludarabine - Busulfan (Flu-Bu) conditioning and the remaining (n= 17) received other conditioning

regimens. Thirty one percent of the patients were not in remission at the time of transplantation. The median follow up of the entire cohort was 336 days (range: 6-3713). The median RFS was 192 days (95% CI: 113- 270) in the Flu- Treo cohort, 366 days(95% CI: 173-1749) in the Flu-Bu cohort, however it was not reached in the Flu-Mel cohort (p= 0.018%). Fludarabine-Melphalan had a significantly better OS than the other conditioning regimens . [median OS- 366 days: entire cohort; 206 days: Flu-Treo; Not reached: Flu-Mel, 492 days: Flu-Bu and 260 days: others, respectively (p= 0.025)] (Fig 1A & 1B). In multivariate analysis incorporating the above mentioned variables, only conditioning type was statistically significant for RFS (p=0.03) and there was trend towards better survival for OS (p=0.059).

Conclusion: Flu-Mel conditioning is independently associated with the best survival outcomes with the least relapse rates in patients undergoing allogeneic HSCT in AML.

*No conflict of interest to disclose.

Impact of donor chimerism monitoring following allogeneic stem cell transplantation : Single-centre experience in Malaysia

by Mohd Yazid Zamri | Bee Ping Chong | Gan Gin Gin | Shasha Khairullah | Cheong Chin Sum | Liong Chee Chiat | Edmund Chin Fui Min | Universiti Malaya | Universiti Malaya | Universiti Malaya | Universiti Malaya | Universiti Malaya | Universiti Malaya | Universiti Malaya

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Topic: Leukemia
Keywords: acute GVHD, chimerism, relapse

Background: Chimerism analysis determines success of an allogeneic stem cell transplantation (AHSCT) by measuring the relative amount of donor stem cell and residual recipient’s stem cell. The target is to achieve full donor chimerism after AHSCT in haematological cancers as it is predictive of lower risk of relapse. Chimerism analysis is usually clinically useful if it is monitored over time rather than one time point. However, this investigation may not be freely available in certain transplant centres in particular in the low to middle income nations, either due to cost or expertise. Therefore, this study aims to determine the relationship of the different time-point of chimerism monitoring with its impact on AHSCT outcome such as relapse, graft versus host disease (GVHD) in adult AHSCT recipients.

Methodology: All adult patients who underwent AHSCT for underlying haematological cancers at Universiti Malaya Medical Centre from December 2008 until December 2022 were reviewed. Recipients with minimum one chimerism result were included and those without any chimerism result were excluded. Patient's outcome such as incidence of acute GVHD, relapse and mortality were collected.Patients were followed up for a minimum 6 months. Acute GVHD was defined according to standard criterion following European Society for Blood and Marrow Transplantation. In this study, acute GVHD is categorized into 2 groups, acute GVHD grade 1 and below, and grade 2 to 4. In our centre, chimerism was done using short tandem repeat polymerase chain reaction at time point of day 30,60,90 and 120. For this study, the chimerism status was grouped into less than 96% and 96-100%. Log rank pairwise comparisons were run to determine relationship between chimerism status with relapse and acute GVHD.

Result : A total of 101 AHSCT recipients were included in this study with the median age of 38 years. Majority of the patients had underlying acute myeloid leukemia (63.4%) followed by acute lymphoblastic leukemia (22%). More than two third (72.3%) were matched sibling donor AHSCT while 22.8% were haploidentical donor AHSCT. 71.3% had grade 2 and above GVHD.

Chimerism status was observed at day 30, 60, 90 and 120 post AHSCT. There was a

significant association of chimerism results with disease recurrence at day 60 ($p < 0.001$), day 90 ($p = 0.001$) and day 120 ($p = 0.028$). There was no significant association of chimerism status with acute GVHD.

Table 2 showed chimerism status at the different time points. Almost all had more than one time point monitoring and only 10% had one chimerism result.

Conclusion: Chimerism status at day 60 to 120 predict disease recurrence .In centre with limited resources, day 60 chimerism monitoring may be most useful time point. However, prospective study is needed to confirm this especially the sample size in this study is small and is retrospective in nature.

A RETROSPECTIVE ANALYSIS OF BK VIRUS HEMORRHAGIC CYSTITIS AFTER ALLOGENIC HEMOPOIETIC CELL TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

by Deepika Gupta | Priyanka Moule | Chetan Aggarwal | Nitin Gupta | Clinical Hematology, Sir Ganga Ram Hospital, New Delhi, India | Clinical Hematology, Sir Ganga Ram Hospital, New Delhi, India | Clinical Hematology, Sir Ganga Ram Hospital, New Delhi, India | Clinical Hematology, Sir Ganga Ram Hospital, New Delhi, India

Abstract ID: 48
Event: 28th Annual Meeting of APBMT
Topic: Leukemia
Keywords: BK virus, Cidofovir, hemorrhagic cystitis

Background: BK virus (BKV) hemorrhagic cystitis (HC) continues to be a serious cause of morbidity and mortality which complicates 5-40% of allogenic hemopoietic cell transplants. Low dose cidofovir has shown efficacy in the management of BK virus hemorrhagic cystitis. There is lack of data about the occurrence and management of BKVHC specially from developing countries.

Methods: Retrospective review of adult patients who underwent allogenic transplants at Sir Ganga Ram Hospital was done and data of patients with symptomatic BK virus hemorrhagic cystitis was analysed from 2017 to 2022.

Results: A total of 50 patients underwent allogenic transplants during this period. Six patients 6/50 (12%) patients developed symptomatic HC. Transplant characteristics and HC treatment outcome are as mentioned in table 1. Mobilized peripheral blood hemopoietic cells were the graft source in all patients. Hemorrhagic cystitis presented with severe dysuria, urinary frequency and hematuria requiring urinary catheterization. Continuous blood irrigation and analgesia with tramadol or morphine was received by all. Five out of six patients were on increased immunosuppression for GVHD. In none of the patients, BK virus was detected in blood. Cidofovir was given as a loading dose of 2 mg/kg then 1 mg/kg weekly as an IV infusion over1 hour without probenecid. In all except one patient, intravesical Cidofovir 1mg/kg was instilled in bladder by the CBI catheter weekly till the catheter lasted. In all patients there was rapid decline in urine BK virus load and symptoms of hemorrhagic cystitis. None of them developed renal toxicity. One patient died due to pneumocystis jiroveci pneumonia as he was on intensive immunosuppression with multiple drugs for refractory acute gut GVHD.

Discussion: We found HC in 12% of our allogenic stem cell transplant patients. It was more common in patient who had received myeloablative conditioning regimen and in patients with active GVHD who were on intense immunosuppression. Out of six patients, five were treated successfully and one succumbed to infection. Ganguly et al used low dose cidofovir

for the treatment of BK virus hemorrhagic cystitis and 13/18 (72%) patients responded without significant side effects. Our experience is also consistent with the above study with rapid resolution of symptoms of HC and viruria.

Conclusion: High clinical suspicion should be kept in patients who present with severe dysuria post allogenic transplant and urine sample should be sent for BK virus testing. Early administration of intravenous and intravesical Cidofovir is required for successful management of this severely troublesome condition.

Retrospective Analysis of Allogeneic Transplants in Lymphoma from 2013 to 2022 ; An Experience from Tertiary Care Centre, India

by Sundar, Shewale1, Rajat Pincha[1], Ashwini Naraynkar[1], Dibakar Poddar[1], Debranjani Chattopadhyay[1], Arijit Nag[1], Rizwan Javed[1], Saurabh Bhave[1], Jeevan Kumar[1], Asish Rath[2], Sushant Vinarkar[2], Deepak Mishra[2], Mammen Chandy[1], Reena Nair[1]. | DrNB Clinical Hematolgy & BMT resident physician

Abstract ID: 110
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: Allogeneic hematopoietic cell transplantation, graft-versus-leukemia effect, lymphoma, relapse, survival outcomes., treatment-related mortality

Introduction: The prognosis for lymphoma patients who have relapsed after autologous hematopoietic cell transplantation (HCT) or have become refractory to multiple lines of therapy remains poor. Allogeneic HCT offers the potential for a Graft versus Leukemia effect, which may provide a therapeutic benefit in such cases.

Aim & objective

This retrospective study aimed to evaluate the response and survival outcomes of lymphoma patients who underwent allogeneic HCT.

Material and Methods

We conducted a retrospective analysis of patients who underwent allogeneic HCT between August 2013 and December 2022. Variables such as age, gender, number of previous chemotherapy regimens, disease status prior to allo HCT, conditioning regimen type (myeloablative vs reduced-intensity), median days to neutrophils & platelet engraftement, graft-versus-host disease (GVHD), treatment-related mortality (TRM), disease progression, and overall outcome were documented. Survival curves were analyzed using SPSS software.

Results

Among 133 lymphoma bone marrow transplants; 26 patients underwent Allogenic HCT while 107 undergone autoHCT during August 2013 to December 2022.

Out of Allo HCT cohort, 17 were Non Hodgkin lymphoma and 9 were Hodgkin lymphoma. Within this group 18 underwent haplo match while 6 were full(10/10) match related and 2 full match unrelated HCTs.

The median age was 31 years (range 12-59), with predominance of male (57%). A total 13 events (50%) were recorded with 12 deaths(46%) and 1 case with progression which further underwent 2nd allogeneic transplant.

Median follow up of 45 months was noted in surviving patients

Patients aged <20 years were 6, 21-40 years were 11, and 41-60 years were 9.

Patients had undergone median 3 lines of chemoimmunotherapies (1-5) prior to Allo HCT. Eight patients had underwent 1-2 chemoimmunotherpies while 18 had >3 lines.

Among prior lines of therapies 5 patient were progressed after auto HCT while one was progressed after Allo HCT.

Prior to Allo HCT, 19 patients were in complete remission, and 7 were in partial remission/stable disease.

The median time to neutrophil engraftment was 18 days(9-35 days), while median platelet engraftment occurred at 21 days(8-36 days).

GVHD was observed in 46% (12/26) of patients at D+100. Among them, 8 patients had Grade >3 GVHD and 4 had Grade 1-2 GVHD. Treatment related mortality(TRM) was recorded in 46% patients (12/26) and 1 case showed disease progression after 11 months. The most common cause of death was bacterial neutropenic sepsis, accounting for 83% (10 out of 12 cases), followed by fungal sepsis, which accounted for 16% (2 out of 12 cases). Median overall survival was 46% while median progression free survival was 42%.

Conclusion:

Allo HCT has high treatment related mortality.(TRM). TRM in our cohort was high in 41 to 60 years age group. But this is curative option for patients who relapsed after multiple lines of chemoimmunotherapy and auto HCT.

5-hydroxy-1,4-naphthoquinone Alleviates Acute Graft-versus-host disease Without Compromising Graft-versus-leukaemia Activity via Modulation of Immune responses in Mice

by Dievya Gohil | Vikram Gotal | Advanced Centre for Treatment Research and Education in Cancer, Navi Mumbai, Maharashtra, India and Homi Bhabha National Institute, BARC, Mumbai, Maharashtra, India | Advanced Centre for Treatment Research and Education in Cancer, Navi Mumbai, Maharashtra, India

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Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: Juglone, cellular redox, graft-versus-host disease, graft-versus-leukaemia, immunomodulation

AIM: Acute graft versus host disease (GVHD) is a major cause of non-relapse mortality after allogenic hematopoietic stem cell transplantation (allo-HSCT). Current prophylactic regimens show limited success in clinics and are associated with severe toxicities, development of steroid refractory GVHD, increased incidence of infections and relapse. Further, it is now well established that immunosuppression is not the best strategy for GVHD prophylaxis. Thus, developing novel strategies/ pharmacological agents that can modulate donor immune response in favor of anti-tumor immunity while suppressing allogeneic immune response is an unmet need in the field of allo-HSCT. Juglone or 5-hydroxy-1,4-naphthoquinone, a redox active phytochemical found in walnuts, has shown potent anti-inflammatory effects in various disease models like colitis and inflammatory bowel disease. However, its effect on T-cell mediated adaptive immune responses is largely unknown.

METHODS: In the present study, we have evaluated the prophylactic efficacy of oral administration of 5NQ using a murine model of allo-HSCT based on MHC-I mismatch.

RESULTS: We observed that treatment with 5NQ inhibits mitogen induced activation, proliferation and cytokine secretion of murine lymphocytes. Additionally, 5NQ treatment inhibited upregulation of MHC-II following mitogenic stimulation on dendritic cells in vitro and in vivo. Furthermore, treatment with 5NQ resulted in increased expression of CD95 (Fas) and CD152 (CTLA4) on activated CD4 T cells in vitro and in vivo causing them to become anergic and exhausted. Oral administration of 5NQ to mice transplanted with allogenic cells led to a decrease in the number of CD4 and CD8 naïve T-cells and increase in CD4 and CD8 central memory T-cells. Anti-tumor activity of donor graft was studied in vitro and in vivo using A20 and EL4 syngeneic murine leukemia cells. Treatment with 5NQ preserved the anti-tumor activity of the graft while alleviating GVHD. Mechanistic studies revealed that 5NQ upregulated expression of the Nrf-2/HO1 antioxidant response signaling in these cells by modulating cellular redox status.

CONCLUSION: Our study demonstrated that the GVHD prophylactic effect of 5NQ is because of its ability to modulate inflammatory innate and adaptive immune responses.

No conflict of interest to disclose

A RETROSPECTIVE COMPARISON OF THE TRANSPLANTS DONE FOR THALASSEMIA MAJOR -FINDING A DONOR FOR ALL!

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Abstract ID: 157
Event: 28th Annual Meeting of APBMT
Topic: Pediatric Transplantation
Keywords: Haploidentcal TCR alpha beta depleted CD45 RA depleted transplant, T Cell replete Haploidentical transplants, Thalassemia major

INTRODUCTION: Allogeneic hematopoietic stem-cell transplantation (HSCT) remains the key curative treatment option for Thalassemia. An HLA-matched donor has traditionally been the donor of choice in HSCT. Unfortunately, it is sometimes challenging to identify HLA-matched donors, and so the donor pool has been expanded to include "alternative" donors such as haploidentical parents or siblings and even mismatched unrelated donors.

AIMS: This was a retrospective single-centre analysis of the pediatric transplants done at our centre to compare matched family donors, Matched unrelated donors (MUD), and haploidentical transplants. We looked at the median Average Length of stay(ALOS), 100-day mortality, the incidence of GVHD, and 1-year survival in our cohort of patients transplanted between August 2018 and April 2023 for Thalassemia major.

RESULTS: A total of 41 transplants were done in this period for thalassemia major. Demographics, the median ALOS, median CD34 dose, days to neutrophil and platelet recovery, and survival at 100 days, 6 months, and 1 year are shown in Table 1. A myeloablative conditioning regimen was used in all patients.

Of the matched family donors (15 MSD and 2 MRD), all children engrafted but one child died on Day 39 post-transplant due to acute RSV infection. Only 2 children developed acute graft versus host disease(GVHD) (Skin) Grade 2 which responded to steroids.

4 children underwent a MUD transplant- one had primary graft failure, one died of acute respiratory distress syndrome associated with engraftment syndrome; the other 2 are doing

well.

The T cell replete group was the worst affected- 4 were haploidentical T cell replete with PTCy and 2 were 1 antigen mismatched matched sibling donors treated with PTCy regimen. One child had a poor graft function and succumbed to Dengue at Day +137; 2nd succumbed to MRSA (Day +180) and the 3rd child died due to pulmonary haemorrhage on Day +69. These children had not achieved platelet engraftment either. Acute GVHD was seen in 2 children and one child went on to develop chronic GVHD gut and then succumbed to toxic epidermolysis and Gram-negative sepsis at Day +400 post-transplant.

Of the 14 TCR alpha beta-depleted CD45 RA-depleted haploidentical transplants, all engrafted and were alive at 100 days. The acute GVHD was Grade 1-2 in 4 children only and responded well to steroids. There was only one mortality at 8 months in a child who had a secondary rejection following late CMV infection and later developed a fungal infection of the brain.

CONCLUSIONS: The outcomes of TCR alpha beta depleted CD45 RA depleted haploidentical transplants are comparable to Matched family donors in our cohort with faster engraftment, a shorter length of stay in the hospital, and good survival at 1-year post-transplant. T Cell replete transplants tend to have more complications post-transplant and a poorer outcome. While MSD continue to be the standard of care, we believe that haploidentical TCR alpha beta depleted CD45RA depleted transplants should be offered to those that do not find a match.

NURSE MEET
in Session 2

A study to assess perceived stressors and coping strategies adopted by post HSCT patients in selected hospital India.

by Mr .Bhushan Ramdas Shelar | Advanced center for treatment research & education in cancer ,Tata Memorial Center ,Maharashtra ,Navi-Mumbai

Abstract ID: 28
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Stressors, coping strategies, fear of relapse.

To find out types of different stressors on post HSCT patients.

Method

Survey method was undertaken in tertiary care cancer center on 30 patients. Who discharged from the unit and were willing to be part of study were given a semi structured questioner .Data was analyzed using descriptive and informational statistics.

Result

30 patients completed the survey majority 77% were male and mean age of patients was 36.26 years . Most 63 % were employed but only 27% had income above Rs 40000 per month. Around 63% of patients had undergone allogenic transplant. The complication experienced by patients was mucositis (97%), diarrhea (60%) and around (33%) had GVHD and neutropenic sepsis. VOD was diagnosed in (7%) of patients .In physical stressors (83%) patients experienced fatigue other stressors included pain and anorexia (77%) and (70%) had nausea and vomiting ,fullness of abdomen . In psychological stressors fear of disease relapse (83%), guilt due to dependency on other (73%). In social stressors lack of family support (50%) and social isolation (57%) .Financial stressors experienced by (73%) while (70%)experienced spirituality stressors . The coping strategies adopted was taking rest(60%),taking prescribed medication in time (70%), taking plenty of oral fluid (83%) ,pray to god by (70%) ,adhere to medical regime (100%).Most (82%) of patients also mentioned that they participate in selfcare activities and try to connect with friends and family members through social media .Financial issues were overcome by financial trust was (82%) .Fear of treatment outcome was significant in patients with ALL (p-0.019). Patients with neutropenic sepsis had higher incidence of skin problrm (p-0.05) and constipation (p-0.001). Female experienced dryness of mouth (p-0.002).patients felt discontinue the treatment is higher in GVHD complication (0.009)

Conclusion

Most common perceived stressors among post-transplant patients is fatigue and fear of

disease relapse .Nurses need to plan their activity and ensure adequate comfort and rest is achieved .Fear of disease relapse has positive impact with all patients adhere to medical regime counselling (multidisciplinary approach) will help in decreasing fear ,anxiety.

No conflict of interest to disclose.

The Successful Treatment of Severe Oral and Nasal Ulcer with Barkin Yufu Ointment on a Relapsed AML Patient Before Secondary HSCT

by xiaoxia wang | yongqiang zhao | fang fang | zhenghong hu | dandan song | xiaoteng liu | dongfang yang | feng zhang | tong wu | fengying chen | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital | Beijiing boren hospital

Abstract ID: 19
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Oral and Nasal Ulcer, Relapsed AML, Secondary HSCT

Aims: To summarize the sincere cooperation between doctors, nurses, and patients, and to share the experience of using Buck Jade Skin Lotion, Skin Code, and Jinyufu Cream in combination to cure a patient with severe oral and nasal ulcers who relapses after AML HSCT and plans to undergo secondary transplantation

Methods: The patient, female, AML, had neutrophils as low as 0.36 and platelets as low as 4 after chemotherapy in February 2023; Ulcers, bleeding, old blood scabs blocking the nasal cavity and inability to breathe through the nose appear in the mouth and nose; Mouth breathing leads to dry mouth, blood scab formed on lips, four grade ulcer in the mouth, bleeding in the upper jaw and two molars, serious bleeding every morning, swollen gums, pain of 7 points, inability to eat, affecting drinking water and high fever. The treatment and nursing plan is as follows: after basic care, a small amount of jade skin solution is used to clear the scab on the blood scab area, the affected area is sprayed with skin code, oxygen is blown dry, thick layers of Jinyufu ointment gauze are applied, the oral cavity is occluded, the nasal cavity is gently inserted with gauze into the middle nasal passage, 8 layers of sterile gauze are covered on the outside of the mouth and nose, and adhesive is fixed to observe the patient's feelings and local conditions at any time. Change dressing twice a day. After eating and drinking water midway, reapply Jinyufu ointment to maintain moist healing therapy.

Results: On February 17th, during the dressing change, Jin Yufu ointment was effective in stopping bleeding in the mouth and nose for 2 minutes, reducing the patient's pain. In the afternoon of the dressing change, 90% of the blood scabs on the lip and right nasal cavity had fallen off, and the right nasal cavity was ventilated; The next day, 50% of the blood scab on the left nose fell off and was partially ventilated; On February 19th, both nasal cavities were ventilated, and the pain score decreased to 5 points. Solid food could be consumed,

and the body temperature dropped to normal; Afterwards, the ulcer area gradually decreased significantly and healed quickly; On February 20th, parenteral nutrition infusion was stopped. On February 23rd, the mouth and nose were basically healed, with 0 points of pain. Normal breathing and eating were allowed. After the doctor's evaluation, arrange for radiation therapy to enter the warehouse for secondary transplantation.

Conclusions: The patient's AML has undergone allogeneic transplantation, relapsed, and experienced a decline in the tertiary system during further consolidation chemotherapy, leading to common complications such as bleeding, ulcers, and infections in hematological patients. Medical care only takes 7 days to complete the repair, helping patients stop bleeding, nutrition, antibiotics and other medications as soon as possible, reducing blood transfusion volume, shortening the course of the disease, and alleviating patients' pain and economic burden.

Long-term outcome of children undergoing hematopoietic stem cell transplantation for inborn errors of immunity: a twenty-year follow-up study from India

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Abstract ID: 113
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: HSCT, IEI, Karnofsky score, Psychosocial aspects

Background

Hematopoietic stem cell transplantation (HSCT) is the only available curative option for children with inborn errors of immunity (IEI) in low-and-middle income countries. There is paucity of data on long-term outcomes following HSCT and the quality of life. We present our data of twenty-year follow-up in children with IEI post HSCT and the implications of sequelae on quality of life.

Patients and methods

We conducted our study at the Department of Pediatric BMT Nursing and included children up to 18 years of age who underwent HSCT for IEI from January 2002 to December 2021. We used a telephonic questionnaire and interviewed the parents using the proxy Kiddy Kindl ^{R} and assessed the six dimensions*: physical wellbeing, emotional wellbeing, self-esteem, family, friends,* and *everyday functioning* to produce *a total score of 100.* We also recorded data on active infections, current height and weight and puberty changes as per Tanner in children above 10 years and current medications. We applied the Karnofsky score for assessing activities of daily living.

Results

One hundred seventy-two children underwent HSCT for IEI from 2002 to December 2021, with 108 (62%) alive at the last follow-up. We obtained responses from 65(60%) of these children. Six children were less than three years of age at follow-up and did not start schooling but had normal developmental milestones with no sequelae. Of the 59 children above three, 56 (94%) attended full-time school.

Twelve children (18%) had sequelae including seizure disorder in 2, bronchiectasis and

recurrent respiratory infections in 1, surgery for post-infective scarring around the alae nasi in 1, mastoidectomy for CSOM in 1, colostomy closure in 1, sequelae due to prior TB meningitis in 2 and thyroid supplementation and having delayed growth in 4 children with height less than 3rd centile who had received prolonged steroids.

The median Karnofsky score was 90 to 100 in 96% of the children. The parent reported total HRQoL score was 74.8 as per the KINDL questionnaire with good scores in the physical and psychosocial domains.

Conclusion

Our study reports optimal quality of life and development, including schooling, in over 95% of children undergoing HSCT for IEIs. All residual sequelae were related to infections before HSCT in 18% of children. We conclude that early HSCT before organ involvement is the key to decreasing morbidity and improving quality of life. We plan to conduct a study comparing the HRQoL between parent and patient reported domains in children between 6 and 16 years to obtain more insights into the psychosocial aspects in our population.

POSTER SESSION

Chimeric Antigen Receptor T cell (CAR-T) therapy for relapsed childhood Acute Lymphoblastic Leukaemia (ALL) in Indonesia

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Event: 28th Annual Meeting of APBMT
Topic: Leukemia
Keywords: Acute Lymphoblastic Leukemia, Chimeric Antigen Receptor T cell

Background

ALL is the commonest childhood cancer which is curable but survival remains sub-optimal in developing countries. This is due to both relapse and treatment related mortality (TRM). There is difficulty in achieving the optimal balance between under and over-treatment, which is compounded by the challenges of inadequate manpower and infrastructure, high therapy abandonment, limited access to risk stratification tools and under-developed stem cell transplant (SCT) services.

CAR-T is potentially a leapfrog technology in Indonesia:

- CAR-T is an easy to administer single-dose therapy, thus avoiding prolonged treatment with current treatment protocol. This is attractive wherever oncology resources are limited and concentrated in major cities.
- CAR-T is a relatively low-cost therapy, possibly even lower than chemotherapy. The cost of CAR-T was only USD45,000 per patient treated in Indonesia.
- CAR-T is highly effective with remission rates of ~80%. The longest observed patient survival to date is 10 years.
- CAR-T is also safe with minimal TRM. It is certainly safer than SCT and likely safer than prolonged chemotherapy in this setting too.

We report here our experience with the first introduction of CAR-T to treat relapsed ALL in Indonesia.

Methods

This is an observational cohort study to evaluate the outcome of relapsed ALL among children and young adult who had received re-induction chemotherapy followed by CAR-T as consolidation. Between October 2017 and December 2019, we had treated 6 patients with relapsed ALL. 13 children who were referred failed to make it to treatment and had subsequently died because of relapse or TRM, or they were unable to raise the financing.

Results

The mean age of the 6 patients treated was 14 (range 6 to 24), all scored ECOG 1 or 2, one had prior allo-SCT, 2 had CNS leukemia. All patients had received a standard course of re-induction therapy, and had failed to achieve remission prior to CAR-T infusion. The mean dose of CAR-T infused was $2.1x10^6$ cells/Kg body weight (range 1 to 4.3). All patients were discharged no later than day-3 post infusion, except 2 who had Cytokine Release syndrome, which was treated with Tocilizumab. No patients had neurotoxicity.

Three patients had achieved complete remission, 2 however had relapsed within 12 months post infusion while one had remained in remission (57 months to date). One patient with relapsed CNS leukemia had failed to achieve remission, another 2 patients had treatment failure possibly related to inadequate cells shipment.

Conclusion

Our observation with the limited data to date attests to the administrative simplicity and safety of CAR-T. The efficacy of CAR-T, especially its ability to achieve long term durable remission in this setting, was demonstrable in one patient. However there remains huge challenges in providing CAR-T therapy in Indonesia. Early preparation of patients for CAR-T soon after relapse before they succumb to relapse or TRM is critical. There were also issues related to shipping cells across borders between Indonesia and the production lab, the obvious solution is to localize production in Indonesia.

Pretransplant and Posttransplant Minimal Residual Disease in CBF-AML: Implications for Allo-HSCT Outcomes

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Topic: Leukemia
Keywords: Minimal residual disease, core-binding factor acute myeloid leukemia, quantitative polymerase chain reaction

Aims

Minimal residual disease (MRD) detection is commonly used for assessing disease status. Pretransplant and posttransplant MRD detection is crucial for risk stratification and

decision making after allogeneic hematopoietic stem cell transplantation (HSCT). Polymerase chain reaction (PCR) -based MRD detection is commonly used in clinical settings for core-binding factor acute myeloid leukemia (CBF-AML), but the interpretation of MRD results in the context of HSCT remains under discussion.

Methods

Using Kyoto Stem Cell Transplantation Group registry data, we included 96 patients who underwent their first HSCT between 2000 and 2019 for AML with inversion 16 (inv16) or AML with t(8;21). Primary endpoint was overall survival (OS), and secondary endpoints was relapse free survival (RFS). Threshold for MRD positivity was 50 copy/μgRNA for quantitative polymerase chain reaction (qPCR) with GAPDH control and 3 log reduction for qPCR with ABL control. The threshold for post-transplant MRD was defined by the point maximizing sensitivity and specificity (Liu, 2012). In multivariate analysis, disease status at HSCT, patient age (50 years or older), conditioning intensity, donor source and performance status are considered as covariates.

Results

To assess pretransplant MRD, qPCR with GAPDH control was the most frequently used method (n=66), followed by nested PCR (n=18), qPCR with ABL control (n=8), and conventional PCR (n=4). Of the patients assessed by qPCR with GAPDH control, the median age of the patients at transplantation was 39 years, with an interquartile range (IQR) of 28-53. Among the patients, 20 had AML with inv(16), and 46 had AML with t(8;21). A total of 39 patients received HSCT in their first complete remission (CR), 20 patients underwent transplantation after their second or after CR and 7 patients received HSCT in non-CR.

In patients with hematological CR whose MRD was quantified by qPCR with GAPDH control, the MRD-negative group (n=25) exhibited favorable OS (91.8%) and RFS (87.4%) at 2 years, compared to the MRD-positive group (n=31) with OS (61.6%) and RFS (59.6%) (hazard ratio [HR]: OS-3.78, 95% confidence interval [CI]: 1.07-13.34; RFS-2.61, 95% CI: 0.83-8.16).

In patients with pretransplant hematological CR, those with lower maximum post-transplant MRD values (<=350 copy/μgRNA) during the half-year posttransplantation period (group 2, n=12) showed comparable OS (81.5%, HR 0.64, 95% CI 0.14-3.02) and RFS (72.9%, HR 0.86, 95% CI 0.23-3.25) to MRD-negative patients during the half-year posttransplantation period (group 1, n=32). In contrast, patients with higher maximum post-transplant MRD values (>350 copy/μgRNA) during the half-year posttransplantation period (group 3, n=13) had significantly lower OS (22.2%, HR 4.92, 95% CI 1.54-15.72) and RFS (12.5%, HR 7.58, 95% CI 2.32-24.71). Median days until the discontinuation of immunomodulatory agents used for graft-versus-host disease prophylaxis were 716.3 in group 1, 603.0 in group 2, and 214.5 in group 3, respectively.

Conclusions

Our study highlights the significance of pretransplant MRD assessment, especially using qPCR with GAPDH as an internal control. The interpretation of posttransplant MRD positivity should be approached with caution, particularly in cases of low-level positivity, as it may diminish over time. These findings can aid in the decision-making process for CBF-AML patients after HSCT.

Allogeneic Hematopoietic Stem Cell Transplantation in Elderly Patients with Hematological Malignancies: Comparison of Different Conditioning Regimens

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Event: 28th Annual Meeting of APBMT

Topic: Leukemia

Keywords: allogeneic hematopoietic stem cell transplantation, conditioning, elderly, hematological malignancy

Introduction: The prognosis of elderly patients with hematological malignancies by chemotherapy is poor. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has remarkably improved long-term survival in this setting.

Aim: In present study, the outcomes of allo-HSCT in elderly patients with hematological malignancies by reduced-intensity conditioning (RIC) or myeloablative conditioning (MAC) are investigated. The risk factors for prognosis post-HSCT are also analyzed.

Methods: Between May 2019 and March 2023, 38 patients over 55 years with hematological malignancies who underwent allo-HSCT were enrolled. The median age was 62 (55-72) years. The diagnosis included myelodysplastic syndrome (n=10), acute myeloid leukemia (AML, n=15), acute lymphoblastic leukemia (n=10), chronic myelomonocytic leukemia (n=2) and diffuse large B-cell lymphoma (n=1). The disease status pre-transplant was complete remission (CR) in 20 (52.6%) cases and non-remission (NR) in 18 (47.4%) cases. The types of transplants included haploidentical (60.5%), unrelated (21.1%) and identical siblings (18.4%). Either RIC (n=13, 34.2%) or MAC (n=25, 65.8%) regimens was applied. For RIC cohort, the regimen with total body irradiation (TBI, 6-7Gy, fractionated), fludarabine (30mg/m^2, 5 days) and cytarabine (1g/m^2, 3 days) was used. For MAC cohort, the regimen with TBI (8-10Gy, fractionated, n=8)/total marrow irradiation (10-12Gy, fractionated, n=2) or busulfan (0.8mg/kg q6h, 3 days, n=15), fludarabine (30mg/m^2, 5 days) and cytarabine (1g/m^2, 3 days) was used. Antithymocyte globulin was used in unrelated and haploidentical transplants. Cyclosporine, mycophenolate mofetil and short-term methotrexate were employed for GVHD prophylaxis.

Results: Thirty-five of 38 patients achieved full donor chimerism because 3 patients with AML (minimal residual disease positive in 1, NR in 2 pre-transplant) had active disease at their first disease evaluation post-HSCT. The median time to neutrophil and platelet recovery was 14.5 (8-22) days, 13(8-27) days respectively. With a median follow-up of 10.6 (1.6-47.7) months, 1-year overall survival (OS) and disease-free survival (DFS) rates were 61.8%, 60.6% respectively. Nine (23.7%) patients relapsed and 14 (36.8%) patients died. The causes of death included graft-versus-host disease (GVHD, n=2), infections (n=5) and disease progress (n=7). Transplant-related mortality (TRM) was 18.4%. There was a trend of lower TRM (20% vs. 44.4%) and higher relapse rate (30.7% vs. 20%) in RIC cohort compared with MAC cohort but without significant differences. Therefore, no remarkable differences were found in OS and DFS between two cohorts. However, the disease status pre-HSCT had remarkable impact on OS (44.4%vs.85%, p=0.004) and DFS (38.9%vs.85%, p=0.001) between NR and CR cohorts.

Conclusions: Under our protocol, OS and DFS have been improved remarkably by allo-HSCT in elderly patients with hematological malignancies. Although RIC regimen has resulted in lower TRM, but the relapse rate was higher compared with MAC regimen, which transplanted into similar survival between two cohorts. The disease status pre-transplant is a key factor for prognosis of allo-HSCT in elderly patients with hematological malignancies.

Haploidentical stem cell transplant : single centre experience in Malaysia

by Mohd Yazid Zamri | Universiti Malaya

Abstract ID: 142
Event: 28th Annual Meeting of APBMT
Topic: Leukemia
Keywords: GVHD, Haploidentical, relapse

Haploidentical haematopoeitic stem cell transplant (Haplo-SCT) has successfully expands the donor pool for many patients with haematological malignancies. Recent studies have demonstrated that survival is similar in patients who had haplo-SCT and matched sibling donor SCT. Due to the relative convenience of finding a suitable haplo-identical donor, there has been a significant increase in haplo-SCT being performed globally. This study aims to report on the outcome of haplo-SCT in a tertiary medical centre in Malaysia.

Methodology: This was a retrospective study conducted at a tertiary medical centre where all patients who had haplo-SCT were included. Patient's sociodemographic and clinical characteristic were reviewed. Transplant related complications such as graft versus host disease (GVHD) and survival status were described.

Results: A total of 23 patients who underwent haplo-SCT were analyzed. The median age was 34 years (range 19 to 64 years). More than half (56.5%) had underlying acute myeloid leukemia (AML). Table 1 showed the patient's characteristics. All patients except acute lymphoblastic leukemia (ALL) patients received Busulfan, Cyclophosphamide, Carmustine and Cytarabine conditioning chemotherapy. ALL patients had total body irradiation as part of conditioning regimen. All patients received anti-thymocyte globulin for in-vivo T cell depletion. None had post- transplantation cyclophosphamide. All stem cell sources were from marrow and peripheral blood. All patients received mycophenolate mofetil, ciclosporin and methotrexate as GVHD prophylaxis.

Almost all patients (21 patients, 91.3%) developed acute GVHD, of which only 33% had grade 3 and above. Chronic GVHD occurred in 13 patients (56%). At the time of this study, nine (39%) patients passed away. Infection was the most common cause of death (5 patients, 56%) while 22% were due to relapse and 11 % each from severe GVHD and graft failure.

Summary: The incidence of GVHD is similar to report elsewhere. Haplo-SCT is a feasible alternative transplantation option especially for patients who had no HLA-matched sibling.

Allogenic Stem Cell Transplantation In Chronic Myeloid Leukemia Patients- A Single Centre Experience From South India

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Abstract ID: 146
Event: 28th Annual Meeting of APBMT
Topic: Leukemia
Keywords: Blast Crisis, CML, GVHD, HaploHSCT, Relapse, TKI Intolerance

Aim:

The indication for transplant in Chronic Myeloid Leukemia patients in TKI era is limited. There is only limited data from resource constrained settings. We present our experience of HSCT in CML patients.

Methods:

Medical records of CML patients who underwent transplant at our centre between 2017 to 2022 were taken and descriptive statistical analysis was done.

Results:

Total of seven CML patients were included. All patients were male with median age of 37 years (31-39). Out of the Seven patients, five had blast crisis. One patient presented with denovo myeloid blast crisis was treated with Decitabine plus Venetoclax plus Dasatinib, whereas four patients had progression from chronic phase due to poor compliance. Three of them had myeloid blast crisis treated with 7+3 induction with Cytarabine + Daunorubicin along with TKI in two and only Decitabine plus dasatinib in one. One patient had lymphoid blast crisis treated with steroid plus vincristine plus dasatinib. One patient in chronic phase CML was intolerant to multiple TKIs. One patient in accelerated phase was resistant to multiple TKIs. TKD mutation analysis was not done in 2 patients, no mutations were detected in 3 patients, while 2 patients had mutations. Dasatinib and nilotinib were given in 4 and 3 patients respectively. All patients had morphological Complete Remission before HSCT. The patient with lymphoid blast crisis achieved molecular remission prior to transplant. The mean time to transplant after the diagnosis of blast crisis was 4.5 months (4-5 months). Matched Sibling Donor (MSD) transplant was done in 3 patients. Haploidentical transplant was done in 4 patients. Myeloablative conditioning was used in all patients. Peripheral blood mobilised stem cell was used in all. The median CD34+ stem cell dose was 8.28 x 10^6 cells/mm^3 (6.5-9.5 x 10^6). Neutrophil and platelet engraftment was observed at a median of 15 days (range: 10–24 days) and 15 days (range: 11–25 days)

respectively. PTCy was given on days +3 and +4 in HaploHSCT patients. Post HSCT TKI maintenance was given in all patients. Acute GVHD (liver) developed in two patients. They were treated with steroids ande etanercept. One of these two patients with acute liver GVHD succumbed. Chronic GVHD (limited skin) developed in four out of seven patients. One patient developed musculoskeletal chronic GVHD. One patient developed Pott's spine treated with AntiTuberculous therapy. One patient presented with CNS relapse on day 243, later had medullary relapse and succumbed to illness. Five patients survived with a median follow up duration of 18 months (10- 71 months).

Discussion & Conclusion:

Achievement of remission is critical for better survival outcomes in CML patients with Blast crisis. Outcome of these patients without HSCT is dismal. Both Matched Sibling Donor and Haploidentical HSCT results in improved survival outcomes in CML Blast crisis patients.

No conflict of interest to disclose.

Health-Related Quality of Life in Acute Leukemia Patients Receiving Hematopoietic Stem Cell Transplantation: A Systematic Review and Meta-Analysis

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Abstract ID: 205
Event: 28th Annual Meeting of APBMT
Topic: Leukemia
Keywords: Acute leukemia, health-related quality of life, hematopoietic stem cell transplantation

Acute leukemia, as the most prevalent pediatric cancer, requires fast-paced advancements in therapy. Hematopoietic stem cell transplantation (HSCT) is a life-saving yet intensive procedure associated with potentially severe adverse effects. This study evaluated the health-related quality of life (HRQoL) of acute leukemia patients undergoing HSCT compared to standardized therapy. Using relevant keywords, a systematic search was conducted using MEDLINE, Web of Science, and ScienceDirect up to June 2023. From 2052 potential studies, seven were finally included in the systematic review, and four were analyzed further in meta-analysis. The study was conducted according to the Preferred Reporting Items for Systematic and Meta-analyses (PRISMA) protocol and registered in PROSPERO. The outcomes measured were mean and standard deviation (SD) focusing on physical and emotional functioning, measured by SF-36. The outcomes were calculated in standardized mean difference (d) with a 95% confidence interval (CI) using Review Manager 5.4 in a dichotomous analysis. From 1605 patients comprised, this study revealed that patients receiving HSCT had a significantly worse physical functioning outcome (d=-0.37 [-0.63,-0.10] Z=2.73 (P= 0.006)) compared to chemotherapy treatments. However, there is no significant difference in emotional functioning between the groups (d= -0.12 [-0.27, 0.04] Z=1.48 (P=0.14). These findings can be attributed to suboptimal patient selection for HSCT, which was exclusively administered to individuals with a poor prognosis and late disease stage, neglecting the optimal time for HSCT administration. Therefore, although HRQoL is generally satisfactory in acute leukemia patients undergoing HSCT, its inferiority compared to conventional therapy must be assessed through the selection criteria of HSCT recipients and optimal timing for the administration. Further research in optimizing HSCT outcomes must also be conducted to enhance therapeutic benefits.

Outcomes of initial pediatric autologous HSCT at a tertiary care public centre in India: achieving comparable outcomes with adaptations

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Abstract ID: 9
Event: 28th Annual Meeting of APBMT
Topic: Pediatric Transplantation
Keywords: autologous HSCT, non positive pressure rooms, non-HEPA filter rooms

Background : Autologous hematopoietic stem cell transplant(HSCT) is a standard treatment for many solid-tumors. It is recommended that the patients undergoing autologous HSCT be cared for in a dedicated HSCT-unit with isolation-rooms having high-efficiency-particulate-air(HEPA) filters and positive-pressure. We report the outcomes of our first twenty pediatric patients , who underwent autologous-HSCT in isolation rooms that had no HEPA-filters and had no positive- pressure. The isolation rooms were not a part of a dedicated HSCT-unit.

Methods: The prospectively recorded data of patients was analysed retrospectively. All patients underwent autologous-HSCT after harvest and cryopreservation of the hematopoietic stem cells(HSC). All patients received myeloablative-conditioning.

Results: The commonest indications for the autologous-HSCT were high-risk neuroblastoma(HR-NB)(n=9) ,refractory/relapsed Hodgkin-lymphoma(HL)(n=6). The median CD-34 positive-HSC administered were4.5(0.8-21.9)million stem cells per-kg of recipient body weight. The median-time to neutrophil engraftment was 16.5(10-35)days and the median-time to platelet engraftment was 19(10-87)days. There was one transplant-related mortality(TRM) and the mean time to discharge from hospital was 27.6±8.3 days. The mean duration of follow up of the patients was 850days. The overall survival for all our patients was 75%. The overall survival for the HL patients was 85.7% and for the NB was 66.7%.

Conclusion :This study provides evidence that autologous-HSCT can be safely performed in non- HEPA filtered and non-positive pressure isolation rooms if expertise and good supportive care is available. In resource limited settings such a model could help in setting up low-cost HSCT units .

Pediatric allogeneic HSCT (including alternate donor HSCT) – a low cost model with acceptable outcomes

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Event: 28th Annual Meeting of APBMT
Topic: Pediatric Transplantation
Keywords: allogeneic HSCT, non-HEPA filter rooms, non-positive pressure rooms, pediatrics

Introduction

Recommendations state that patients undergoing allogeneic hematopoietic stem cell transplant (HSCT) be cared for in a dedicated HSCT unit with a minimum number of isolation rooms. The setting up of an HSCT unit in resource intensive and poses a significant financial burden.

Methods

We report the outcomes of the first twenty pediatric patients who underwent allogeneic HSCT , at our centre that had started its HSCT program . The HSCT was done in rooms that had no HEPA filters ,no positive pressure, no laminar flow of air and the rooms were not part of a HSCT unit.

Results

The median age of the patients at the time of HSCT was 6(1-20)y and that of the donor was 9.5(3-42)y. There were 18 males . In fifteen the indication for HSCT was an underlying malignant condition. Twelve patients were MSD HSCT , two were MUD and the rest were mismatched related donors/haploidentical donors.

The mean stem-cell dose transfused was 8.2$\pm$3.0 million CD 34+ cells per-kg. The neutrophil engraftment for 19 patients occurred at a mean of 17.0$\pm$8.07 days and the platelet engraftment for 18 patients at 18.8$\pm$10.1 days. The mean time to discharge after the infusion of the HSC for 18 patients was 30.9$\pm$10.04 days.

90 % of patients developed febrile neutropenia on follow up for which they required empiric antibiotic administration. In 6 instances there was blood culture positivity for an organism. In 2 cases evidence of fungal infection in the form of budding yeast cells in blood or a positive galactomannan were there. There were four cases of CMV reactivation, two patients with BK viremia and one case with parainfluenza pneumonia. In all cases except one the infections were successfully treated.

Six out of twenty patients had manifestations of acute GVHD. The acute GVHD was of grade I in one patient and it improved with topical steroid cream application, grade II in one and it required systemic steroids , grade IIa in three patients and they were treated with oral budesonide and grade III in one requiring steroids and ruxolitinib. Three patients with a follow up of more than one year were free of disease and have not had manifestations of chronic GVHD. One patient has had moderate chronic GVHD and in five the chronic GVHD has been severe. There were no mortalities within 30 days. Between day 30 and day 100 there were 3 deaths. One was due to relapse and progressive disease after cure post HSCT , one due to primary graft failure and in one due to multiple infections post HSCT. Beyond day +100 there were three mortalities, two due to relapse after cure post HSCT , and one due to SARS-COV2 infection.

Conclusions

The outcomes of our patients who had undergone allogeneis HSCT including alternate donor HSCT, in non positive pressure , non HEPA filtered rooms that were not a part of a HSCT unit were acceptable

The First Beta-Thalassemia Major Patient in Indonesia's First Pediatric Hematopoietic Stem Cell Transplantation Unit: A Case Report

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Topic: Pediatric Transplantation
Keywords: HSCT, case report, pediatric, thalassemia major

Introduction Currently, the mainstay treatment of pediatric beta-thalassemia major cases involves lifelong transfusion and chelation therapy. Recently, we established Indonesia's first official pediatric hematopoietic stem cell transplantation (HSCT) unit to decrease the disease burden in Indonesia. This case aims to report our unit's ongoing first case complicated with several findings based on the result of clinical and laboratory examination, who are currently in the screening phase. We also aim to briefly describe the establishment and status of pediatric HSCT unit in Indonesia.

Case Report A 10-years old girl was referred to our hospital for HSCT. The patient received monthly blood transfusion of two packed red cells with daily deferoxamine for iron chelation and have had a total of three liters of red blood transfused up until now. Currently, the patient and her parents reported no significant complaint. Physical examination found Cooley's facies, darkened skin, anemic conjunctiva, mildly icteric sclerae, and minimal hepatomegaly. HLA typing found that her younger brother, aged six years old, was perfectly matched with our patient. Data from additional examinations concluded that the patient is classified as Pesaro class 2. MRI testing found that the patient had mild cardiac hemosiderosis. On laboratory examination, both the donor and the recipient were found to have positive interferon gamma release assay (IGRA) result. Confirmatory examination of thoracal and abdominal computed tomography (CT) without contrast of the recipient revealed multiple mesenterial lymphadenopathy of the lower right quadrant of the abdomen. In addition, the recipient was also found to have mild hepatosplenomegaly, minimal free fluid in the pelvic cavity, thickening of urinary vesica with asymptomatic bacteriuria, high titer of *Salmonella typhii* IgM, partial clouding of maxillary sinus, and positive extended

beta-lactamase CTX-M *Klebsiella pneumoniae* on rectal swab. Since mesenterial biopsy was not possible, the recipient was prescribed with nine months of anti-tuberculosis (TB) therapy, in which the patient may proceed to HSCT after two months of anti-TB if follow-up examinations revealed acceptable improvements. In addition, she was also prescribed oral cefixime for ten days, oral cotrimoxazole for two weeks, and oral amoxicillin-clavulanic acid for five days. As for the donor, he was also found to have high titer of *Toxoplasma sp.* IgM and IgG with a history of frequent playing with street cats. For this, the donor was prescribed isoniazid for TB prophylaxis for three months and cotrimoxazole for two weeks.

Conclusion Presently, HSCT is one of the only definitive treatment of beta-thalassemia major in Indonesia. The presence of infections prior to HSCT may present as future complications after the procedure, hence requiring therapies before HSCT may proceed. The development of the first pediatric HSCT unit in Indonesia sheds a ray of hope for Indonesian children currently living with beta-thalassemia major.

Post-Transplantation Lymphoproliferative Disorder (PTLD) Following Pediatric Liver Transplantation: Case Reports

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Abstract ID: 118
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Topic: Pediatric Transplantation
Keywords: Liver transplantation, PTLD, treatment

Background: Post transplantation lymphoproliferative disorders (PTLDs) are a diverse group of potentially life-threatening conditions that affect solid organ and hematopoietic cell transplant recipients and commonly related to Epstein-Barr virus (EBV) infection. However, development of PTLD in EBV negative patients is not uncommon. Treatment approach consists of reduction of immunosuppression, chemotherapy, rituximab, adoptive immunotherapy, and antiviral. While the incidence of PTLD remains unknown in Indonesia especially in the pediatric population, it is important to understand this condition as it may lead to poor prognosis.

Aim: to describe two PTLD cases following pediatric liver transplantation in Cipto Mangunkusumo Hospital.

Case 1: A five-year-old girl received a living donor liver transplantation (LDLT) for biliary atresia at 11 months old, with her mother as the donor. The donor had reactive anti CMV IgG and anti-EBV VCA IgG. Immunosuppressants methylprednisolone and tacrolimus were administered. After three years, elevated liver enzymes led to a biopsy showing early chronic rejection and stage F2 fibrosis. Mycophenolate mofetil (MMF) was added. Five months later, a palpable mass appeared in the upper abdomen. Doppler ultrasound indicated an allograft liver with enlarged lymph nodes, suggesting a post transplant lymphoproliferative disorder (PTLD). The CT-scan showed lymphadenopathies causing vein stenosis. A tumor biopsy indicated non-Hodgkin Lymphoma, consistent with monomorphic PTLD (M-PTLD), B-cell, plasmablastic lymphoma subtypes with negative CD20 and positive EBER ISH. Positive EBV was also found in blood, bone marrow, and pleura. Immunosuppressant was reduced, antiviral treatment given, and chemotherapy (R-CHOP protocol followed by methotrexate) were initiated. The response to chemotherapy was poor. Unfortunately, the patient died after multiple organ dysfunction due to severe sepsis and tumor lysis syndrome.

Case 2: A six-year-old girl who underwent LDLT at the age of nine months has been experiencing complaints of frequent choking, sore throat, and hoarseness for the past month before admission. She was taking tacrolimus and methylprednisolone. The laryngoscopy revealed epiglottis, adenoid and severe diffuse laryngeal oedema.

Tonsillectomy and adenoidectomy were performed, and histopathology results showed lymphoid hyperplasia suggesting a non-destructive PTLD. It was positive for CD20 and negative for EBER ISH. Due to impending airway obstruction, tracheostomy was performed. Ganciclovir was administered, and immunosuppressants were reduced. We initiated Rituximab treatment for three weeks, but the response was poor, so we continued with the R-CHOP protocol. Three cycles were completed with a partial response. Our plan is to continue up to a minimum of six cycles.

Conclusion: The management of post-transplant lymphoproliferative disorders (PTLDs) during long-term follow-up after solid organ transplantation is challenging. The mortality rate is high especially in cases unresponsive to chemotherapy. Although PTLD is rare, recognizing this disease as early as possible is crucial. A multidisciplinary approach is necessary to ensure comprehensive management.

DIABETES MELLITUS AFTER HEMATOPOEITIC STEM CELL TRANSPLANTATION IN CHILDREN WITH ALPHA THALASSEMIA : CASE REPORT

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Abstract ID: 120
Event: 28th Annual Meeting of APBMT
Topic: Pediatric Transplantation
Keywords: Diabetes mellitus, Hematopoietic stem cell transplantation, Thalassemia

Background:

Indonesia is located along the 'Thalassemia Belt" and a hotspot for hemoglobinopathies. Anemia of the most severe form of the disease, known as beta thalassemia major or transfusion dependent thalassemia is treated with lifelong red blood cell transfusion associated with chelation therapy in order to limit chronic complication dan premature death. Hematopoietic stem cell transplantation (HSCT) is curative treatment for beta thalassemia patient. Survivors of pediatric hematopoietic stem cell transplantation are known to be at risk developing endocrine abnormalities, but occurrence of diabetes mellitus (DM) is a relatively recent observation.

Aims: To describe a case diabetes mellitus condition after hematopoietic stem cell transplantation in children with Alpha thalassemia.

Case:

The patient was diagnosed with Alpha thalassemia at age of 2 month by DNA analysis examination (HbH with 2 deletion and 1 mutation). Patient born by ceasarean section in 34 weeks gestational age, 2100 gram with hemoglobin (Hb) level 10.1 g/dL, breathe spontaneously without oxygen supplementation. Her mother was reffered to fetomaternal in our hospital with fetal hydrops and received twice intrauterine transfusion. Since being diagnosed with Alpha Thalassemia at months, the patient routinely gets blood transfusion every 3-4 weeks with maintaining pretransfusion Hb levels above 9 g/dL until age 8 years.

When the patient was 8 years, haploidentical transplantation bone marrow, father donor was performed. After HSCT, several early complications occurred, mucositis, fever,

pneumonia, and acute respiratory failure and treat with mechanical ventilation (± 14 days).

The Hemoglobin level and platelet was still low and he still received transfusion every week until two years after HSCT.

Two years after undergoing HSCT, the patient's condition has decreased. He had hypertension, seizures, and increased intracranial pressure. Blood glucose became elevated dan diabetes mellitus was diagnosed. At that time, his pH status was with normal range and the patient had glycosuria without ketonuria. Initially, only short-acting insulin was given subcutaneously before meal. At that time, C-peptide was normal. It was impossible to assess antibodies associated with diabetes due to administered immunosuppressant drugs.

Currently, he is 13 years old and currently he is controlled regularly in Diabetic outpatient clinic and received short acting combination with long acting insulin. He is in a good general condition and continuous his education in a public school. He participates in physical exercises on a regular basis. Despite the correct fitting of insulin does, a tendency to labile blood glucose is still observed.

Conclusions

Survivors of pediatric HSCT are known to be at risk of developing endocrine abnormalities, but occurrence of DM is relatively recent observation. Diabetes mellitus after HSCT in this patient may have a multifactorial origin. Moreover, diabetes could be associated with GvHD and prolonged corticosteroid exposure. The possible multifactorial origin of DM after HSCT highlights that it is difficult to classify and treat this type of diabetes.

Blinatumomab prior HSCT in MRD-positive pediatric ALL patients

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Topic: Pediatric Transplantation
Keywords: BCP-ALL, Blinatumomab, HSCT

Aims:

Blinatumomab is a CD3/CD19-directed bispecific T-cell engaging antibody with efficacy in children with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (BCP-ALL). Aim of this study was to evaluate data of patients who were treated with blinatumomab as “bridge”- therapy prior to allogenous hematopoietic stem cell transplantation (HSCT).

Methods:

We retrospectively analyzed medical data of 33 pediatric patients aged from 4 to 17 with refractory or relapsed BCP-ALL who were treated with blinatumomab followed by HSCT in the single center. Eight patients had initially refractory course of BCP-ALL, 20 – were in 1^{st} relapse, 5 - in 2^{nd} relapse. Genetic aberrations were found in 7 cases (21%): CRFL2 in 3, KMT2A in 2 and PDGFRB and E2A in one case each respectively. All patients achieved morphological remission (<5% blasts in bone marrow) and had minimal residual disease (MRD) status measured by immunologic flow cytometry ≥ 10^{-3} before initiation of blinatumomab therapy. All children received one 28-day cycle of blinatumomab with further evaluation of response. Toxicity of treatment was evaluated according to CTCAE v5.0.

Results:

MRD-negative status after one cycle of blinatumomab was achieved in 30 (90%) cases. The progression of BCP-ALL after blinatumomab was seen in other 3 children, who successfully received alternative immunotherapy and achieved MRD negative status afterwards. Grade 3 toxicity (according to CTCAE) was observed in one case (severe Henoch–Schönlein purpura with skin, limbs and abdominal involvement). Three patients required tocilizumab administration due to refractory fever and transaminitis. No cases of severe neurological toxicity were detected. No course of blinatumomab was interrupted due to its side effects. All patients were transplanted in MRD negative status. In 29 cases - from haploidentical donors, in 3 cases - from matched siblings and in one case - from 9/10 matched unrelated

donor. Three patients had grade 3 graft versus host disease (GVHD). Thirty children survived. Three died (one - from GVHD, one - from primary non engraftment, one – from relapse). Three of 30 survived children relapsed after HSCT, but were successfully treated by blinatumomab and second HSCT from alternative donor.

Conclusions:

Blinatumomab is effective and well-tolerated therapy in pediatric BCP-ALL patients with MRD-positive status.

Conflict of interest

No conflict of interest to disclose.

Gastric Immunoglobulin Light Chain (AL) Amyloidosis-Associated Multiple Myeloma Presenting With Upper Gastrointestinal Bleeding: A Case Report

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Abstract ID: 25
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: Autologous Stem Cell Transplant, Gastric AL Amyloidosis, Multiple Myeloma

Rationale and Objectives Immunoglobulin light chain amyloidosis can be diagnosed with the presence of multiple myeloma, however, diagnosis may be delayed until organ-specific symptoms arise. Symptomatic amyloidosis of the gastrointestinal tract is rare. Studies showed that autologous stem cell transplant is an effective therapy for multiple myeloma-associated amyloidosis with improvement of organ function, quality of life, and survival.

Case Report A case of a 62 year old, male presenting with melena. Esophagogastroduodenoscopy (EGD) revealed multiple gastric ulcerating submucosal nodules. Gastric biopsy showed gastric antral-type mucosa with lambda- light chain restricted plasmacytosis and amyloid deposits, positive for congo red stain. Bone marrow aspiration and core bone biopsy showed atypical plasmacytosis compatible with plasma cell myeloma. Patient was treated with 6 cycles of bortezomib, cyclophosphamide, and dexamethasone (CyBorD regimen), with good response. However, persistence of monoclonal spike two months post-chemotherapy was noted. Patient then underwent high dose chemotherapy with Melphalan (200 mg/m^2) followed by autologous hematopoietic stem cell transplant. Three months post-transplant, he was started on lenalidomide. Repeat Esophagogastroduedenoscopy showed absence of submucosal nodules.

Discussion and Summary Patients with amyloidosis-associated multiple myeloma should be monitored closely since these two diseases may occur at the same time, and the presence of organ-specific complications identified. In our patient's case, he presented with gastrointestinal bleeding and subsequently treated with standard systemic chemotherapy with autologous stem cell transplant which resulted to better outcome.

No conflict of interest to disclose.

Autologous PBSCT for Second Relapse of Diffuse Large B-Cell non-Hodgkin Lymphoma

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Abstract ID: 35
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: Autologous Stem Cell Transplantation, Indonesia, Non-Hodgkin Lymphoma, Relapsed/Refractory

Introduction: Non-Hodgkin Lymphoma (NHL) is the seventh most common cancer in Indonesia.[1] In 2020, there were 16,059 new cases of NHL in Indonesia.[1] Chemotherapy remains the first-line therapy for aggressive lymphomas. However, 20–30% of patients with NHL will relapse after initial therapy.[2] Here, we present the case of relapsed diffuse large B-Cell (DLBC) NHL who underwent first autologous stem cells transplantation (ASCT) at Dharmais National Cancer Center Hospital.

Case Presentation: A 43-year-old man was diagnosed with diffuse DLBC NHL in 2017. He received the R-CHOP (Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone) chemotherapy for six cycles, achieving complete remission (CR) but then relapsed in 2019. He was then treated with second-line chemotherapy regiment, R-ICE (Rituximab, Ifosfamide, Carboplatin, and Etoposide), for four cycles resulting in CR again. The disease relapsed again in December 2022 when PET/CT examination revealed multiple enlarged lymph nodes entirely supradiaphragmatic with extra-nodal involvement at retropharyngeal. The rebiopsy was done and confirmed the relapse of DLBC NHL with germinal center B-like (GCB) subtype stage II-E (retropharyngeal). The patient was then planned to undergo ASCT and thus treated with salvage chemotherapy regimen, R-DHAP (Rituximab, Dexamethasone, Cytarabine, and Carboplatin) for three cycles. Following the third cycle, peripheral blood stem cells (PBSC) were mobilized and cryopreserved. Evaluation by PET/CT imaging revealed a complete metabolic response (CMR). In May 2023, the patient underwent conditioning chemotherapy with BEAM (Carmustine, Cytarabine, Etoposide, and Melphalan) regimen, followed by ASCT. A total of 8.42 x 10^6 /kg

bodyweight CD34+ PBSC were administered on Day 0 dan Day+1. Neutropenic fever happened on Day+8 but then subsided after administration of antibiotics. Engraftment was achieved on Day+13 and the patient was sent home the day after. Routine blood examination after one month of transplantation indicated full hematopoietic reconstitution with WBC 7.63 x 10^3/µL, HGB 11.8 g/dL, and PLT 256 x 10^3/µL. Adjuvant radiotherapy for the extra-nodal (retropharyngeal) involvement was planned afterward. The first post-ASCT evaluation will be done on Day+120.

Discussion: High-dose chemotherapy and ASCT have been the standard treatment for relapsed/refractory high-grade NHL. Five-year overall survival (OS) for B-cell NHL undergoing ASCT was 60%.[3] Commencing ASCT in Indonesia is so much different from the western countries due to multiple factors such as social factors, lack of drugs or facilities, and high cost involved playing a significant role. Lots of Indonesian patients must go to neighboring countries to get this service. With special effort to overcome the obstacles, we show that Dharmais Hospital as Indonesian NCC can serve a safe and high quality ASCT service for R/R DLBC NHL patient aligning with the international standards. The patient's disease-free period will be measured and reported periodically. The financial aspect continues to be the biggest challenge since ASCT is still not fully covered by many private medical insurances or even the National Health Insurance in Indonesia.

Conclusion: Implementing a safe and high quality ASCT in Indonesia is achievable. The financial aspect is the biggest challenge to overcome.

No conflict of interest disclosed.

Autologous Stem Cell Transplant in Relapsed Refractory Classical Hodgkin Lymphoma: A systematic review

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Keywords: autologous stem cell transplant, classical Hodgkin Lymphoma, refractory relapse

Aims

This systematic review aims to analyze the available literature on Autologous Stem Cell Transplant (ASCT) in classical Hodgkin Lymphoma (cHL), including its efficacy, safety, predictors of outcomes, and the role of salvage therapies.

Methods:

A comprehensive search of electronic databases which includes PubMed central/MedLine (PMC), SCOPUS, and EMBASE via OVID was conducted to identify relevant studies. Inclusion criteria were applied to select studies that examined ASCT in cHL. Data extraction and critical appraisal were performed on the included studies. Evaluation quality of studies were conducted by 3 independent reviewers. Newcastle Ottawa scale were used for cohort studies and JADAD scale were used for randomized controlled trial (RCT).

Results:

A total of 13 studies were included. The sample sizes ranged from 50 to 500 patients. ASCT was consistently associated with high response rates, with complete remission (CR) achieved in the majority of patients. ASCT was particularly beneficial in patients with high-risk features, such as relapsed or refractory disease and bulky tumors. However, the

occurrence of treatment-related adverse events, such as infection and organ toxicity, was not negligible, emphasizing the importance of appropriate patient selection and supportive care. The Progression free survival (PFS) and Overall survival (OS) after ASCT were ranged from 62-79% and 71-89%, respectively, at five years. Salvage regimens, disease status at ASCT, mobilization strategies, specific high-dose chemotherapy regimens, and post-transplantation approaches all play important roles in determining outcomes. Quality assessment of included studies were moderate to good.

Conclusions:

ASCT remains a standard of care treatment for relapsed or refractory cHL after frontline chemotherapy. Further studies were needed to evaluated the role of ASCT compared to CAR-T cell therapy and combination with Antibody Drug Conjugate (ADC) for initial or maintenance therapy.

"No Conflict of interests to disclose".

Nutritional Therapy in Autologous PBSCT for Second Relapse of Diffuse Large B-Cell non-Hodgkin Lymphoma

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Abstract ID: 47
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Topic: Lymphoma/Myeloma
Keywords: Autologous Stem Cell Transplantation, Energy. Protein, Indonesia, Non-Hodgkin Lymphoma, Nutritional Therapy

Introduction

Non-Hodgkin's lymphoma (NHL) is a prevalent form of hematological cancer, accounting for 3% of cancer cases and deaths worldwide.[1] A significant proportion of patients (20-30%) experience relapse after initial therapy, and the standard approach is salvage chemotherapy followed by high dose chemotherapy (BEAM) and autologous hematopoietic stem cell transplant (HSCT).[2] Patients undergoing HSCT are at risk of malnutrition, which is associated with poor clinical outcome, decreased OS, higher risk of infectious and immunologic complications, delayed neutrophil engraftment, and prolonged hospital stay.[3] Here, we present nutritional therapy in the case of relapsed diffuse large B-Cell (DLBC) NHL who underwent first autologous stem cells transplantation (ASCT) at Dharmais National Cancer Center Hospital.

Case Illustration

A 43-year-old man was consulted from haematology and medical oncology division with relapsed DLBCL NHL stage II E (retropharyngeal) undergoing ASCT. He was already in mild malnutrition state because of inadequate food intake (as a result of gum problem, causing the decrease of his ability to chew) and 3% decrease in body weight. Laboratory results showed hyperbilirubinemia, leukopenia, thrombocytopenia, hypokalaemia, hypomagnesemia and hyponatremia. Initial nutritional therapy was started with oral and parenteral nutrition, adapted to patient’s situation to fulfil the energy (40 kcal/kg body weight) and protein (1.5 g/kg body weight) requirements. Before ASCT, the patient received 29 – 36 kcal/kgBW of energy and 1.3 – 1.5 gram/kgBW of protein accompanied with educational therapy of nutrition, resulting in the increase of his body weight to 3.4 kg in 3 weeks. During ASCT, he received 36 – 53 kcal/kgBW of energy and 1.4 – 2.1 gram/kgBW of protein orally. The patient experienced the side effects of conditioning chemotherapy (such as dry mouth, febrile neutropenia, bloating, and diarrhea), which led to a lower appetite and the decrease of his body weight (3 kg in a course of 9 days). The patient was finally discharged on D+14 after achieving engraftment status.

Discussion

This case highlights the crucial role of nutritional therapy include educational therapy particularly in terms of protein and energy intake, before ASCT, during BEAM conditioning chemotherapy and ASCT. Moreover, the underlying disease and chemotherapy after-effects can potentially deteriorate the patient's nutritional status. Due to hypercatabolic status, energy requirements may increase in HSCT patients, which corresponds to 30 – 50 kcal/kg BW/day. Protein requirements ranging from 1,4 to 1,5 g/kg BW/day, and may reach up to 2 g/kg BW/day.[4] The patient in this case report was able to fulfil energy and protein requirement with the support from multi-disciplinary teamwork in Dharmais Cancer Hospital and his family.

Conclusion

Patients undergoing ASCT are often at nutritional risk or already malnourished due to their underlying disease, pre-transplantation chemotherapy administration, and ASCT treatment-related toxicity. Improving the nutritional status of ASCT patients by managing each of these particular complications with appropriate nutritional approach is essential for successful engraftment.

Outcomes of Autologous Hematopoietic Stem Cell Transplantation Among Adult Patients with B-cell and T-cell Lymphoma in St. Luke's Medical Center

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Topic: Lymphoma/Myeloma
Keywords: Autologous Hematopoietic Stem Cell Transplantation, Hodgkin lymphoma, Non-Hodgkin Lymphoma

Background

Hodgkin and Non-Hodgkin lymphomas were treatable hematologic malignancy. Autologous stem cell transplantation (ASCT) is the recommended therapy for primary progressive or relapsed lymphomas. This study is to describe the clinical profile, progression-free survival, and 1-year and 3-year overall survival of adult patients with B-cell and T-cell Lymphomas after autologous stem cell transplant.

Methods

This is retrospective and descriptive study of all patients 18 years and older diagnosed with B-cell and T-cell lymphoma who underwent autologous hematopoietic stem cell transplant in St. Luke's Medical Center – Quezon City and Global City, between January 1, 2002 – December 31, 2020.

Results

A total of 23 patients with B-cell and T-cell Lymphomas were included in this study, 16 with Hodgkin's and 7 with non-Hodgkin's. The median age was 29 years old with male dominance. Ki 67 was assayed immunohistochemically in the tissue samples, and the median Ki 67 was high at 80%. The median Ki 67 was higher in NHL group (90 % vs 40%), which shows a poor prognosis. There was no detected double or triple hit expressor by FISH or IHC. The presence of B symptoms was seen in 69.57% patients, and it was more common in the NHL group (85.71% vs 62.5%). In staging of lymphoma, many patients were under Ann-Arbor Classification IV 47.83% and 30.43% had IPI score of 4. Many had Lugano Response score of 3 (47.83%) and 4 (39.13%). RCHOP was used by all 7 patients in the NHL group while RICE was used by 71.43% patients in the same group. Brentuximab and

ABVD were used by 25% and 100% patients respectively, in the HL group. Majority had pre-HSCT radiotherapy (60.87%), and it was more used by the HL group (62.50% vs 57.14%). A relapse pre-HSCT was seen in all patients of both groups.

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During the transplant regimen, chemotherapy as a conditioning regimen was used by all patients in both groups while a few had radiotherapy. The source of stem cells used by all patients were peripheral blood stem cell.

The recurrence-free survival at 1 year is 69% overall, and 73% for HL and 63% for NHL patients. At three years, this decreases to 55% overall; 50% for HL and 63% for NHL patients. For overall survival, it is at 91%; 100% for HL and 67% for NHL patients at 1 year; and 79% at three years; 80% for HL and 67% for NHL.

Conclusion

The overall recurrence-free survival at 1 year, and 3 years, of HL and NHL lymphoma patients who underwent autologous hematopoietic stem cell transplantation at St. Luke's Medical Center – Quezon City and Global City are 69% and 55%, respectively. The overall survival at 1 year, and 3 years, of HL and NHL lymphoma patients are 91% and 79%, respectively.

No conflict of interest to disclose.

Tandem vs. Single Autologous Hematopoietic Stem Cell Transplant in Relapsed/Refractory Hodgkin Lymphoma: a Systematic Review

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Keywords: autologous, hematopoetic stem cell, lymphoma, systematic review

Introduction

Hodgkin Lymphoma (HL) is a lymphatic system tumor distinguished by the presence of Reed-Sternberg cells. While therapy breakthroughs have resulted in better results, a percentage of patients develop relapse or refractory disease, necessitating novel therapeutic methods. Hematopoietic Stem Cell Transplantation (HSCT) has emerged as an important therapy option for such patients, with the possibility for long-term remissions. Among the emerging techniques, the use of tandem HSCT, which involves two consecutive transplants, has received attention due to its potential to improve therapeutic efficacy. The purpose of this systematic review is to examine and compare the outcomes between tandem and single autologous HSCT for relapsed/refractory Hodgkin Lymphoma patients.

Method

A systematic and literature search based on PRISMA 2020 will be conducted across electronic databases such as Google Scholar, PubMed, MEDLINE, Embase, and ProQuest until August 4, 2023, reported in any language that compared tandem with autologous HSCT in patients with relapsed/refractory Hodgkin lymphoma. The search will encompass articles published from inception to the present, using a combination of Medical Subject Headings (MeSH) terms and keywords related to "Hodgkin Lymphoma," "hematopoietic stem cell transplant," and "tandem transplant." The outcomes of the study were to compare efficacy, evaluate disease control, analyze risk-adapted approaches, assess adverse effects, and examine secondary failures.

Results

A total of 3 studies were included in this study. Tandem autologous HSCT showed potential for poor-risk cases. Intermediate-risk patients benefited from single autologous HSCT. Tandem autologous HSCT reduced second failures. Overall, tandem autologous HSCT

displayed efficacy in poor-risk patients, while single autologous HSCT suited intermediate-risk patients, underlining the significance of risk-adapted strategies. The observed reduction in second failures associated with tandem autologous HSCT highlights a potential advantage of this approach in mitigating disease relapse. By targeting residual disease more aggressively through sequential transplantation, tandem HSCT may contribute to improved long-term disease control, particularly in patients at higher risk of relapse. It was noted that tandem transplantation appeared to be associated with a higher incidence of certain adverse events, including graft-versus-host disease (GVHD) and treatment-related mortality.

Conclusion

Tandem transplantation might be more appropriate for certain subsets of patients with specific high risk factors, such as high disease burden or unfavorable genetic profiles, whereas single autologous HSCT could be a viable option for patients with lower risk profiles in patients with relapsed/refractory Hodgkin Lymphoma.

Maintenance therapy after autologous BMT in MM

by Mehrdad Payandeh | Kums

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Topic: Lymphoma/Myeloma
Keywords: MM, lenalidomid, thalidomide

After autologous BMT in MM. cases we treated them with anti angiogenesis drug in two groups , first groups (35) with thalidomide for 10 years , second groups (35) for 5 years during last years .
in our analysis no differences between two group in relapse and PFS.
Most toxicity in thalidomide been peripheral neuropathy.

in lenalidomide group most toxicity been neutropenia.

in conclusion , maintaining in importance for prolonged the OS and PFS in our payient.

Brentuximab combined with oral alkylating drugs after relapsing in autologous HD

by Mehrdad Payandeh | Kums

Abstract ID: 88
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: HD, brentuximab, chlorambucil, procarbazin

We presented 10 cases of HD that after autologous BMT , after 12 months relapsed and after low dose chemotherapy with Gemara and oxaliplatin for three months we decided treated them in follow with combination of chlroambucil and procarbazine and brentuximab , after 18 months 7 of them Been stable and free of complained

in conclusion metronomic therapy after BMT can prolong life in relapse HD cases

Autologous Hematopoietic Stem Cell Transplant in Relapsed Hodgkin’s Lymphoma in the Philippines : A Retrospective Single-Center Case Series and Review of the Literature

by Pia Maeven M. Edejer MD | Sofia Dominique D. Unson MD | Francisco Vicente F. Lopez MD | Jose Roberto G. Amparo MD | St. Luke’s Medical Center - Global City, Department of Medicine | St. Luke’s Medical Center - Global City, Institute of Oncology | St. Luke’s Medical Center - Global City, Blood and Marrow Transplant and Section of Medical Oncology | St. Luke’s Medical Center - Global City, Institute of Oncology

Abstract ID: 107
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Topic: Lymphoma/Myeloma
Keywords: Autologous HSCT, HSCT, Hodgkins, Immunotherapy, Lymphoma

BACKGROUND

Hodgkin's lymphoma (HL) is a hematological malignancy that is often curable with initial chemotherapies. However, for patients who relapse to frontline treatment, the standard of care involves salvage chemotherapy followed by autologous hematopoietic stem cell transplantation (HSCT). While this approach can be effective, a subset of patients experience disease progression after autologous HSCT or are unable to undergo the procedure due to various medical reasons. In this case series, we present the clinical outcomes of patients with relapsed HL.

OBJECTIVES

We aim to present a single-center study and retrospective evaluation of the outcomes of patients with Relapsed Hodgkin’s Lymphoma who underwent Autologous HSCT and compared our results with literature.

METHODS

We retrospectively analyzed institutional data of 17 patients with Relapsed Hodgkin’s Lymphoma who underwent high-dose chemotherapy followed by Autologous HSCT between May 2012 to February 2023 in St Luke’s Medical Center Global City. Pre-transplant, post-transplant treatment and outcomes were all recorded.

RESULTS

In a retrospective study spanning ten years and nine months, we documented seventeen cases of relapsed Hodgkin's Lymphoma. All patients underwent high-dose chemotherapy followed by Autologous Hematopoietic Stem Cell Transplant. The patient cohort consisted of ten (58%) males and seven (41%) females, with a median age of 26.4 (range 18 to 47) years old. The majority of patients (88%) received Doxorubicin, Bleomycin, Vinblastine, Dacarbazine (ABVD regimen) as their initial treatment, with an average of 6.07 cycles. Patients remained in remission for an average of 15.5 (range 4 to 37) months before experiencing relapse, leading them to necessary salvage chemotherapy and HSCT.

Before HSCT, patients received high-dose salvage chemotherapies, with Carmustine, Etoposide, Cytarabine and Melphalan (BEAM) being the most common (73%). All seventeen patients underwent Autologous HSCT, with a median engraftment time of 10.5 days.

Post-transplant, five patients relapsed after HSCT and were given Pembrolizumab (1 of 5), Brentuximab vedotin (2 of 5) and Brentuximab vedotin followed by Pembrolizumab (2 of 5) as salvage therapy, wherein four obtained complete remission. One patient required salvage chemotherapy and obtained a complete remission and proceeded to an allogeneic HSCT with his twin brother as donor. Four patients received Brentuximab vedotin as maintenance therapy.

These therapies contributed to the improved outcome of the study, with 15 patients achieving complete remission and only two patients succumbing to death from relapse disease.

SUMMARY/CONCLUSION

Overall, our research indicates that the use of high-dose chemotherapy followed by Autologous HSCT is an important treatment option for relapsed lymphoma. However, our study also highlights the growing role of novel therapies such as Brentuximab vedotin and Pembrolizumab in improving survival outcomes, especially in Hodgkin Lymphoma as salvage therapy post transplant or maintenance treatment.

Tailoring of maintenance therapy in multiple myeloma based on Measurable residual diseases (MRD) by multiparametric flow cytometry (MFC) post induction and autologous stem cell transplant: A pilot study

by Dr.Priyanka Moule | Dr.Sabina Langer | Dr.Deepika Gupta | Dr.Chetan Agarwal | Dr.Amrita Saraf | Dr.Pallavi Prakhar | Dr.Jyoti Kotwal | Dr.Nitin Gupta | Department of hematology and BMT, Sir Gangaram Hospital, New Delhi | Department of hematology, Sir Gangaram Hospital, New Delhi | Department of hematology and BMT, Sir Gangaram Hospital, New Delhi | Department of hematology and BMT, Sir Gangaram Hospital, New Delhi | Department of hematology, Sir Gangaram Hospital, New Delhi | drjyotikotwal@gmail.com | drjyotikotwal@gmail.com | Department of hematology and BMT, Sir Gangaram Hospital, New Delhi

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Keywords: MRD, Maintenace therapy, Multiparametric flowyctometry, Multiple myeloma

Introduction :
Assessment of measurable residual disease (MRD) in bone marrow is of prognostic relevance in patients with multiple myeloma (MM) and MRD negativity showed improvement in progression-free survival (PFS) and long-term survival (OS). However, the use of MRD results to make clinical decisions in the maintenance therapy of myeloma is under evaluation.

Aims & Objectives:
1. To study the MRD with multiple parametric flow cytometry (MFC) in myeloma patients post autologous stem cell transplant and its effect on disease relapse.
2. Feasibility of deciding about consolidation vs maintenance therapy based upon MRD results.

Materials & Methods:
Prospective study of patients with multiple myeloma who underwent transplant at our centre from Jan 2021 to Dec 2022. Ten patients were to be enrolled. Patients were monitored with SPEP, IFE and SFLC and MRD by multiparametric flow cytometry (MFC) on Day+100 of ASCT. MFC was done on EDTA bone marrow (BM) samples using standard lab protocol for the Stain-Lyse-Wash technique on 12 colours, 3 laser flow cytometer BD FACSLyric. The antibody panel used included CD45, CD138, CD38, CD19, CD117, CD28, CD27, CD319, CD81 and CD56 and cytoplasmic kappa and lambda. (BD Biosciences, San Jose, CA). Forward and side scatter, CD38/CD138, CD45/CD38 and CD319/CD138 to gate plasma cells were used. A minimum of 2.5 million events were acquired. The limit of detection was 10^-5. Patients who were MRD-negative were given lenalidomide maintenance while MRD-positive patients received consolidation chemotherapy similar to their pre-transplant induction chemotherapy for 2 cycles and then bone marrow MRD was

repeated. PFS was calculated at the time of relapse or last follow-up in patients with remission.

Results: Ten patients were included in the study. The demographic, clinical and laboratory details of patients are given in Table 1. All patients underwent high-dose chemotherapy with Inj Melphalan 200mg/m2 followed by ASCT. Day+100 MRD was assessed for all these patients post-ASCT. 4 patients were MRD negative by MFC and were put on maintenance with lenalidomide. Six were MRD positive as mentioned in table 1. All 6 MRD-positive patients received consolidation therapy. Out of these 2 have relapsed, 2 have achieved MRD negativity status while the other 2 were low MRD positive but are in complete hematological remission.

Discussion and Conclusion: MFC has become a valuable tool to monitor MRD and evaluate the depth of response in MM. MFC is relatively rapid, has wider applicability, and is cost-effective. In various studies, MRD positivity at various time points is associated with inferior PFS and higher relapse rate but there is a paucity of data using MRD-based modification of post-transplant management. A large study, FREEDOM Trial is ongoing to assess the MRD-based therapy in myeloma. Our pilot study has confirmed the prognostic value of MRD measurement and a subset of patients benefitted from the addition of consolidation therapy. In conclusion, post-transplant maintenance should be modified to achieve MRD-negative status which can improve PFS. Future work needs to be done with larger studies and longer follow up to validate our findings.

“No conflict of interest to disclose”

AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA – A SINGLE CENTER EXPERIENCE FROM NORTHERN INDIA

by Nitin Gupta | Priyanka Moule | Deepika Gupta | Sabina Langer | Pallavi Prakhar | Amrita Saraf | Jyoti Kotwal | Sir Ganga Ram Hospital, New Delhi | Sir Ganga Ram Hospial, New Delhi | Sir Ganga Ram Hospital New Delhi | Sir Ganga Ram Hospital, New Delhi | Sir Ganga Ram Hospital, New Delhi | Sir Ganga Ram Hospital, New Delhi | Sir Ganga Ram Hospital, New Delhi

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Keywords: autologous bone marrow tranplant, multiple myeloma

Introduction:

Even in the current era of novel agents, many studies have shown a significant improvement in progression-free survival (PFS) with autologous hematopoietic stem cell transplantation (ASCT) in multiple myeloma (MM). It results in deepening of responses including achievement of MRD negativity which leads to prolongation of duration of remission which is particularly relevant in a developing country like India where median age of myeloma patient is younger than western world and access to newer salvage therapies is limited due to cost and availability. Here we report our experience of ASCT in myeloma at our tertiary care center from Northern India.

Aims & Objectives: To study the demographics, clinical profile, laboratory features, complications, response and progression free survival of myeloma patients undergoing ASCT at our tertiary care center.

Materials & Methods: A retrospective study of patients who underwent ASCT at our center between January 2016- December 2022. Progression Free Survival (PFS) and Overall Survival (OS) were determined for patients with more than 6 months of post-transplant follow up. Data are expressed as median and interquartile range (IQR).

Results: Thirty-seven patients were transplanted during study period, The median age was 52 years (23-68), 24 (64%) were males and 13 females. The most common immunoglobulin isotype was IgG 23 (62%) followed by IgA 9 (24%) and light chain only 5 (13.5%). ISS stage was 3 in 21 patients (57%), 2 in 7 patients (18%) and 1 in 9 patients (24%). FISH reports were available in 23 patients (62%), out of which 8 (34%) had high-risk cytogenetics were identified. Triplet induction consisting of Bortezomib, dexamethasone, and IMiD was the most common induction regimen in 30 patients (81%) while 7 received CyBorD protocol.

Most patients (19, 51%) were transplanted in first complete remission (CR1). high dose melphalan was dosed at 200mg/m2 in 32 of 37 patients (86%) while 5 patients (13.5%) received a reduced dose (140mg/m2) in view of reduced GFR, poor ECOG performance status and other co-morbidities. The median stem cell dose was 5.31 $x10^6$/kg (1.96-11.2 x 10^6/kg). The median time to engraftment was 11 days (9-13). Mucositis was the most common complication post ASCT (35, 94%), and grade 3/4 mucositis occurred in 7 (18%). One patient (2.7%) died before engraftment due to sepsis. Another patient died 3 months after transplanting due to stroke. Out of the remaining 35 patients, 11 patients relapsed (31%) out of which 5 have died due to progressive disease. The median duration of response was 23 months post ASCT while median PFS has not been reached. Overall survival was 81 % at median follow up of 27 months (6-84). Flowcytometry post-transplant was done in 10 patients, 4 were negative and 6 were positive. Two out of the six MRD positive patients have relapsed.

Discussion and Conclusion: ASCT results in prolongation of remission duration and deepening of the responses which is especially relevant in developing countries where access to newer therapies is limited. There is a need to tailor post-transplant treatment to achieve MRD negative status.

Overall Survival and Progression-Free Survival on DLBCL Patients After Autologous Hematopoietic Stem Cells Treatment: Systematic Review

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Keywords: autologous hematopoietic stem cell, diffuse large B-cell lymphoma, overall survival, progression-free survival

Aim: To assess the survival rate, particularly overall survival (OS) and progression-free survival (PFS), of diffuse large B-cell lymphoma and its contributing factors after autologous hematopoietic stem cells therapy (AHSCT)

Methods: A systematic literature search was undertaken across PubMed, ScienceDirect, and Google Scholar databases using related keywords to synthesize the overall survival and progression-free survival of DLBL patients following AHSCT. This literature review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results: Six retrospective cohort studies were included in this review. Most studies included DLBCL patients who received AHSCT intervention after first-line chemotherapy. The results revealed that the 1-year, 2-years, 3-years, and 5-years OS range were 62-70%, 58-71%, 50-77%, and 52-86%, respectively. Meanwhile, 1-year, 2-years, 3-years, and 5-years PFS range were 55-56%, 48-65%, 41-72%, and 43-81%, respectively. Improvement of OS and PFS was observed across studies which increased over time after AHSCT. Only one study reported decreased survival over time after AHSCT which included subjects >60 years old. Factors predicting worse survival identified in the studies were older age, early relapse after first-line chemotherapy (<6 months), and relapse after AHSCT before 24 months.

Conclusion: Autologous hematopoietic stem cell transplantation improves overall survival and progression-free survival in diffuse large B-cell lymphoma patients, especially in younger patients with late relapse. Selection criteria for AHSCT recipients is necessary to gain the utmost benefit from stem cells.

No conflict of interest to disclose.

A 60-Year-Old Male with Ulcerative Colitis in Multiple Myeloma Post-Autologous Bone Marrow Transplantation: A Case Report

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Topic: Lymphoma/Myeloma
Keywords: Autologous Bone Marrow Transplantation, Multiple Myeloma, Ulcerative Colitis

Introduction

Multiple myeloma (MM) is a neoplastic plasma cell disorder that represents approximately 10% of all hematological malignancies. It is characterized by uncontrolled clonal proliferation of malignant plasma cells in the bone marrow. Common presentations include anemia, renal failure, hypercalcemia, increased susceptibility to infection, and bone pain. Intensive therapies, including autologous bone marrow transplantation, have become an integral part of advanced MM management. However, post-transplant complications, such as colitis, can disrupt disease trajectory. Colitis is marked by chronic diarrhea, being one of the most prevalent causes of morbidity in patients undergoing autologous bone marrow transplantation, resulting in a significant decline in the patient's quality of life. The causes of colitis are mainly related to patient immunity, toxicity of high-dose chemotherapy schemes, irritation of the epithelia and mucosa of the digestive tract, and various infectious conditions.

Case Illustration

A 60-year-old male with multiple myeloma underwent autologous bone marrow transplantation involving mobilization using the Cyclophosphamide and Mesna protocol, along with conditioning utilizing the High-Dose Melphalan protocol. During the bone marrow transplant procedure, the patient got diarrhea and hypovolemic shock. The patient currently presents with chronic diarrhea and abdominal discomfort. Physical examination does not indicate signs of dehydration. Various diagnostic tests have been conducted, including stool analysis, colonoscopy, and histopathological examination of colon tissue. Routine stool analysis and fecal culture were sterile, while colonoscopy revealed pan-colitis, that was further confirmed by histological examination of colon tissue, showing features of active chronic colitis with cryptitis and crypt abscesses. The patient's final diagnosis is ulcerative colitis associated with post-autologous bone marrow transplantation. Anti-inflammatory treatment and adjustment of post-transplant therapy were administered under close monitoring. The patient was given Loperamide, Mesalazine to alleviate his diarrhea and abdominal pain symptoms, while post-transplant therapy included Bortezomib and

Lenalidomide.

Discussion

Ulcerative colitis is a chronic inflammation marked by mucosal inflammation involving the colon and rectum in a continuous pattern. The disease is characterized by inflammation, sores, and ulcers on the intestinal mucosa, leading to symptoms like bloody diarrhea and abdominal pain. Ulcerative colitis is a rare complication in MM patients post autologous bone marrow transplantation, particularly in autologous bone marrow transplantation. Patients' compromised immunity, toxicity of high-dose chemotherapy schemes, irritation of the epithelia and mucosa of the digestive tract, various infectious conditions, and using of immunosuppressive therapies increase the risk of intestinal inflammation. Proper management involves a multidisciplinary approach, including symptomatic treatment, monitoring of post-transplant therapy, and anti-inflammatory therapy.

Conclusion

This case underscores the significance of vigilant monitoring for post-autologous bone marrow transplantation complications in MM patients. Although rare, complications like ulcerative colitis can have a significant impact on a patient's quality of life. Awareness of these potential complications and a holistic management approach are crucial to provide optimal care to MM patients post-autologous bone marrow transplantation.

Treatments Option Relapse or Refractory Diffuse Large B Cell Lymphoma Other than AHSCT and CAR T Cell :A Systematic Review

by Ni Putu Merlynda Pusvita Dewi | Hematologi Onkologi Medik Universitas Indonesia

Abstract ID: 187
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: , Antibody drug conjugated, Ineligible AHSCT and CART cell, Lymphoma non hodgkin, Relaps refractory

Aim:

To know the eficacy of antibody drug conjugated to be treatment Option Relapse or Refractory Diffuse Large B Cell Lymphoma.

Methods:

Comprehensive search of electronic databases including PMC, ASH Publication, ESBCO, and ASCO to identify relevant studies. Autologous Hematopoietic Stem Cell Transplantation (AHSCT) and Chimeric Antigen Receptor (CAR) T Cell exclusion criteria in searching. We assessed the feasibility of performing an Indirect Treatment Comparison (ITC) or Network Meta-Analysis (NMA). The Newcastle Ottawa scale was used for the cohort study and the JBI scale was used for randomized controlled trials.

Results:

A total of 11 studies were included. The sample sizes ranged from 30 to 450 patients. While AHSCT and CAR T have demonstrated durable remissions for patients who respond to treatment, patients who are ineligible, unable to access these therapies, or who fail treatment often experience poor outcomes. DLBCL patients in this setting have many options for new therapies, including loncastuximab, tesirine, polatuzumab vedotin, selinexor, tafasitamab, ofatumumab and rituximab in combination with cisplatin, cytarabine, and dexamethasone (DHAP). Among 145 patients who received at least 1 dose of loncastuximab, the ORR was 48.3% (95% CI, 39.9-56.7), including 35 patients (24%) who had CR. Selinexor yields an ORR of 28%, including a CR of 12%. With an average follow-up of 15 months, the mean duration of response, duration of response, and overall survival were 3, 9, and 9 months, respectively. The response rate for O-DHAP was 38% (CR, 15%)

versus 42% (CR, 22%) for R-DHAP. Naratuximab was the most common side effect occurring at grade ± 3 treatment was neutropenia (54%), lymphopenia (17%), and thrombocytopenia (11%). In the 74 patients evaluated with DLBCL, the ORR and CR rates were 43 and 32%, respectively. Zilovertamabis Its toxicity is mainly neutropenia (grade ± 3, 34%) and peripheral neuropathy (44%; grade three, 13%).

Conclusion:

Treatment option of R/R DLBCL other than AHSCTH and CAR T Cell are Antibody Drug Conjugated is a new treatment is needed, there is no difference in the efficacy of the results between previous treatment. Further studies are needed to evaluate the specific role and specific drugs for R/R DLBCL.

No conflict of interest to disclose

A Remarkable Outcome of Autologous Stem Cell Transplantation (ASCT) Followed by Pembrolizumab Treatment in Classical Hodgkin Lymphoma Relapse: A Case Report and Literature Review

by Mila Astrilia | Budi Setiawan | Daniel Rizky | Eko Adhi Pangarsa | Damai Santosa | Catharina Suharti | Internal Medicine, Faculty of Medicine, Diponegoro University | Hematology and Medical Oncology Division , Department of Internal Medicine, Faculty of Medicine, Diponegoro University | Hematology and Medical Oncology Division , Department of Internal Medicine, Faculty of Medicine, Diponegoro University | Hematology and Medical Oncology Division , Department of Internal Medicine, Faculty of Medicine, Diponegoro University | Hematology and Medical Oncology Division , Department of Internal Medicine, Faculty of Medicine, Diponegoro University | Hematology and Medical Oncology Division , Department of Internal Medicine, Faculty of Medicine, Diponegoro University

Abstract ID: 194
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: ASCT, Hodgkin Lymphoma, Pembrolizumab

Introduction

In 2020, a total of 83,087 new cases of Hodgkin Lymphoma were reported, with an incident rate 0.98 per 100,000 people. Recently, the prognosis of Classical Hodgkin Lymphoma (cHL) has improved due to advancement of novel treatment strategies. In this report, we will present a successful cHL treatment with autologous stem cell transplantation (ASCT) followed by administration of pembrolizumab.

Case Illustration

A 34-year-old man presented with a lump on his left neck with a size of 10 cm, fever, night sweat and a progressive weight loss. The patient was previously diagnosed with Hodgkin lymphoma and had undergone ABVD chemotherapy in 2019. Relapsed Hodgkin lymphoma was suspected and the patient underwent biopsy procedure and pathological examination with a confirmatory diagnosis of Classical Hodgkin lymphoma. Patient was programmed for BV and ESHAP chemotherapy and further planned to undergo ASCT. Mobilization step was completed in the mid of June 2021 with Cyclophosphamide and Mesna protocol. Harvesting step was completed by the end of June 2021 and conditioning step was completed with BeEAM protocol which was performed by the mid of August 2021. Subsequently, stem cell infusion of 535 mL CD34+ cells with 70% viability was performed. Patient was discharged 21-day post stem cell transplantation with a fit condition. After ASCT, a 16-cycle of BV chemotherapy was planned for the patient. Patient experienced a relapse episode with fever, night sweat, progressive weight loss, lump appearance, and the PET scan showed nodule activity, therefore BV chemotherapy was stopped and changed to pembrolizumab chemotherapy every 3 weeks up to 2 years since March 2022. To date, the patient has

undergone 15 cycles of pembrolizumab chemotherapy. Patient is currently in a fit condition and does not experience relapse post pembrolizumab administration.

Discussion

ASCT is the treatment-of-choice for Hodgkin lymphoma in a young and healthy subject. Initial treatment before ASCT is aimed at producing a high-quality transplant response. In this report, the patient was treated with BV-ESHAP chemotherapy prior to transplant mobilization. Previous studies have found that 94% cases prescribed with BV–ESHAP regimen were properly mobilized. During the conditioning phase, the BeEAM regiment was generally applied in patients with Hodgkin lymphoma which was proven to have a better progression free survival (PFS) in comparison to other regiments. Consolidation after ASCT aims to provide an effective anti-lymphoma regiment immediately after ASCT. In this patient, BV chemotherapy was given after ASCT. BV was considered as a suitable agent for a pre-emptive treatment promptly after ASCT with a lower frequency of hematological toxic effects, and has an effective mechanism of action in patients with HL. Once after receiving the BV chemotherapy, the patient experienced a relapse episode, therefore the regiment was discontinued and replaced with pembrolizumab. Clinical evidence has approved the administration of 200 mg pembrolizumab every 3 weeks is effective for a relapsed Hodgkin lymphoma.

Conclusion

ASCT treatment in cHL successfully increases both overall survival and progression free survival rate. In Addition, pembrolizumab is a promising novel therapy for relapse cHL after ASCT procedure.

Unraveling Thrombocytopenia after Autologus Stem Cell Transplantation in Multiple Myeloma: A Case Report

by Ika Kartiyani | Damai Santosa | Department of Internal Medicine, Dr. Kariadi General Hospital/ Diponegoro University, Semarang, Indonesia | Division of Hematology and Oncology, Dr. Kariadi General Hospital/ Diponegoro University, Semarang, Indonesia

Abstract ID: 195
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: ASCT, CyBorD, Multiple Myeloma, Thrombocytopenia

ABSTRACT

Introduction

Multiple myeloma (MM) is a malignant clonal plasma cell dyscrasia characterized by the clinical constellation of anaemia, nephropathy, and bone disease. Multiple myeloma is not curable with currently available therapies; however, overall survival and quality of life have dramatically improved by autologous stem cell transplant (ASCT) for eligible patient. Autologous stem cell transplant can provide significant remission that is both long and deep, extending survival.

Case Presentation

A 58-year-old woman presented with a 3-month history of refractory anaemia. Complete blood test revealed anemia, thrombocytopenia, and azotemia. Punched-out lesions in multiple bones were observed in the bone survey examination. Serum protein electrophoresis showed M-spike of the gamma globulin. Hypercellular bone marrow with 32% plasmocytes were found in the bone marrow puncture. The patient had anemia, renal insufficiency, and bone lesions as the myeloma-defining events. The International Myeloma Working Group (IMWG) criteria was fulfilled, hence the diagnosis of multiple myeloma was established. The patient received chemotherapy with CyBorD (Cyclophosphamide, Bortezomib, and Dexamethasone) regimen. Bone marrow evaluation results showed less than 5% plasmocytes with good clinical improvement. Subsequently, the patient underwent autologous bone marrow transplantation with high dose mephalan conditioning

The patient experienced engraftment after 13 days of infusion. Some of the symptoms that appeared during treatment were nausea, vomiting and diarrhea which were finally handled properly. On the 14th day the patient comes out of the isolation room and discharged home in good condition and visit the doctor every month. She had been grappling with mild thrombocytopenia for a span of 6 months following the infusion which was treated well with daily eltrombopag. No indications of anemia were present, and there were no discernible signs or symptoms of relapse.

Conclusions

Autologous Stem Cell Transplantation (ASCT) has emerged as a significant therapeutic intervention for patient with multiple myeloma. The procedure offers promising outcomes

by combining high-dose chemotherapy with stem cell support, effectively targeting malignant plasma cell. This approach often leads to deep and durable remissions, improving overall survival and quality of life. However, despite its advantages, ASCT is not without risks and requires careful patient selection and management of potential complications. Continued research is essential to refine patient selection criteria, optimizing conditioning regiments, and explore novel adjunctive therapies to further enhance the efficacy and safety of ASCT in the treatment of multiple myeloma

No conflict of interest to disclose

Secondary aplastic anemia after autologous bone marrow transplantation in multiple myeloma : a case report

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Abstract ID: 197
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: aplastic anemia, autologous bone marrow transplantation, high dose melphalan, myeloma

Background: Aplastic anemia is a relatively severe hematological condition but is rarely associated with hematopoietic failure resulting in decreased or absent hematopoietic precursor cells in the bone marrow. Aplastic anemia can occur at any age with the same distribution between sexes and races. Three known mechanisms of aplastic anemia include direct injury, immune-mediated disease, and bone marrow failure. The most common etiology of aplastic anemia is considered to be idiopathic. Patients usually come with non-specific complaints such as fatigue, shortness of breath on exertion, paleness, and bleeding. The main treatment for aplastic anemia is to eliminate the causative agent. In patients in whom a reversible cause is not found, the management of the patient depends on the age and severity of the disease. We present the case of a 68-year-old man with a history of autologous bone marrow transplantation due to multiple myeloma, laboratory results showed cytopenia and had an excellent response to immunosuppressive therapy.

Case report: A 68-year-old man came with complaints of frequent weakness, fatigue and low back pain since last month. The patient had a history of autologous bone marrow transplantation due to multiple myeloma in 2013, with conditioning high dose melphalan. Physical examination found pale palpebral conjunctiva, no active bleeding. Routine blood tests revealed cytopenia. Because this patient had history of multiple myeloma, he was suspected a case relapsed. Serum protein electrophoresis showed that there was no monoclonal gammopathy, then bone marrow biopsy examination found a hypocellular bone marrow cellularity, confirmed as an aplastic anemia. The patient was given immunosuppressive therapy, cyclosporine, with a dose of 50 mg/ day. After 3 months of therapy, the patient's condition improved. The dose of cyclosporin was tapered down.

Conclusion: Patients after autologous bone marrow transplantation especially in this case for indications of multiple myeloma, should be monitored for a relapse case. But in this case, from bone marrow biopsy found that aplastic anemia. The possible cause of aplastic anemia is bone marrow failure. The diagnosis in this patient was known quickly, then given immunosuppressive therapy for 3 months. The outcome of patient's clinical condition improved until now.

Lenalidomide Maintenance for Transplant Ineligible Newly Diagnosed Multiple Myeloma : A Mini Systematic Review

by Vania Tryanni | department of internal medicine, university of indonesia

Abstract ID: 209
Event: 28th Annual Meeting of APBMT
Topic: Lymphoma/Myeloma
Keywords: Ineligible transplant, Keyword: Lenalidomide maintenance, newly diagnosed Multiple Myeloma

Please write your abstract n

Introduction

Multiple myeloma is an incurable plasma cell disorder and prevalent in aged 65 or older. From the last decade, there was advancement in MM treatment with used of Proteosome inhibitor and immunomodulatory drugs but ASCT still the mainstay treatment of MM. Unfortunately, many of Indonesian is ineligible for transplant, because of economical or medical reason. Lenalidomide maintenance in post transplant population showed benefit in OS and PFS, but it advantage for transplant ineligible patients still unclear. This study purpose is to look for benefit of lenalidomide maintenance for transplant ineligible newly diagnosed multiple myeloma (NTE-NDMM).

Method

We conduct a systematic searching through PubMed, Embase and Clinical Key with "Continuous lenalidomide" or "Maintenance lenalidomide" or "long term lenalidomide" and "Newly diagnosed multiple myeloma" and "transplant ineligible" as keyword. We include systematic review and meta-analysis study of RCT , RCT and observational studies in the last 12 years. Studies that are not available in English, or full text, using indirect comparison, and no control were excluded. Critical appraisal is done with Oxford Centre for Evidence Based Medicine Levels of Evidence.

Result

We found 10 studies in PubMed, 91 in Embase and seven in science direct. After abstract screening and screening double total of four studies were included. All four article are considered valid. Palumbo in 2012 found significant benefit using lenalidomide maintenance compare to induction with 9 cycles MPR with PFS of 31 months vs 14 months (HR 0.49, $P<0.001$). Facon found similar result with benefit of maintenance lenalidomide compare to use of MPT or RD alone (26 months vs 21.9 months vs 21 months, with HR 0.63 and 0.71 respectively). Jakson found that lenalidomide maintenance associated with prolong PFS compare to placebo despite of the induction regime (39 months vs 20 Months, HR 0.46). Last study by Sharpley showed benefit of PFS in patients receiving maintenance with PFS of 25.7 months vs 9 months (HR 0.54).

Discussion

Lenalidomide maintenance showed significant benefit for PFS in NTE-NDMM. It is associated with increased infection, with ARR of 0.2 and NNH of 5 and other adverse events are similar. There was not drug related death reported from Jakson's study. Lenalidomide usage also did not correlate with secondary malignancy. Patient's HRQoL is preserved. It also showed to be cost effective compare to VMP. Its showed similar benefit when compared to proteosome inhibitor-based induction treatment.

Conclusion

Maintenance treatment with lenalidomide showed significant benefit in PFS for NTE-NDMM with acceptable toxicities. There should be further studies to look for benefit when using lenalidomide maintenance after proteasome inhibitor-based induction regimen.

Chronic Graft versus Host Disease post Allogenic Bone Marrow Transplant in Relapsed Acute Lymphoblastic Leukemia: A Case Report

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Abstract ID: 43
Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: Hematopoietic stem cell, bone marrow therapy, graft versus host disease

Introduction

Hematopoietic stem cell transplantation (HSCT), also known as bone marrow transplant (BMT), is a treatment option available for children with haematology or oncology diseases. Chronic graft versus host disease (cGvHD) is a consequential non-relapse cause of morbidity and mortality after allo-HSCT for malignancies, which may be in any organ, especially noticeable on the skin and eyes. This case reported an Indonesian boy participated with two paediatric-oncologists from Indonesia, from the HSCT screening process in Italy, until the latest post-transplant monitoring.

Goal: To raise awareness and remind the novel cutaneous and ocular manifestation of the cGvHD.

Case Report

An 8-year-old boy has undergone bone marrow transplant for relapsed acute lymphoblastic leukaemia (ALL) at 22 December 2014 in Cagliari, Rome, with his sibling as the donor. His conditioning regimen consisted of total body irradiation (TBI) and cyclophosphamide. For GvHD prophylaxis, cyclosporin A (CSA) was started one day before BMT (D-1). Early complication showed acute GvHD (aGvHD) grade I-II on his skin and gut system, which was treated with steroid followed by gradual dose reduction.

One year after BMT therapy (January 2016), patient revealed several cGvHD manifestations. His skin showed erythematous rash with 54% body surface area (BSA) covered with movable sclerosis, mostly at both arms and thighs. The sclerosis appeared hyperpigmented, asymmetrical, and distinct, while also felt rough scaly texture with elevated lesions. Non-movable sclerosis with subcutaneous sclerosis covered 70% of BSA, found mostly at trunks and legs, with initial stiffness at joints skin surface such as wrist, elbow, and knee. Some of the skin sclerosis showed hardening felt even at muscle tissue level. Schirmer’s tear test

highlighted bilateral lack of tear production. The treatment plan goal to control cGvHD by adjusting the immunosuppressants, corticosteroids, and antibiotics with additional supplements, thus the treatment plan consisted of CSA 30 mg twice a day, methylprednisolone 4 mg per day, imatinib 100 mg once a day for a month after meal.

After two years of follow-up cGvHD assessment showed improvement. The distinct movable sclerosis, mostly at both arms and thighs, appeared to be mildly diffused. Schirmer's tear test also showed improvement of ocular tear function. After 4-5 years of follow-up, there was improvement of skin sclerosis in all body surface, subcutaneous, dermis, except in arm and medial chest areas. The skin lesions started to become smoother and the colours become less distinct. Patient showed consistent adherence and tolerance towards the medication, without any major side-effects or complications.

On the latest follow-up (6 years after BMT therapy), patient showed good clinical condition, without active cGvHD. At skin findings, there was dry skin, with only cutaneous outcomes of chronic GvHD such as skin discolorations with hypochromia and hyperchromia.

Conclusion

This case report showed classic cGvHD clinical manifestations, which involve multiple organs, but particularly noticeable on cutaneous tissue and eyes. Thus, it is necessary to continue developing strategies to evaluate and improve cGvHD to enhance survival and quality of life after allo-HSCT.

Bronchiolitis Obliterans Syndrome: A Rare Complication of Graft Versus Host Disease in an Allogeneic Hematopoietic Stem Cell Transplant Patient

by Arielle Nicole Y. Cheng | Camille A. Pestaño | Ruth Marie R. Divinagracia | Francisco Vicente F. Lopez | Department of Internal Medicine, St. Luke's Medical Center – Global City | Department of Internal Medicine, St. Luke's Medical Center – Global City | Institute of Pulmonary Medicine, St. Luke's Medical Center – Global City | Blood and Marrow Transplant and Section of Hematology, St. Luke's Medical Center – Global City

Abstract ID: 55
Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: Allogeneic hematopoietic stem cell transplant, Bronchiolitis Obliterans Syndrome, Graft-Versus-Host Disease

We report a case of a 37 year old female with Pre B Cell acute lymphoblastic leukemia presenting with dry cough and exertional dyspnea 21 months post allogeneic Hematopoietic Stem Cell Transplant (HSCT). A pulmonary function test (PFT) revealed an obstructive pattern with no bronchodilator response. CT scan of the chest (inspiratory and expiratory phases) showed air trapping and hyperinflation. A diagnosis of Bronchiolitis obliterans syndrome (BOS) was made. Bronchoscopy with bronchoalveolar lavage showed no evidence of any active infection or malignant cells. She was started on Azithromycin 250mg 3 times a week, Fluticasone furoate/Vilanterol 100/25 mcg 1 puff once daily, Tiotropium bromide 2 puff once daily along with adequate immunosuppressive regimen led to a significant improvement in symptoms within 4 weeks. A repeat PFT after 3 months showed improvement in the FEV1 by 22%. The conference of challenges in diagnosing BOS, its rarity and poor prognosis, make it important to recognize such cases in a timely manner, so that proper management can be initiated.

No conflict of interest to disclose.

Lithium combined with classic GI GVHD in treated grade 3-4

by Mehrdad Payandeh | Kums

Abstract ID: 89
Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: GVHD, lithium, toxicity

In 15 cases of GIGVHD we added lithium 309 mg at night , and can treated and have a good controlled of GI symptoms and sever diarrhea .
in conclusion severe GI GVHD in life threatening in post allogeneic transplant and need combined therapy in cases and lithium is new drug with light toxicity .

A Case report The use of ruxolitinib for steroid dependent chronic GVHD of scleroderma in a patient of ALL post allo-HSCT

by Hardy Indradi | Tzu Chi Hospital Jakarta

Abstract ID: 90
Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: case report, chronic GVHD, ruxolitinib, scleroderma

Chronic graft-versus-host-disease (GVHD), a major complication of allogenic stem cell transplantation. Standard first-line treatment of chronic GVHD consists of systemic glucocorticoids; however, in approximately 50% of patients, the disease becomes glucocorticoid-refractory or glucocorticoid-dependent, greatly increasing the risk of poor outcomes. Ruxolitinib, a Janus kinase (JAK1-JAK2) inhibitor, showed potential efficacy in patients with glucocorticoid-refractory or glucocorticoid dependent chronic GVHD. Ruxolitinib blocks janus kinases 1 and 2 , which are required to mediate the downstream signalling of multiple cytokine receptors.

A case presentation

A 35-year-old Indonesian male was diagnosed with Acute Lymphocytic Leukaemia (ALL) with a positive Philadelphia chromosome. After induction chemotherapy, he was declared in complete remission and advised to have allo-hematopoietic stem cell transplantation. Hence, three months after his complete remission, he proceeds with the transplantation with a fully matched donor from the patient's elder brother in Hualien Tzu Chi Hospital. He got discharged from the hospital on the fifty-first day after transplant.

During follow up, he was diagnosed with chronic graft versus host disease (GVHD) in skin, oral mucosa, and liver manifestation. These chronic GVHD can be well controlled with steroids and tacrolimus. Imatinib was added to the medication for relapse prevention purposes.

11 months after the transplant, the patient began to gain weight, swelling in the lower extremities and getting tired quickly. There was skin thickening in his forearms, upper arms, lower leg and thighs. The patient began to feel stiff throughout the body and had difficulty performing certain movements such as squatting and opening his mouth wide. There was an increase in gamma-glutamyl transferase (GGT) and D-dimer, according to the laboratory result. The symptoms have led the patient to be diagnosed with scleroderma. Clinically, the patient's condition improved after being given steroid injection for a while. However, the signs and symptoms begin to recur after a reduction in steroid doses. With the consideration to reduce the side effects of long-term use of high-dose steroids, patients began to be given ruxolitinib. Several months after administration of ruxolitinib, GVHD was

successfully controlled with mild sequelae accompanied by decreased values of GGT and D-dimer. As such, the use of steroids was able to be lowered to minimal doses.

Discussion: This case illustrates the use of ruxolitinib in steroid dependent chronic GVHD which leads to improved clinical outcome and avoids the side effects of long-term use of high-dose steroids.

Transplant-Associated Thrombotic Microangiopathy (TA-TMA) and Mucormycosis as Complications of Chronic Graft Versus Host Disease (GVHD)

by Ludi Dhyani Rahmartani | Ganda Ilmana | Nina Dwi Putri | Eka Laksmi Hidayati | Pustika Amalia Wahidiyat | Suradej Hongeng | Universitas Indonesia - Cipto Mangunkusumo National Hospital | Universitas Indonesia - Cipto Mangunkusumo National Hospital | Universitas Indonesia - Cipto Mangunkusumo National Hospital | Universitas Indonesia - Cipto Mangunkusumo National Hospital | Universitas Indonesia - Cipto Mangunkusumo National Hospital | Ramathibodi Hospital - Mahidol University

Abstract ID: 214
Event: 28th Annual Meeting of APBMT
Topic: GVHD
Keywords: GVHD, HSCT, Mucormycosis, TA-TMA, thalassemia

Background:

Transplant-associated thrombotic microangiopathy (TA-TMA), a severe hematopoietic stem cell transplantation (HSCT) complication, impacts multiple organs. Mucormycosis, an invasive fungal infection, poses a significant threat to immunocompromised patients. Both conditions contribute to high morbidity and mortality rates.

Aim:

This study aims to describe a case of mucormycosis and suspected transplant-associated thrombotic microangiopathy as complications of graft-versus-host disease (GVHD) in a pediatric patient.

Case:

A 17-year-old Indonesian boy with transfusion-dependent HbE/β thalassemia received a matched sibling donor HSCT two years prior in Thailand. After successfully HSCT, he experienced multiple episodes of chronic GVHD (skin and gastrointestinal) and was given prednisone and sirolimus. He complained of high peak fever, cough, and mild sore throat three days before admission. Being treated with antibiotics, the fever persisted, along with an ulcer in the palate. Evaluation for mucormycosis was planned, but he had a sudden onset of diabetic ketoacidosis and was admitted to the intensive unit. The ulcer became more severe and progressed to a perforation. Brain CT showed bilateral sinusitis of the maxillary, ethmoid, sphenoid, and frontal region with erosion in maxillary and ethmoid sinus, Keros type II, soft tissue defect in palatum durum without infiltration to intracranial. Debridement was done, and the pathology result was consistent with invasive fungal infection (Mucorales). Isavuconazol and micafungin were administered. Despite aggressive management for diabetes, sepsis, and fungal infection, the condition deteriorated. There was a decreased consciousness, which was seen as a temporal hyperacute infarct in brain

MRI. The laboratory result showed elevated LDH and D-dimer, proteinuria with acute kidney failure, anemia, thrombocytopenia, and schistocyte in peripheral blood smear. The ADAMTS13 activity and sC5-9 could not be measured due to limited facilities. Diagnosis of TA-TMA was established, and we performed seven cycles of therapeutic plasma exchange. Unfortunately, the condition worsened, and he underwent continuous renal replacement therapy (CRRT). We did not have Eculizumab available in the country. Unfortunately, he died after 21 days of intensive care.

Conclusion:

Combining TA-TMA, mucormycosis, and multiple organ failure could contribute to significant morbidity and mortality, leading to high fatality rates.

Role of Prophylatic Low dose Cidofovir in preventing CMV Reactivation and Related Complications in Patients undergoing Allogeneic HSCT

by Shubh Sanket Purohit | Physician/Trainee

Abstract ID: 78
Event: 28th Annual Meeting of APBMT
Topic: Infections
Keywords: CMV, GVHD., HSCT, cidofovir, prophylaxis

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Abstract Text

Aim:

Cytomegalovirus (CMV) remains a major cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (Allo-HSCT). New strategies and methods for prevention and management of CMV infection are urgently needed. We aim to review the role of prophylactic low dose cidofovir for prevention of CMV viremia and its related complications in allo-HSCT recipients.

Methods:

We retrospectively assessed 26 patients (12 MRD, 10 Haplo and 4 MUD) who underwent allo-HSCT from 1st January 2022 to 30th June 2023 at our centre. These 26 patients were stratified into a low dose cidofovir prophylaxis group (n = 6) and a non-cidofovir prophylaxis group (n = 20). Prophylactic cidofovir was given at a dose of 2.5 mg/kg once a week starting at 3-4 weeks after allo-HSCT. CMV viremia was monitored by quantitative real time PCR (RQ-PCR) for CMV DNA at weekly interval or more frequently when indicated. Low dose cidofovir prophylaxis was continued till 12 weeks post allo-HSCT in patients who continued to be tested negative for CMV viremia.

6 more patients are currently under low dose cidofovir prophylaxis at our centre, however they were not included in this study as they have not completed 24 weeks post allo-HSCT.

Results:

Patients in the low dose cidofovir prophylaxis group had a lower possibility of CMV

reactivation by 24 weeks post allo-HSCT than those in the non-cidofovir prophylaxis group (33% versus 70% respectively). Odds for low dose cidofovir prophylaxis given and no reactivation of CMV was 4.6 (95% Confidence interval: 0.66-32.74). Also there was a significant decrease in the incidence of acute severe GVHD (≥ Grade 3) in patients who received prophylactic cidofovir compared to non-cidofovir prophylaxis group. None of the patients in cidofovir-prophylaxis group had acute severe GVHD, while 20% patients in the non-cidofovir prophylaxis group had acute severe GVHD. The overall survival was 100% in the low dose cidofovir prophylaxis group when compared to 80% in the non-cidofovir prophylaxis group at week 24 post transplant.

Conclusion:

Although the sample size is small and needs further correlation, low-dose cidofovir prophylaxis could be an option to prevent CMV reactivation in patients undergoing allo-HSCT, especially in resource-limited countries.

Conflict of interest: No conflict of interest to disclose.

A CASE SERIES OF CYTOMEGALOVIRUS COLITIS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS IN A TERTIARY CENTER IN THE PHILIPPINES

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Cytomegalovirus (CMV) infection is one of the most common opportunistic infections in immunocompromised hosts, including transplant recipients. CMV colitis has been documented to be the most common focus of infection based on the European Conference on Infections in Leukaemia (ECIL 7), presenting with diarrhea, hematochezia, and abdominal pain. The diagnosis is based on triad of gastrointestinal symptoms, visualization of characteristic lesions on endoscopy, and cytoplasmic inclusions on histopathology.

Generally, any immunocompromised patient is at risk for CMV infection. However, in hematologic malignancy settings other than the allogeneic hematopoietic stem cell transplantation (aHSCT), the most relevant risk factors for CMV appear to be CMV-negative donor CMV-positive recipient serostatus, acute or chronic graft-versus-host disease, and unrelated or mismatched donor.

In actual clinical practice, only a minority of these patients present with the classic clinical triad of CMV colitis, and the serologic tests have poor diagnostic sensitivity and specificity, hence making the diagnosis of CMV colitis very challenging, especially in the Philippines where there has been no documented report post aHSCT. Because of these challenges, we present four cases of histologically confirmed CMV colitis in patients who underwent aHSCT, illustrating the classic approach to the diagnosis. These cases also illustrate the myriad combination of the different diagnostic tests for CMV and will summarize which among these tests correlate strongly with CMV colitis.

Pattern of Invasive Fungal infection in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Retrospective Analysis from a Tertiary Care Centre

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Introduction:

Invasive Fungal infection (IFI) is an important cause of mortality and morbidity among recipients of hematopoietic Stem cell transplantation (HSCT). The problem is compounded by emergence of antifungal resistance and breakthrough infection despite prophylaxis. Hence study of the patterns of fungal infection and antifungal prophylaxis will provide useful insight for prevention and treatment of IFI in these high-risk patients.

Methods:

This is an observational retrospective analysis. Patients undergoing both autologous and allogeneic transplants were studied. We included a total of 638 cases from Jan 2012 to Dec 2022 in this analysis. Patients with invasive fungal infection (IFI) were diagnosed as per the EORTC MSG criteria. For patients on antifungal prophylaxis, eligibility for breakthrough fungal infection was assessed by comparing date of sample collection with the date of last antifungal therapy.

Results: Of the 638 included patients, 20 cases of confirmed fungal infection were identified. Responsible pathogens were identified as Aspergillus species: 15 cases (14 by Galactomannan antigen test, 1 by DNA PCR from blood), Candida species: 4 cases (1 by PCR, 1 by blood culture, 2 by mannan antigen) and Fusarium species: 1 case by blood

culture (Fig: 1)

Number of patients receiving (treatment/prophylaxis) each type of antifungal agent is shown in Fig. 2. Antifungal prophylaxis was administered in 619 patients (Fluconazole n=259, 41.8%; Voriconazole n=2, 0.3%; Posaconazole n=344, 55.6%; Amphotericin B n=14, 2.3%; see Fig. 3). Further analysis yielded 18 cases of BIFI (11 on Posaconazole, 6 on Fluconazole and 1 on Liposomal amphotericin B prophylaxis).

Conclusion:

These result suggest that the incidence of breakthrough fungal infection is considerably low and similar to that described in literature.

- No conflict of interest to disclose.

Assessing the effectiveness and safety of Double Lumen Femoral Venous Catheters in adult Peripheral Blood Stem Cell Harvest: Insights from a new Bone Marrow Transplant Centre

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Keywords: Bone Marrow, CVC, DLBCL, PBSC, PICC, PTCL

Autologous peripheral blood stem cell (PBSC) transplantation has become increasingly important in the treatment of various malignancies. However, obtaining an adequate product for autografting requires processing large volumes through apheresis, and a significant proportion of eligible patients lack sufficient venous access for repeated apheresis procedures. Additionally, high flow rates are essential for withdrawing and returning large volumes during each apheresis which can be challenging to achieve through peripheral veins, especially in patients who have undergone extensive chemotherapy. Traditionally, many centers rely on a femoral sheath and peripherally inserted central catheter (PICC) for apheresis procedures. However, there is limited published data on the efficacy and safety of double lumen femoral central venous catheters (CVCs).This approach has been discouraged in the past due to the concerns about a higher incidence of infections and thromboembolic complications. To evaluate the feasibility, safety and efficacy of short-term femoral venous dialysis catheters used for the collection of peripheral blood stem cells (PBSCs). This is a retrospective observational study of PBSC harvests in adult patients collected from June 2022 to July 2023. The efficacy and safety of 36 short-term double lumen polyurethane femoral CVC used for the PBSC was evaluated. There were a total of 33 patients with male to female ratio 2.6:1 with a mean age of 36.5 years. A total of 36 apheresis procedures were performed. The longest duration a catheter remained in situ was 3 days. No prophylactic antibiotic or antithrombotic therapy was used. The target CD 34 count was kept 2- 6 X 10^6 cells/kg. (84%) of patients achieved this target or above. 11 (33.3%) of the cases were refractory /progressive Hodgkin lymphoma, 9(27.2%) were multiple myeloma, 4(12.12%) were Peripheral T-cell lymphoma (PTCL), 3 (9.09%) were Diffuse large B-cell lymphoma (DLBCL), 1(3.03%) was anaplastic large cell

lymphoma,1(3.03%) was angioimmunoblastic lymphoma,1(3.03%) was neuroblastoma and 1(3.03%) was plasma cell leukemia, 1 (3.03%) was mantle cell lymphoma and 1 (3.03%) was a allogenic donor. The average CD 34 +cell count per session was 8.39 X 10^{6} cells/kg. There were no insertion-related complications, no infection or thrombosis documented. There were minimal mechanical problems. CVC removal was uneventful in all the cases.Using femoral venous catheters for PBSC collection on a short term basis proves to be both safe and effective. This approach streamlines the procedure, enhances patient comfort, and reduces overall costs.

The effect of thirst quenching herbal medicine in the treatment of oral mucositis in bone marrow transplant candidates

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Topic: Conditioning Regimens
Keywords: GVHD, MUCOSITIS, conditioning

Introduction: The Scrophularia striata plant with the local name of thirst quencher is a perennial plant from the monkey flower, which the people of Kermanshah province have been experimentally using this plant in various forms such as edible decoction, incense and poultice in the treatment of disease.

Discussion: The conditioning regimen has led to the development of mucositis or painful oral ulcers, which often causes swallowing disorders and malabsorption of food in these patients. In a study that was conducted on ten transplant patients suffering from oral mucositis, consumption of the decoction of the thirst-quenching plant as a gargle was observed to have significant effects on the resolution of mucositis compared to chlorhexidine mouthwash. In this method, pour 20 grams of dry herbs or 40 grams of fresh herbs with 750 ml of cold water into a container (pot) and put it on a low flame of the stove for 20-30 minutes until it boils and the volume of the remaining liquid in the container It reaches two thirds of its initial volume (500 ml).Then pour the cooled and strained decoction into a suitable glass container with a lid and store it in the refrigerator. The amount prepared is enough to consume 3 doses for the same day. The decoction should be prepared fresh and daily.

Conclusion: The effect of regular consumption of the decoction of thirst-quenching plant in the form of gargle in the treatment of patients with oral mucositis was observed after 3-4 days, and about fifty percent recovery was achieved

ROLE OF N. ACETYL CYSTEINE IN REDUCING THE MUCOSITIS IN BONE MARROW TRANSPLANTATION

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Keywords: Mucositis, N acetyl cystein, Oral mucosal score

INTRODUCTION

Oral mucositis [OM] is a complications of high dose conditioning chemotherapy which is frequently observed in hematopoietic stem cell transplant settings.OM is a major morbidity which will reduces the calorie intake and poor absorption of immunosuppressive therapy. Antioxidants like N acetyl Cysteine [NAC] proposed to prevent the OM. In the present observational study to evaluate the effects of NAC on OM incidence and severity.

METHODS & RESULTS

Methods:

The current study includes both pediatric and adult patient who were enrolled for both autologous and allogenic SCT received high dose chemotherapy or Myeloablative chemotherapy. Total 50 patients were enrolled as observational study. NAC was given as parenteral route until the conditioning therapy complete and there after prescribed oral NAC until the engraftment at 10mg/kg/dose Q6thrly.OM assessed with Oral Mucosa Assessment scale. OM score was monitored during transplant period until engraftment.

Results:

In this observational pilot study total 50 patient were included,90% (n=45) were children less than 18years old and 10%(n=5) were adults. Among type of transplants, 14%(n=7) were autologous transplants and 86%(n=43) were allogenic transplants, In allogenic group 58% (n=25) haploidentical and 42%(n=18) Matched related donor transplants. Conditioning regimen in all patient were Myeloablative conditioning. Disease characteristics and conditioning protocol-Multiple Myeloma (n=2)- High dose Melphalan 200mg/m2; Relapsed Lymphoma(n=3)-BEAM conditioning; Neuroblastoma (n=1)- Bu Mel conditioning; Severe aplastic anemia[SAA](n=4)-Fluderabine + Cyclophosphamide and ATG; Hyper Ig E syndrome (n=1)-Flu + CTx +Bu+ TBI with PT/Cy, Congenital megakaryocytic thrombocytopenia (n=1) -Flu + CTx +Bu +TBI with PT/Cy; Acute Lymphoblastic Leukemia(n=6)-CTx+TBI/Flu-TBI;Acute Myeloid Leukemia(n=2)-Hopkins protocol/FTT; Primary Immunodeficiency(n=10)-CTx-Flu-Bu-TBI/FTT; Constitutional aplastic anemia (n=4)-Flu-CTx-TBI; Thalassemia major/Hemoglobinopathies (n=12)-FTTA; Metachromatic Leukodystrophy (n=1)-Flu-BU; Osteopetrosis (n=1)-FTT; Neiman Pick disease(n=1)-FTTA;

Hyper IgD syndrome(n=1)-FTTA; Mucositis assessment score- Grade 2 [erythema] in 40% (n=4) and Grade 1[soreness] in 60% (n=6). All, except one patient(JMML) were engrafted, among Allogenic stem cell transplantation group One patient with SAA developed lower gut GVHD grade 4 (grossly blood diarrhea) from Day+60, steroid responsive restarted NAC when GVHD was started stool volume and color of stool improved by Day7 of steroid initiation.

CONCLUSIONS

The NAC significantly reduces the OM in high dose chemotherapy setting, which may reduces the bacterial translocation and therefore gram negative sepsis, NAC did not affect engraftment and transplant outcomes. We also observed reduced stool volume in case of Gut GVHD and faster recovery when used for gut GVHD along with steroids, though numbers were small may need larger study to confirm this phenomena.

Viability and Engraftment of Non-cryopreserved Stem Cell in Autologous Transplant for Lymphoma using Modification of BEAM Protocol

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Keywords: Modification of BEAM, engraftment, non-cryopreserved stem cell, viability of stem cells

Aim:

In recent years, Myanmar has come across many limitations to perform autologous haematopoietic stem cell transplantation (ASCT) due to economic recession and irregular electricity, in particular, ASCT for relapse/refractory (R/R) lymphoma which requires cryopreservation of stem cells to undergo standard BEAM protocol of 6 days duration. By modification of BEAM after approval from the institutional review board made reinfusion of stem cells possible after 5 days of chemotherapy and helped bypass resource-intense cryopreservation. Here, we report our observation on viability and engraftment of such ASCT cases carried out at the North Okkalapa General and Teaching Hospital, Yangon, Myanmar between September 2017 to August 2023.

Method:

Conditioning with the modified BEAM protocol consisted of carmustine 300mg/m^2 on day −5; cytarabine, 550 mg/m^2 intravenously daily, from day −4 to day−2; etoposide, 275mg/m^2 intravenously daily, from day −4 to day −2; and melphalan, 140 mg/m^2 intravenously on day −1. Harvested stem cells were stored at 4’C in a blood bank refrigerator. Stem cell dose and viability were tested after collection and rechecked before reinfusion, using BD FACSCanto flow cytometer and BD stem Cell Enumeration Kit containing 7 Amino Actinomycin D stain.

Results:

Three primary refractory Hodgkin lymphomas and five relapsed refractory diffuse large cell B cell lymphomas, two female and six male patients at a median age of 46 years underwent ASCT. One patient died on day+17 from severe pneumonia. Of remaining 7 cases, mean

interval from stem cell harvest to reinfusion was 121.4 ± 10.6 hours ie. within 6 days. Mean viable CD34+ cell count was 3.36 ± 0.83 x10^6 cells/kg and mean viability was 80 ± 5.7 %. Mean engraftment day of neutrophil was 13 ± 4 days and that of platelet was 20 ± 14 days. All patients achieved engraftment and there was no graft failure. Among seven cases engrafted, one died from liver failure, and one died of relapse. Five cases remained alive at the end of the study.

Conclusion:

In this study, even without cryopreservation, modification of BEAM protocol allowed good viability of stem cells at the time of reinfusion on day 6 leading to engraftment and made ASCT feasible in resource limited countries. Further studies are needed to investigate drug toxicities, engraftment sustainability and outcome in lymphoma patients.

Reduce Intensity Conditioning Allogeneic HSCT For Young Adults Man With T-Cell Acute Lymphoblastic Leukemia: A Case Report

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Keywords: Allogeneic HSCT, Reduce Intensity Conditioning, T-cell ALL.

Introduction

Reduced Intensity Conditioning (RIC) may be indicated for patients with ALL who require allo-HSCT, but are ineligible for a dose-intensive conditioning. Such indications include: poor performance status, active infections, significant organ dysfunction, or advanced age. Indications of allogeneic hematopoietic stem cell transplantation (allo-HSCT) for T-ALL are also similar to those for Ph-negative B-ALL, including those for patients in their first Complete Remission (CR1) who have high-risk features of relapse, patients in ± CR2, and patients in relapse and with refractory conditions. However, toxicity of treatment remains a significant problem, with previous studies reporting 10% to 30% transplantation-related mortality (TRM) in AYA patients who underwent HSCT for ALL, mostly due to graft-versus-host disease (GVHD) and infection.

Case Illustration

A 26-year-old man was diagnosed with type T-cell acute lymphoblastic leukemia (T-ALL) in March 2021. He received the Indonesian ALL regimen for 1 year. After CR1, in August 2022 the patient presented for thrombocytopenia for which bone marrow aspirate showed relapsed disease. He received the Hyper-CVAD regimen for 4 cycles with 25% restriction dose. In November 202, patient achieved a second complete remission. He underwent allogeneic stem cell transplant from matched-related donor in January 2023 using conditioning with fludarabine and melphalan. He received tacrolimus and leucovorin as graft-versus-host disease prophylaxis. The patient's engraftment and full-donor cell engraftment were established, but patient showed febrile neutropenia for several days and improved by received antibiotics appropriate with blood culture result. Disease evaluation at day 30 post-transplant and 180 days after, patient showed no evidence of leukemia by clinical features and haematology profile.

Discussion

Patient diagnosed with T-cell ALL with relaps disease, received Indonesian ALL regimen and hyper-CVAD regimen before his CR2 achieved, and underwent allogeneic HSCT followed after his CR2. Patient received the reduced intensity conditioning regimens, GVHD prophylaxis, as per local protocol and management of infection condition. Patient showed improvement showed by clinical features and haematology profile, rather than other examination such as morphology and flow cytometry, molecular studies for TCR rearrangement, cytogenetics and monitoring donor chimerism.

Conclusions

Acute lymphoblastic leukemia with high-risk features has a poor prognosis in young adults or advance age despite aggressive chemotherapy. Reduced-intensity conditioning (RIC) is a lower toxicity alternative for high-risk patients requiring HSCT, however, it has not been widely used for ALL. The outcomes of allo-HSCT for T-ALL with RIC in this patient was safe and effective.

Fludarabine-Treosulfan-Thiotepa Has Comparable Outcomes With Lesser Toxicity Than Busulfan Cyclophosphamide In Transfusion-Dependant-Thalassemia Patients Undergoing Allogeneic Stem Cell Transplant

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Topic: Hemoglobinopathies, primary immune deficiency disease and metabolic disorders
Keywords: Allograft, Bu/Cy, FTT, Thalassemia

Aims:

To study the clinical outcomes of patients with transfusion dependent thalassemia (TDT) undergoing matched sibling and matched unrelated donor allogeneic stem cell transplant (HSCT) and compare the clinical outcomes (including toxicity and survival outcomes) between patients receiving two different conditioning regimens [Busulfan/Cyclophosphamide (Bu/Cy) and Fludarabine/Treosulfan/Thiotepa(FTT)].

Methods:

69 patients with TDT undergoing HSCT from a HLA-matched (sibling and unrelated) donor between Jan 2012 to December 2022 were analysed. Categorical and continuous variables were presented as counts (with respective percentages) and median (with range) values, respectively. Overall survival (OS) was defined as the time from transplant to death. GVHD-free Transfusion-free Survival (GTFS) was analysed as a composite end-point. The events in GTFS included acute GVHD grade 3-4, extensive chronic GVHD, onset of regular transfusion and death. Kaplan-Meier product-limit-estimate was used to calculate OS and GTFS. Log-rank test was used to compare the outcomes between the conditioning regimens. Transplant related mortality (TRM) was defined as death due to a transplant-related cause other than relapse. Competing event analysis was used for calculating TRM and the Fine-Gray test was used to compare the outcome between conditioning regimens. For the statistical analyses, $p < 0.05$ was considered significant.

Results:

27 patients underwent conditioning with Bu/Cy and 42 with FTT. The FTT cohort had a higher median age (9.5 Vs 5, p <0.001) and more patients in Pesaro Class III [including Very High Risk (VHR)] (26.2 vs 7.4, p:0.002). Peripheral blood stem cell (PBSC) graft was the predominant graft source in the FTT cohort (97.6 Vs 11.1, p<0.001). More patients in the FTT group received graft from a matched unrelated donor (28.6 vs 3.7, p<0.001). In spite of this, rATG use as a GVHD prophylaxis was lesser in the FTT cohort (45 Vs 100, p<0.001).

Clinical outcomes were mostly comparable across the two regimens (Bu/Cy, FTT). There was a trend to faster platelet engraftment in the FTT group (14 Vs 20 d, p: 0.05). No pulmonary toxicity (acute or long-term) was experienced in either group. The incidence of veno-occlusive disease (VOD) was lesser in the FTT group (7.5 Vs 25.9%, p:0.004) in spite of having a higher risk cohort (Pesaro Class III and VHR group). Overall survival at 1 and 2 years was 92% (95% CI:81.9-96.6). TRM at 2 years was 7.7 % (95% CI: 2.8-15.9) with 5 (7.2%) deaths. GTFS at 1 and 2 years was 55.5% (95% CI: 42.9-66.5) with no significant difference across groups.

Conclusions

Conditioning with FTT offers comparable outcomes to Bu/Cy with lesser incidence of VOD, even in patients with high-risk categories undergoing HSCT from HLA-matched donors in TDT. This widens the ambit of patients who can undergo HSCT with minimal toxicities.

Conflict of Interest Statement:

No conflict of interest to disclose

A Case Series of Clinical Presentations, Management, and Outcomes of Hemophagocytic Lymphohistiocytosis (HLH) in A Tertiary Care Center in The Philippines

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Topic: Bone Marrow Failure Syndromes Including MDS
Keywords: H-score, HLH, HLH-2004, HSCT, Hemophagocytic Lymphohistiocytosis, stem cell

AIMS: This study aims to enhance understanding of adult Hemophagocytic Lymphohistiocytosis (HLH), a complex, life-threatening hyperinflammatory syndrome often mistaken for sepsis due to its nonspecific symptoms, which often lead to misdiagnosis and delayed treatment. By presenting a series of four diverse cases, the study offers a broadened perspective on HLH manifestations, provides insights into diagnostic challenges, and explores diverse therapeutic strategies.

METHODS: Four adult female patients aged between 23 and 67 from 2022-2023, were diagnosed with HLH based on the H-score and HLH-2004 diagnostic criteria, combining clinical presentations, laboratory findings, and bone marrow results. Underlying causes included malignancy, autoimmune disorder, infection, and chemotherapy. Upon diagnosis, immediate treatment was initiated, with therapies tailored to individual cases.

RESULTS: Three out of four patients fulfilled at least 5 out of 8 clinical and lab diagnostic criteria of HLH-2004 but all four have high probability for HLH by H-score. The clinical features and laboratory findings of patients are summarized in Table 1. Common presentations included fever, splenomegaly, cytopenia, hypertriglyceridemia, and hyperferritinemia, with hemophagocytosis evident in two patients' bone marrow smears. At time of diagnosis of HLH, two patients had underlying hematologic malignancies (pre B Cell ALL, Diffuse large B Cell lymphoma) and one had systemic lupus erythematosus in flare. The other patient also with SLE but not in flare at time of HLH diagnosis. Various treatment strategies, including induction chemotherapy, dexamethasone, and hematopoietic stem cell transplantation (HSCT), were administered upon diagnosis which can be seen in Table 2. Two patients achieved remission following HSCT, while two succumbed to the disease.

CONCLUSION: Adult HLH is frequently misidentified as sepsis due to similar clinical

presentations and laboratory results, which can impede the swift diagnosis of HLH and effective administration of immunosuppressive agents and/or chemotherapy. Utilization of HLH-2004 diagnostic criteria and the H-score proved effective in these cases, aiding in differentiating HLH from sepsis and informing treatment approaches. This case series emphasizes the urgent need for prompt recognition and accurate diagnosis of adult HLH to facilitate immediate and appropriate treatment, reducing adverse outcomes and mortality. This study also highlights the life-saving potential of HSCT, as evidenced by two patients achieving remission following the procedure. Lack of available data on the prevalence of HLH among patientscalls for future comprehensive local research and clinical trials aiming to yield robust clinical data and immunologic information to enhance understanding and effective management of this syndrome, and possible development of targeted therapies.

No conflict of interest to disclose.

The Promising Stem Cell Transplantation Outcomes in Pediatric Patients with Inherited Neutropenia and Thrombocytopenia

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Topic: Bone Marrow Failure Syndromes Including MDS
Keywords: Congenital Amegakaryocytic Thrombocytopenia, Hematopoietic Stem Cell Transplantation, Severe Congenital Neutropenia

Aims

Severe congenital neutropenia (SCN) and congenital amegakaryocytic thrombocytopenia (CAMT) are characterized as pre-malignant syndromic bone marrow failure (BMF) entities, which are genotypically and phenotypically heterogeneous. Hematopoietic stem cell transplantation (HSCT) is the only curative modality for hematologic manifestation in affected patients. We aim to evaluate the HSCT outcome in the pediatric cohort affected by SCN and CAMT.

Methods

Eight hereditary pediatric neutropenia (n = 4) and thrombocytopenia (n = 4) patients underwent HSCT at Children’s Medical Center between May 2020 and February 2023. The diagnosis was confirmed by mutation analysis consequent to the BM workup. All patients were HLA-matched in donor selection except for one case of SCN. Four patients were transplanted from siblings, while related and unrelated donors were in two patients apiece. The stem cell source was peripheral blood in all patients except for one cord blood (CB). The Fludarabine-based reduced-intensity regimen besides Melphalan and anti-thymocyte globulin was used in SCN cohorts, while the myeloablative protocol concerning Busulfan and Cyclophosphamide was utilized in CAMT patients. Patients received Cyclosporin A as a graft versus host disease (GvHD) prophylaxis regimen. In addition, SCN and CAMT patients were administered Methylprednisolone and Methotrexate, respectively.

Results

The mean HSCT age of SCN and CAMT patients was 5.6 (2 – 13) and 5.2 (1.5 – 9) years. The female-to-male ratio in each BMFS group was 1:1. The mean number of harvested MNC was 7.33 and 7.75 × 10^8 cells/kg in SCN and CAMT cohorts, respectively. Correspondingly, the mean $CD34^+$ cells of 8.73 and 5.22 × 10^6 cells/kg were grafted. All patients were efficaciously engrafted. The SCN patients ensued neutrophil and platelet on the median time of +12.5 (11 – 27) and +7 (2 – 12) days, while the CAMT cohort on +14 (11 – 26) and +10 (6 – 17) days. All SCN patients experienced acute GVHD grade I-II and III-IV in two apiece, while three CAMT patients presented grade I-II. Chronic GvHD occurred in one-fourth of the patients, one in each BMF syndrome. Approximately 60% of patients were infected by *Cytomegalovirus*, two neutropenia and three thrombocytopenia. The posterior reversible encephalopathy syndrome complication was observed in one SCN and one CAMT. Likewise, one SCN and one CAMT patient presented hemorrhagic cystitis. Throughout a median one-year follow-up, overall and disease-free survival rates were 87.5% in all patients. Septic shock was the cause of death of the SCN patient in the CB setting. In the last follow-up, GvHD- disease-free survival was 62.5% as well.

Conclusions

Although HSCT is associated with various outcomes in patients affected by inherited neutropenia and thrombocytopenia, promising HSCT outcomes exist. These data indicate full-matched related donor is the best option concerning these BMF syndrome subcategories. Furthermore, it is recommended to utilize peripheral blood SC as an appropriate source in a transplant setting.

Real-World Impact of Time From Leukapheresis to Infusion (Vein-to-Vein Time [V2VT]) in Patients With Relapsed or Refractory (R/R) Large B-cell Lymphoma (LBCL) Treated With Axicabtagene Ciloleucel (Axi-Cel)

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Topic: Cell and Gene Therapy
Keywords: Axi-Cel; CAR T-cell therapy; large B-cell lymphoma; vein-to-vein time; manufacturing

Aims: Axi-cel was associated with shorter median V2VT versus other CAR T-cell products (real-world: axi-cel, 28 days versus tisagenlecleucel, 45 days; clinical trial: lisocabtagene maraleucel, 37 days; Riedell et al. *Transplant Cell Ther*. 2022; Abramson et al. *Lancet*. 2020). Reduced wait time in JULIET was associated with increased efficacy (Chen et al. *Value Health*. 2022). Here, we assessed the real-world impact of V2VT on outcomes with axi-cel in R/R LBCL.

Methods: Patients treated with commercial axi-cel for R/R LBCL between October 2017-August 2020 were identified from a non-interventional post-authorization safety study using the CIBMTR registry. Reasons for patient exclusion are shown (**Table 1**). Effectiveness outcomes were overall and complete response rates (ORR and CR rates), duration of response, progression-free survival, and overall survival (OS). Key adverse events included cytokine release syndrome (CRS; Lee et al. *Blood*. 2014), immune effector cell-associated neurotoxicity syndrome (ICANS; ASTCT grading), and prolonged neutropenia and thrombocytopenia. Odds and hazard ratios were estimated using logistic and Cox regressions after adjustment of key prognostic factors (**Table 2**). Adjusted curves were generated based on direct adjusted survival function (Makuch et al. *J Chronic Dis*. 1982).

Results: In total, 1383 patients from 78 US centers were included. Median V2VT (time from leukapheresis to infusion) was 27 days (IQR, 26-32), including a median of 5 days (IQR, 5-5)

from start of lymphodepleting chemotherapy to infusion. V2VTs were consistent regardless of disease histology, sex, race, ethnicity, ECOG performance status before infusion, or chemosensitivity. Patients with shorter V2VTs were younger and less likely to have comorbidities (**Table 1**). Patients with ±40-day V2VT were more heavily pretreated and more likely to have received bridging therapy.

At 24.2-months median follow-up, better outcomes were observed in patients with shorter V2VTs. CR rates were 60%, 61%, and 50% (ORR 77%, 77%, and 70%) for patients with V2VT of <28, ±28 to <40, and ±40 days, respectively. OS at 24 months was 53% for patients with V2VT of <28 and ±28 to <40 days versus 38% for ±40 days. After adjustment, patients with ±40-day V2VT had significantly lower CR rates and OS versus patients with <28-day and ±28 to <40-day V2VT (**Table 2; Figure 1**).

Any-grade or Grade ±3 CRS and prolonged neutropenia were consistent regardless of V2VT. Patients with <28-day versus ±28 to <40-day V2VT had more frequent any-grade ICANS; Grade ±3 ICANS was not significantly different between these groups (**Table 1**). Among patients alive at Day 30, those with ±28 to <40-day and ±40-day V2VT had higher rates of prolonged thrombocytopenia versus those with <28-day wait time.

Conclusions: In this real-world analysis, most patients received axi-cel within 5 weeks after apheresis. Shorter V2VT was associated with favorable CR rate, OS, and reduced risk of prolonged thrombocytopenia; however, risk of any-grade ICANS may be higher. Overall, these findings highlight the importance of shortening V2VT in patients treated with axi-cel.

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Beyond the Marrow: Strategic Approaches to Stem Cell Mobilization in Multiple Myeloma Therapeutics for Optimal Outcome

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Abstract ID: 172
Event: 28th Annual Meeting of APBMT
Topic: Cell and Gene Therapy
Keywords: Multiple myeloma, autologous stem cell transplantation., stem cell mobilization

Background

Autologous stem cell transplantation (ASCT) is a critical therapeutic modality in multiple myeloma (MM). Successful ASCT relies on efficient stem cell mobilization to ensure an adequate yield of hematopoietic progenitor cells. However, achieving optimal mobilization in MM patients can be challenging due to disease-related factors and prior treatments. This case report aims to demonstrate stem cell mobilization protocol in achieving optimal hematopoietic stem cell yield and successful engraftment in MM patients undergoing ASCT.

Case Presentation

A 42-year-old female was diagnosed with multiple myeloma in 2021. The patient underwent induction chemotherapy with thalidomide and dexamethasone for 6 cycles and achieved complete response (CR). Treatment was continued with an ASCT. In this patient, the mobilization process involved administering mobilization chemotherapy with Vinorelbine 25mg/m2 (on day 1), along with Cyclophosphamide 1500 mg/m2 and Uromintexan 1500mg/m2 (on day 2), followed by the administration of granulocyte-colony stimulating factor (GCSF) injections from day 4 to day 12. The mobilization process was intended to obtain a sufficient number of hematopoietic stem cells from the peripheral blood, with a CD34+ target of > 15 cells/µl. Once the CD34+ count reached the target, stem cell harvesting was performed through apheresis process. For the Peripheral Blood Stem Cell Transplantation (PBSCT) process, the required CD34+ cell count was 2-5 x 106 cells CD34+/kg of the patient's body weight. In this case, the CD34+ target was achieved on days 9 and 10 after mobilization chemotherapy, with CD34+ counts of 26,530 cells/µl and 107,933 cells/µl, respectively. CD34+ counts of 1.97x10^6/kg body weight and 5.02x10^6/kg body weight was obtained. This might have been caused by insufficient flow during the harvest process with the apheresis machine. After the stem cell collection

process, cryopreservation was carried out, and the cells were stored in a container containing liquid nitrogen at a temperature of -196^{o}C. During the cryopreservation process, samples were taken for CD34+ examination and culture testing.

Discussion:

The mobilization process is a crucial step in ASCT, showcased a strategic protocol involving a combination of Vinorelbine, Cyclophosphamide, Uromintexan, and granulocyte-colony stimulating factor (GCSF) injections. This approach is aimed at achieving a suitable quantity of hematopoietic stem cells from the peripheral blood, with a specific CD34+ cell count target. The successful achievement of the CD34+ target after mobilization chemotherapy, resulting in significant counts of 26,530 cells/µl and 107,933 cells/µl on days 9 and 10, respectively, demonstrated the meticulous planning and execution of the mobilization process. In this case, engraftment was achieved on the 10th day after ASCT administration.

Conclusion

The presented case demonstrates the intricate interplay of various therapeutic modalities, including chemotherapy, stem cell mobilization, transplantation, and cryopreservation, in the comprehensive management of MM. Optimal vascular access during the harvesting procedure significantly contributes to the effectiveness of the overall process. The success of the engraftment process during ASCT depends on the number of stem cells harvested during mobilization.

Abstract: Recent Advances in Chimeric Antigen Receptor (CAR) T-Cell Therapy

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Abstract ID: 217
Event: 28th Annual Meeting of APBMT
Topic: Cell and Gene Therapy
Keywords: CAR T-cell therapy, Gene therapy, advancements

Abstract: Recent Advances in Chimeric Antigen Receptor (CAR) T-Cell Therap

Aims: This abstract aims to present the recent advancements in chimeric antigen receptor (CAR) T-cell therapy and their promising outcomes in treating various cancer types, including primary brain tumors, hematological malignancies, and solid tumors.

Methods: We have reviewed the recent scientific literature of innovative approaches within CAR T-cell therapy. Multi-antigen targeting strategies have been developed to address challenges posed by certain malignancies, allowing simultaneous targeting of multiple antigens. Universal CAR-T cell therapy has been explored, involving the design of CARs capable of targeting a diverse array of tumor antigens. Safety and efficacy improvements encompass optimization of manufacturing processes, enhancing CAR-T cell persistence and proliferation, and minimizing treatment-related toxicities. Additionally, methods to overcome obstacles in treating solid tumors, such as the tumor microenvironment and tumor-associated antigens, are being investigated.

Results: Noteworthy advancements in CAR T-cell therapy include the development of multi-antigen targeting strategies, enabling improved treatment efficacy for challenging malignancies. Universal CAR-T cell therapy offers adaptability in target selection, enhancing the therapy's versatility. Safety and efficacy enhancements have been achieved through optimized manufacturing, augmented CAR-T cell attributes, and toxicity reduction. The expansion of CAR T-cell therapy to solid tumors reflects recent successes, as researchers innovate to overcome hurdles related to the tumor microenvironment and antigens.

Conclusions: Recent strides in CAR T-cell therapy underscore its evolving significance in cancer treatment. Multi-antigen targeting, universal CAR-T cell therapy, safety and efficacy improvements, and the extension to solid tumors collectively highlight the field's potential to revolutionize cancer care. Ongoing research and clinical trials contribute to refining therapeutic outcomes, fostering optimism for more effective and precise treatments for cancer patients. The dynamic nature of CAR T-cell therapy signifies its ongoing evolution as a beacon of hope in the realm of cancer therapeutics.

DETECTION OF JAK2 V617F MUTATION IN MONGOLIAN PATIENTS WITH MYELOPROLIFERATIVE DISEASES

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Event: 28th Annual Meeting of APBMT
Topic: Basic Science
Keywords: Gene mutation, Genetic diagnosis, Janus kinase 2, Myeloproliferative disease

Aims: The myeloproliferative disease (MPDs) comprise a group of clonal stem cell disorders associated with a high prevalence of mutations in JAK2 and overproduction of mature blood cells. According to the Surveillance, Epidemiology, and End Results program of the National Cancer Institute, the high-range estimate is that ~20,000 people get an MPDs each year and there are ~295,000 people living with an MPD in the United States. In our country, the number of MPDs also tends to increase slightly in the last few years.

Janus kinase 2 (JAK2) is located on chromosome 9p24, and its structure is highly homologous with associates of the JAK family. Epidermal growth factor, platelet-derived growth factor, colony-stimulating factor, interleukin 3, and erythropoietin mediate cell proliferation, differentiation, and apoptosis via the JAK2 signal transduction pathway. JAK2 (V617F) is a kind of mutation called a point mutation that replaces the reference amino acid valine (abbreviated V) with phenylalanine (abbreviated F). As a result of this mutation, JAK2 is constitutively activated leading to uncontrolled cell growth. Therefore, the JAK2 mutation important diagnostic tool for the detection of MPDs. The JAK2 (V617F) mutation is the most common somatic mutation in the classical MPDs, present in >95% of cases of polycythemia vera (PV) and ±50% of essential thrombocythemia (ET) and myelofibrosis (MF). It is so challenging to cytogenetics and molecular genetics into clinical practice in developing countries. The present study aimed to investigate the detection of the JAK2 (V617F) mutation in patients with MPDs in Mongolia.

Methods: This study was performed in Mongolia. A total of 41 patients referred to The First Central Hospital of Mongolia from 2022-2023 with symptoms of MPDs were included in the study. We studied by comparing some laboratory results and clinical symptoms. Real-time Polymerase Chain Reaction (RT-PCR) was used to detect the presence of the JAK2 (V617F) mutation in the genomic DNA isolated from the patient peripheral blood samples.

Results: The study gender ratio is male/female is 9/32, and the median age is 54.4 (25-74). Of the 41 patients with MPDs, approximately 23 (56%) patients were positive for the JAK2 (V617F) mutation. Cases number and percent Polycythemia Vera n=16 (39%) was the most common MPD, followed by Essential Thrombocythemia n=13 (31.7%), Primary

Myelofibrosis n=10 (24.4%) and Chronic Myeloid Leukemia (CML) n=2 (4.9%). JAK2 (V617F) gene-positive incidence of diagnosed PV n=13(81.25%), ET n=5 (38.5%), and MF n=5 (50%). The relationship between age among all types of MPDs was not significant.

Conclusions: Of the examined cohort in Mongolia, 55% of the patients with MPNs were found to have the JAK2 (V617F) mutation which determines the presence of the JAK2 (V617F) mutation helps to decide the correct form of treatment and diagnostic criteria. In addition, we necessary to check TET2, NFE2, MPL, and BCR-ABL gene mutations by reason of important differential diagnoses by disease. Besides, We will have many opportunities to use new therapeutic target agents in our country.

Src Family Kinase Inhibitor Enhances Cell Death of the Anti-myeloma Agents via Activating Apoptosis

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Abstract ID: 56
Event: 28th Annual Meeting of APBMT
Topic: Basic Science
Keywords: Apoptosis, Multiple myeloma, Src

Aims

In multiple myeloma (MM), it has been described that in cell lines and MM patient-derived tumors, c-Src is constitutively activated. This constitutive activation of c-Src promotes cell survival, proliferation, and chemoresistance, and then inhibition of Src activation enhances chemosensitization. There are a few basic studies on multiple myeloma with Tris (Dibenzylideneacetone) dipalladium (Tris DBA) and dasatinib.

In this study, we investigated whether Src family kinase inhibitor PP2 enhances the effect of the currently used medications for multiple myeloma.

Methods

We treated MM cell line (ARH77) with clinically active agents alone of MM treatment, PP2 (5 uM), and combinations: bortezomib (5 nM), lenalidomide (1.5 mM), dexamethasone (20 uM), PP2, bortezomib plus PP2, lenalidomide plus PP2, and dexamethasone plus PP2.

Results

We found that the combination of PP2 with bortezomib, lenalidomide, or dexamethasone decreased the surviving fraction of MM cells more than each the drugs alone (Figure 1). Treatment of ARH77 cells with PP2, bortezomib, lenalidomide, and dexamethasone alone resulted in 73%, 84%, 79%, and 71% of cell viability, respectively. PP2 combined with bortezomib, lenalidomide, or dexamethasone showed in 57%, 50%, and 41% of cell viability,

respectively. These results suggested that PP2 suppress the MM cells proliferation.

We then tested the effect of PP2 on apoptosis of MM cells (Figure 2). Caspase 3 is a critical executioner of apoptosis. The expression of cleaved caspase 3 was increased when cells treated with bortezomib plus PP2, lenalidomide plus PP2, and dexamethasone plus PP2 than treated alone. It suggests PP2 enhance the induction of apoptosis by bortezomib, lenalidomide, or dexamethasone in MM cells.

Conclusions

PP2, Src inhibitor have been shown to increase the effectiveness of anti-myeloma drugs (ie. Bortezomib, lenalidomide, dexamethasone) and increased apoptosis more than each drug alone. These results suggest the combination of PP2 with anti-myeloma agents may be beneficial as a new therapeutic option in treatments of MM.

Prevention and Nursing of Hemorrhagic Cystitis in the early stage of Hematopoietic Stem Cell Transplantation pretreatment in children with severe β-Thalassemia

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Abstract ID: 10
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Hematopoietic Stem Cell Transplantation Severe β-Thalassemia Hemorrhagic Cystitis Nurse

Aims Exploring Prevention and nursing of hemorrhagic cystitis in the early stage of hematopoietic stem cell transplantation pretreatment in children with β-thalassemia major

Methods In the early stage of hematopoietic stem cell pretreatment, a large amount of uniform fluid infusion was carried out, and the cardiopulmonary function was monitored at the same time. 30 minutes before the application of Cyclophosphamide, 1/5 dose of Mesna was applied intravenously, while Cyclophosphamide was applied, Mesna was infused for continuous detoxification, etc. The alkalized diuretic intravenous fluid infusion was carried out 4~6 hours before the injection of Cyclophosphamide, so that the Cyclophosphamide metabolite Acrolein was fully excreted in kidney urine, and the 24-hour intake and output were accurately recorded, Ensure the balance of intake and output, give Diuretic Furosemide according to the intake and output of children, keep the urine at 100~150ml/h, observe the urine volume, urine color, urination symptoms, and monitor the electrolyte supplement in time.

Results Among the 102 patients, 14 were clinically diagnosed with HC and 3 were suspected of HC, all of which were delayed onset HC. After symptomatic treatment with hydration and alkalization according to medical advice, all were cured, and the blood count returned to normal and transferred out of the laminar flow chamber.

Conclusions During the nurse's pre-treatment period, measures such as fluid replacement, alkalization of urine, and effective detoxification to ensure timely discharge of urine can better prevent the incidence of HC during transplantation in children, alleviate their pain, and create conditions for successful transplantation.

An overview of Clinical Pharmacy Services for Bone Marrow Transplant Patients Receiving Melphalan Therapy at Dr. Kariadi Hospital, Semarang, Indonesia

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Abstract ID: 34
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Bone marrow transplant, Clinical Pharmacy, Melphalan

Abstract

Introduction: Bone Marrow Transplant (BMT) is a procedure to replace damaged blood cells with healthy ones that can be used to treat conditions affecting the blood cells, such as leukaemia and lymphoma. Melphalan is a widely used agent in conditioning regimens prior to BMT and it is the mainstay-conditioning drug for multiple myeloma (MM) and lymphomas. The aim of this study is to provide an overview of clinical pharmacy services in general for CST patients who receive Melphalan therapy at Dr. Kariadi Hospital, Semarang.

Methods: The study was conducted from January 2022 to July 2023 at the Oncology Installation of Dr. Kariadi Hospital. CST patients receiving Melphalan therapy are monitored and evaluated for drug-related problems (prescription and protocol review, drug availability, interactions, side effects, drug preparation, and administration).

Results: A total of 12 CST patients with diagnoses including Multiple myeloma (9 patients), Acute myeloid leukemia (1 patient), Acute lymphocytic leukemia (1 patient), and Lymphoma (1 patient) who received Melphalan therapy were monitored during the study. Review prescriptions and protocols (administrative, pharmaceutical, and clinical), as well as drug therapy training conducted for all patients. A management review and assurance of the availability of Melphalan was carried out for each patient before receiving therapy. Of these, 83.33% received education regarding treatment information directly from the clinical pharmacist; prescription and protocol discrepancies (drug dosage, duration of administration, drug administration restrictions, and completeness of the protocol) by 75%; and 8.33% related to drug side effects.

Conclusion: The clinical role of pharmacy on BMT service contributed to improved patient care dan safety and management of drug-related problems in CST patients receiving melphalan.

The Effects of Oral Cryotherapy on Chemotherapy-Induced Oral Mucositis in Patients Undergoing Bone Marrow Transplantation: A Systematic Review

by Yuswinda Kusumawardhani | RSUP Dr. Kariadi Semarang

Abstract ID: 72
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Bone marrow transplantation, Chemotherapy, Oral cryotherapy, Oral mucositis

Background: Oral mucositis is known to be a frequent and challenging side effect in patients with chemotherapy in bone marrow transplantation. These side effects cause a decrease in quality of life, delay treatment plans, and increase treatment costs. Some literature states that oral cryotherapy has been scientifically proven as a non-pharmacological therapy to reduce the incidence of oral mucositis.

Aims: The purpose of this research is to do systematics literature review and examination of the effectiveness of oral cryotherapy in reducing the incidence of oral mucositis in patients with haematological malignancies under chemotherapy management undergoing bone marrow transplantation.

Methods: A systematic literature search was performed, using the PubMed, Embase, MEDLINE electronic databases and Scopus. A total of 342 papers were identified from 2003 to 2023, and 8 papers were analyzed according to established inclusion and exclusion criteria. Study quality was assessed using the COCHRANE risk bias assessment tool.

Results: Eight randomized controlled trials, analyzing 609 participants; control group (n = 266, mean age ± SD; 41.15 ± 21) and treatment group (n = 343, mean age ± SD; 39.15 ± 20), and the majority were both male in the control group and the treatment group in this systematic review. Seven of the eight studies reported significant effectiveness (p value <0.05), of oral cryotherapy, in reducing the incidence of oral mucositis in the adult population undergoing bone marrow transplantation, especially the regimen protocol including an alkylating agent (melphalan).

Conclusions: This review supports the use of oral cryotherapy for the prevention of oral mucositis in patients undergoing bone marrow transplantation, on the high-dose melphalan protocol. It is recommended that more studies be conducted to compare the effectiveness of oral cryotherapy with other chemotherapeutic agents. The heterogeneity of the trials demonstrates the need for an assessment tool and standardized oral cryotherapy duration for better comparison and analysis of treatment effects based on RCTs.

No conflict of interest to disclose

Efficacy and Safety of Double Lumen Femoral Venous Catheters in Pediatric Peripheral Blood Stem Cell Harvest-An Experience from a New Stem Cell Transplant Centre

by Soumya J | DM Pediatric Oncology Fellow

Abstract ID: 75
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: femoral vein; vascular access; dual lumen polyurethane catheter; PBSC collection.

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Introduction: Pediatric Peripheral Blood Stem Cell (PBSC) harvest is being increasingly performed for many benign hematology diseases, hematolymphoid and solid malignancies. Central Venous Catheter (CVC) with high flow rate is one of the basic necessities. Many centers typically use a femoral sheath and a Peripherally Inserted Vein (PIV)catheter for performing apheresis. There is scant published data regarding the performance and safety of double lumen femoral CVCs in pediatric PBSC which has been traditionally discouraged due to the high incidence of infection rates, thromboembolic complications and belief of low stem cell yield due to mixing of inflow and outflow blood.

Methods: This is a retrospective observational study of PBSC harvests performed in pediatric patients (<15 years) from December 2021 to June 2023 in a state-run autonomous government hospital- Kidwai Memorial Institute of Oncology (KMIO).The efficacy and safety of 23 short-term double lumen polyurethane femoral CVC used for the PBSC was evaluated.

Results:

There was a total of 23 patients with male to female ratio 2:1 with a mean age of 8 years. A total of 38 apheresis procedures were performed. The target CD 34 cell count was kept 6-10 X 10^6 cells/kg body weight.52 % of patients achieved this target or above in only 1 session, 26 % achieved in 2 sessions,17% in 3 sessions and only 1 required 4 sessions for achieving the target count. 11(50%) cases were refractory /progressive Hodgkin lymphoma and11 (50%) were High Risk Neuroblastoma and 1 case was a relapsed Wilms tumor. The average

CD 34 cell count per session was 9.3 X 10^{6} cells/kg and the inlet flow rate was >0.7ml/kg/min in 94 % of cases. The flow related Adverse Events (AE) was documented in 17% cases. There were no insertion-related complications, no infection or thrombosis documented. CVC removal was uneventful in all the cases.

Conclusion: The short-term use of standard dual lumen femoral venous catheters appears safe and effective for PBSC collection, simplifying the procedure, improving patient comfort, and reducing the cost.

Keywords : femoral vein, vascular access,dual lumen polyurethane catheter,PBSC collection, stem cell harvest

Unmet Needs of Pediatric Hematopoietic Stem Cell Transplantation in a Tertiary Government-run Hospital in State of Karnataka, India

by Vasundhara Kailasnath and Lokesh C Rajole | Master of Social Work

Abstract ID: 76
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Keywords : unmet needs, Pediatric HSCT, financial constraint, parental awarenes

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Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is curative treatment for many life threatening benign and malignant diseases. An estimated 2500 HSCTs are performed annually in India as per Indian Society of Blood and Marrow Transplantation (ISBMT) 2021 data. In India, most of these HSCTs happened in private sector run hospitals. Kidwai Memorial Institute of Oncology (KMIO), is an autonomous State-run Government hospital which is one of its kind offering Pediatric HSCTs in public sector in Bangalore, Karnataka, India.

Aims: The purpose of this study is to quantify the demand and unmet needs of HSCT in a newly set up Bone Marrow Transplantation unit in a tertiary Government-run hospital in the state of Karnataka, India.

Methods: We collected demographic, diagnostic and disease related data from patients enrolled during the period of April 2022 till March 2023 (financial year) at KMIO, to get an accurate estimation of pediatric patients requiring HSCT.

Results: A total of 119 patients registered at KMIO, between the period of April 2022 till March 2023, 31.93% were females.

Allogenic Vs Autologous Transplant: Out of the total 119 pediatric HSCT patients registered at KMIO Pediatric BMT Unit, 71.5% (85) required Allogenic HSCT and 28.5 % (34) required Autologous HSCT.

Disease distribution: 77.31% (92 cases) out of 119 total cases were malignant diseases like high risk Neuroblastoma, high risk Medulloblastoma, relapsed Wilm’s Tumor, relapsed Acute Lymphoblastic Leukemia (ALL), relapsed Acute Myeloid Leukemia (AML) and Chronic

Myeloid Leukemia (CML). The benign diseases (27 cases) requiring HSCT comprised of Beta- Thalassemia Major, Aplastic Anemia, Fanconi Anemia, Leucocyte Adhesion Deficiency and Congenital Adrenoleucodystrophy.

Educational Qualification of Parents: 70.6% of parents have secondary level of education,10.92% of parents are uneducated and 4.2% of parents have graduation level of education. (Figure 1)

District wise distribution: Bangalore stands higher with 21.84 % of patient population and Kalaburagi stands second with 7.5%. (Figure 2) 84 % of the patients were from the State of Karnataka and another 16 % from other states.

73.95% of the patients belong to low income (< Rs. 15,000 per month) and only 1.68% belonged to high income (>Rs. 30,000 per month).

Out of the 119 eligible patients registered for HSCT, only 13(10 %) underwent HSCT and all the 13 (100 %) patients underwent autologous HSCTs. Amongst the 106 children waiting for HSCT, 10 (11%) patients expired due to disease relapse and 15 (14) patients were lost to follow up.

Conclusion: Though, this is the data from a new HSCT center spanning over one year, it clearly indicates a huge unmet need of HSCT in economically poor background patients hailing from the state of Karnataka, India. The main drawback for the reception of HSCT is the financial constraint and lack of parental awareness.

The Comparative Analysis of Knowledge Before and After in Blood and Marrow Transplantation Training at Kariadi General Hospital Semarang

by Sri Setyowati | Setyo Budi Raharjo | Emi Tsuwaibah | Sriyani | Kariadi General Hospital Semarang Indonesia | Tugurejo General Hospital Semarang Indonesia | Kariadi General Hospital Semarang Indonesia | Kariadi General Hospital Semarang Indonesia

Abstract ID: 99
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Comparative analysis, blood and marrow transplantation, knowledge, training

Introduction:

Blood and Marrow Transplantation (BMT) is one of therapy used to patients that potentially can provide a long term treatment variety of diseases. In Indonesia based on Pusdatin data has not been found. At Kariadi General Hospital, the prevalence of blood and marrow transplantation during period 2017 until 2022 is 21 patients consist of 76.2% autologous and 23.8% allogeneic. The success rate number of engrafment is 90.5% and the survival rate more than 1 year is 57.1%. Blood and marrow transplantation team has been formed consisting of various health professions. But currently the entire hospital workers has not been able to understood about blood and marrow transplantation. A preliminary study of 10 hospital workers showed that 5 out of 10 did not know about blood and marrow transplantation.

Aims and Method:

This study aims to know value pre and post test trainees blood and marrow tranplantation trainning. This study also to know differences of both pre and post test. This study uses a quasi experimental method with design one group pretest-posttest design. The research was conducted July 2023, located at Kariadi General Hospital. The sampling technique is total sampling. The subjects that were obtained 35 trainees. Subject will given tests before and after treatment/training. Data collected through questionnaires/knowledge test with multiple-choice answer. Knowledge is defined as ability to answer question on pre and post test questions with correct answer. Respondents given the same questions before and after training in accordance with knowledge. The complete data tested normality by Shapiro-Wilk test, next data distributed normally then followed by test statistics inferential with paired T test. In processing pre-test and post-test, researcher use tool analysis data that is program device SPSS software 23.

Results:

Amount participants in this study were 35 trainees. All of participants do the knowledge test

in a manner completed and 35 samples can be analyzed. The result showed pre test assessment prior to training was carried out test scores between 40-77. The result of post-test is between 83 – 100. From the normality test, it was found that the data distributed normal so that used paired T-test. The median value of pre-test score is 61.03 and the post-test score is 91.74. It can be seen that the average value achievement is 91,74. There is none training participants has decrease score before and after doing training. This means that all of trainees increase their knowledge. The knowledge score nothing remain between before and after training. Analysis comparison knowledge result in pre-test and post-test states that *p-value* is 0.000, it is means that value of $p < 0.005$.

Conclutions:

There are significant differences in trainees knowledge before and after blood and marrow transplantation training. For the future research can analyse of differences in knowledge regarding blood and marrow transplantation of trainees can be continued to add variables characteristics of the participants and other factors including level of education, knowledge, occupation (profession), experience, age and interests.

The psychological impact of hematopoietic stem cell transplantation on children and adolescents: a prospective single-arm study from a pediatric blood and marrow transplantation unit in India

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Abstract ID: 101
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: GAD-7, HSCT, PHQ-9, Psychiatrist, Psychological

Background

The psychological impact for children and young people undergoing hematopoietic stem cell transplantation (HSCT) is high. Assessment of their emotional health needs is essential for optimal treatment outcomes. We present prospective data on the extent of depressive and anxiety symptoms in those undergoing HSCT using a uniform questionnaire.

Patients and methods

We used a prospective design and collected data from children and young people who underwent HSCT via in-person interviews from December 2022 to July 2023. The questionnaires used were patient health questionnaires (PHQ-9) and generalized anxiety disorder (GAD-7). For PHQ-9 the scoring system included 5-9 as mild, 10-14 as moderate, 15-19 as moderately severe, and 20-27 as severe. For GAD-7, the scoring included 5-9 as mild, 10-14 as moderate, and 15 and above as severe. We initiated referral to a child psychiatrist for counseling with score in moderate range and started medication on children rated severe. We included demographic data particularly socioeconomic status based on the Kuppuswamy score and type of family – nuclear versus joint. The study was approved by our Hospital Ethics.

Results

Forty children and young people from the ages of 5 years to 18 years of age were assessed. There were 23 males and 17 females (male: female 1.3:1). Twenty-four children (60%) were between 5 to 10 years of age, while 16 (40%) were above ten years of age. Twenty-seven children (67%) had non-malignant disorders, while 13 (33%) had malignant disorders. Based

on the Kuppuswamy socioeconomic scale, the distribution in the cohort was upper lower 16 (40%), lower middle 12 (30%), upper middle 6 (15%), lower 5 (12%), and upper 1. None of the families were separated, 37 (92%) were nuclear families, and 3 (8%) families were joint. Twenty-six children had siblings (65%), while 14 (35%) were the only children in the family.

Based on the PHQ-9 scores, 12 (30%) each had mild and moderate depressive symptoms, and 6 (15%) each had moderately severe and severe symptoms. Based on GAD-7 scores, 9 (22.5%) had minimal anxiety symptoms, 13 (32.5%) had mild symptoms, 12 (30%) had moderate symptoms, and 6 (15%) had severe symptoms. Moderate symptoms were more common in the 5–10-year age group (33%), compared to moderately severe being more common among those above ten (37%). Most families belonged to the upper-lower scale in moderate and severe categories. Among those with siblings, symptoms were predominantly moderate (34%); while among those who were a single child, the majority had mild symptoms (35%).

Conclusion

This study shows that children and young people undergoing HSCT have a significant psychological need for depressive and anxiety symptoms. Those with minimal and mild symptoms can be offered self-help strategies and distraction techniques to help manage their distress. Those with higher levels of depressive and anxiety symptoms found it challenging to engage with the care team and treatment offered. They were highlighted to the Psychiatrist within the team and needed psychological support and medication.

Hypertension in children less than five years of age undergoing hematopoietic stem cell transplantation: challenges in monitoring and management

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Abstract ID: 114
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: HSCT, Hypertension, PRES, Seizures

Introduction

We present data on incidence and nursing management of hypertension in children less than five years of age undergoing hematopoietic stem cell transplantation (HSCT).

Patients and methods

A retrospective study was conducted in children up to five years of age who underwent HSCT from January 2020 to December 2022. Hypertension was defined as per guidelines and anti-hypertensives were introduced if consistently above 50th centile and were escalated if more than 95th centile. We administered the medications in a timed manner through a nasogastric tube starting with nifedepine initially followed by enlapril. Subsequent antihypertensives included oral prazosin and clonidine. Sodium nitroprusside and labetolol were used as intravenous infusions if the hypertension was refractory. All children were on prophylactic levetiracetam till Day 28.

Results

A total of 157 children, 68(43%) being <1 year of age with inborn errors of immunity being the most frequent diagnosis. Hypertension was documented in 70 (44%) children, 16/70 (22%) of these being less than 1 year of age. Thirty-six (51%) children required enalapril and nifedepine combination. 17% required four antihypertensives including clonidine and prazosin, all being <1 year of age. Sodium nitroprusside infusion was required in 7%, and three infants (1.9%) children had seizures. None of the children required intubation for hypertension or seizures and there was no mortality directly related to the above event.

Conclusion

Hypertension can be frequently documented in children less than five years of age undergoing HSCT with infants being particularly vulnerable to developing seizures. Compliance to antihypertensive dosages can be challenging and strict monitoring is required to ensure timely administration of antihypertensives. Nursing interventions include strict adherence to antihypertensive timings administered through a nasogastric tube. Early institution of sodium nitroprusside can help decrease progression to seizures. A seamless communication with the physician team is essential to improve survival.

Role of N- Acetyl cysteine infusion in reducing the severity of mucositis in children with Fanconi anemia undergoing hematopoietic stem cell transplantation

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Abstract ID: 116
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Fanconi, HSCT, Mucositis, NAC

Background

Hematopoietic stem cell transplantation (HSCT) is the curative option for bone marrow failure in Fanconi anemia (FA). Children with Fanconi anemia have the underlying DNA breakage repair defect and more prone for regimen related toxicity even with the reduced intensity conditioning. Anti-oxidants like N- acetyl cysteine infusion helps in scavenging the free radical damage.

Aim of our study

To analyze the effect of N-acetyl cysteine (NAC) infusion in children with FA undergoing HSCT with respect to mucositis and pain relief.

Patients and methods

We conducted a retrospective analysis in our bone marrow transplantation unit and included children with FA who underwent HSCT between January 2015 and September 2022. N- Acetyl cysteine infusion was given at the dose of 10mg / kg / day as a continuous infusion from Day +3 till discharge. Cohort 1 included children who underwent HSCT without the use of NAC and Cohort 2 with concomitant NAC infusion. We documented the grade of mucositis and the need for analgesia and parenteral nutrition in these children from nursing chart reviews.

Results:

Results are enlisted in table 1 as below.

Conclusion

N-Acetyl cysteine infusion helps in reducing the severity of mucositis in the form of pooling of salivary secretions and airway obstruction and hematochezia in all children. The duration of analgesics requirement and parenteral nutrition was lesser in the NAC cohort. We have therefore included NAC in all children with Fanconi anemia.

Evaluate the knowledge of nurses on management extravasation

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Abstract ID: 134
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Nil

Research ABSTRACT

A study to evaluate the knowledge of nurses on management extravasation with chemotherapeutic drugs in a tertiary cancer Care hospital.

Objectives: The objective of the study was, to assess the existing knowledge and Practice of staff nurses on management of extravasation.

PURPOSE:

1.To evaluate the knowledge of nurses on management of extravasation with chemotherapeutic drugs.

BACKROUND: Chemotherapy Constitute one of the treatment modality in cancer management. Nurses play a significant role in administration chemotherapy. The process of administration, though safe significant complications relatively rare does occur which impair the quality of life in individuals. Hence this study was done to evaluate the knowledge of the nurses on management of extravasation.

Methodology: A Descriptive exploratory research approach using a structured questionnaire administered to participants. Consecutive sampling was used. Data was analysed using consequent sampling score >=9/10 was considered as acceptable.

Results: Questionnaire was administered to a total of 15 participants. Statistical interpretation revealed that the mean age of participant was 31 years(min 24 yrs,max 39 yrs)The Median of experience of participants administering chemotherapy was 7 years. Around 26.6%had a score >9 while53.3% had a score between 7-8and 20% of participant had a score between 4-6

Conclusion: Implementation of effective management strategy in the event of extravasation by nurses add to the quality of life in patient.

NURSING IMPLICATION: Ongoing Training is an essential need for nurses in practice to counter the adverse effect of extravasation.

The Characteristics of Patients with Peripheral Blood Stem Cell Transplantation At Dr. Kariadi General Hospital

by Catur Wijayanti | RS Kariadi Semarang

Abstract ID: 176
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: Description, RSU P Dr Kariadi Semarang, peripheral blood stem cells

Aims :

Dr. Kariadi General Hospital has several excellent services including Bone Marrow Transplantation or Hematopoietic Stem Cell Transplantation (HSCT). It can be done by using both bone marrow and peripheral blood stem cell transplant (PBSCT). PBSCT has been done since 2016 at Dr. Kariadi General Hospital, Semarang.

This study described the patients' characteristics who underwent HSCT through peripheral blood stem cell transplant from 2016-2023 at Dr. Kariadi General Hospital Semarang, Indonesia.

Methods :

This study was a quantitative research non-experiment with a design retrospective analysis. Data or sample was taken with a total sampling are 35 patients. Data analysis by describing the criteria or group.

Results :

The result of the study describes that there was a significant increase in the number of peripheral blood stem cell transplants taken though there was a sharp drop in 2020 because of the COVID-19 pandemic. Most of the diagnoses are Multiple Myeloma (60%), then Lymphoma at 34.29 %, and only one patient (2,86%) both with Neuroendocrine Tumor and Leukemia.

Most range ages are at 46-55 years (31%) then followed by 20% at range age 56-65 years, then adolescents (23%), adults (20%), and no children (0 %). The gender of the patients consists of 54% male and 46% who have undergone hematopoietic stem cell transplantation

through peripheral blood stem cell transplantation.

Conclusions :

The data we present is based on documentation conducted by the Peripheral Blood Stem Cell Transplant Team (PBSC) Dr. Kariadi from 2016 to July 2023. The data we present is in the form of patient characteristics based on the number of actions, diagnoses, age, and gender. Health professionals should improve their knowledge and skills to present research data from the perspective of the success of Peripheral Blood and Bone Marrow Stem Cells

Impact of Ice Cube Application during High Dose Melphalan Conditioning on Oral Mucositis after Autologous Hematopoietic Stem Cell Transplantation

by Sri purwoko | Rsup dr kariadi semarang indonesia

Abstract ID: 200
Event: 28th Annual Meeting of APBMT
Topic: Allied (Nursing, technical aspects such as graft processing, cryopreservation etc)
Keywords: hematopoietic stem cell transplantation, ice cube application, oral mucositis

Impact of Ice Cube Application during High Dose Melphalan Conditioning on Oral Mucositis after Autologous Hematopoietic Stem Cell Transplantation

Sri purwoko and Retno Dwi Yuliana

Introduction

Autologous hematopoietic stem cell transplantation is a part of standart therapy in patients with multiple myeloma. Due to the use of high dose of conditioning chemotherapy regimens patients experience a wide variety of toxicities. Oral mucositis is one of the most common side effects of this treatment and it reported by patients as the most deteriorating and decreasing the quality of life. Oral mucositis often causes the need parenteral nutrition but also increases the risk of bacterial translocations and sepsis during cytopenia. One of the strategies used to prevent oral mucositis is cryoprotection with ice cubes applications 5 minutes before, during and 5 minutes after melphalan infusion.

Case illustration

A 59-years-old man with multiple myeloma came for the autologous hematopoietic stem cell transplantation using high dose melphalan conditioning (200 mg/m2). Hematopoietic stem cells were infused with a dose of 514 cc with a total of 200 million stem cells divided into 4 bags which were infused for approximately 40 minutes. Patient was given 3 bags of packed red cells leucodepleted, 2 bags of packed red cells, 5 bags of plateletpheresis and 24 bags of platelets components. On day 12, the engraftment was occurred and the patient can leave the isolation room and continue observation in the normal room. During the treatment, there is no mucositis oral but other complications was arised include nausea, vomiting, and diarrhea. Cryoprotection with ice cubes was applied 5 minutes before, during and 5 minutes after melphalan infusion. The Oral Assesment Guide was used to evaluate changes in the oral cavity.

Discussion

Ice cube application during high dose melphalan conditioning can reduce the incidence of oral mucositis after autologous hematopoietic stem cell transplantation.

Conclusion

The result show that ice cube application is effective intervention in reducing the incidence of oral mucositis after autologous hematopoietic stem cell transplantation. This method is recommended for the prevention of oral mucositis in hematopoietic stem cell transplantation.

Key words: oral mucositis, hematopoietic stem cell transplantation, ice cube application

APPENDIX

Bone Marrow Transplantation in Indonesia

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The Indonesian Society of Hematology-Medical Oncology (ISHMO)

Introduction

Bone marrow transplantation (BMT) or hematopoietic stem-cell transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cells, could be derived from bone marrow, peripheral blood, or umbilical cord blood. BMT / HSCT is conducted in order to prevent the bone marrow ablation due to the myelo-ablative conditioning regimens in autologous HSCT, in which the patient's own stem cells are rescued and re-infused, and in allogeneic HSCT, in which the patients' bone marrow is replaced by the HSC donor, as well as in syngeneic HSCT, in which HSC come from an identical twin. HSCT is reserved for patients with life-threatening diseases. Autologous HSCT is mostly indicated in patients with myeloma multiple (MM) as one episode treatment of palliative treatment, patients with refractory/relapsed (R/R) non Hodgkin lymphomas (NHL) and Hodgkin lymphomas (HL). Whereas, allogeneic HSCT is mostly indicated in acute leukemias to cure. Despite HSCT remains a dangerous procedure with many possible complications, survival following the procedure has increased. Therefore, its use has expanded beyond cancer, such as bone marrow failure (aplastic anemia/AA, myelodisplastic syndrome/MDS), thalassemias, immunodeficiency and others. Referring to the international studies on BMT/HSCT, based on the evidence base medicine (EBM), the BMT /HSCT has become an internationally standard of care in those patients. However, infections and graft versus host disease (GVHD) remain the major complications of allogeneic HSCT. Meanwhile, in autologous HSCT infections remains the major complication.

Multidisciplinary team and accreditations of BMT/HSCT procedures

HSCT requires a multidisciplinary team to conduct , especially in allogeneic HSCT, including the clinical, laboratory and diagnostic medical teams as well as the medical supporting teams, from the pre HSCT until the post HSCT, to achieve a successful outcome. To achieve this goal the most important things are controlling infection and GVHD, beside controlling the other complications, such as veno-occlusive disease (VOD), Those controlling activities will be successful if all HSCT procedures are conducted in a multidisciplinary setting and meet the standard operating procedures (SOP) based on the international standardization in HSCT procedures. Most of the BMT/HSCT services use the Joint Accreditation Committee, ISCT and EBMT (JACIE) in standardization of BMT/HSCT to promote medical practice and laboratory services to comply the best clinical practice in order to achieve the safe and efficacious outcomes. Including into the JACIE accreditation are clinical units, personnel staff, management quality, as well as data and medical record management accreditations. Beside those points of accreditations, there are some other sections to be importantly accredited, comprising standardization of education program, standard operating procedures (SOP) of autologous and allogeneic BMT/HSCT which include recipient selection and

management as well. The assessment of SOP quality outcomes and the BMT/HSCT efficacy and safety results in every hospital are included into the highly important points to be accredited to determine if the BMT/HSCT procedures are permitted to continue or to discontinue temporarily or permanently. Therefore, the local authority should be included into the BMT/PBSCT accreditation and registry and the hospital management should be responsible to the quality of BMT/HSCT as well as the quality of the attending BMT/HSCT physicians.

A selection of an appropriate candidate for the BMT/HSCT program is the first important step prior to the BMT/HSCT procedures. References and supervision from the experts of BMT/HSCT worldwide obviously the key to make the BMT/HSCT program a success in a hospital which intends to initiate this program.

A collection an as well as the stem cell processing and banking are the most important facilities to be standardized, c n order to provide the safe and optimal stem cells. If the allogeneic stem cells are provided by the other institutions beyond by the hospital BMT team, the SOP in these institutions should comply to the JACIE.

The CD 34+ stem cell enumeration and viability assessment, the immunology, microbiology, parasitology and pharmacology laboratories as well as the stem cell processing and banking are the most important facilities to be standardized to provide the safe and optimal stem cells. These safe and sufficient CD 34+ stem cells are most required to achieve a successful BMT outcome.

The facilities and systems which are supporting the BMT/HSCT should meet the international standardization, including the positive pressure rooms which preventing BMT patients from infections due to air born microorganisms as well as the standardization of written protocols with regards to patients monitoring during hospitalization and when being transferred to the intensive care

In addition, a budget support from the government is highly required, not only for the HSCT standardized facilities and procedures, also for the patient whole expe from prior to and during hospitalization until the post BMT/HSCT monitoring period which may be one until two years after BMT/HSCT.

History of BMT/HSCT worldwide and in Indonesia

BMT was initiated in1939 in a woman with AA who received the first human bone marrow transfusion without unexpected reaction. Whereas, HSCT using bone marrow-derived stem cells, was pioneered by a team at the Fred Hutchinson Cancer Research Center from the 1950s through the 1970s led by E. Donnall Thomas whose work was later recognized with a Nobel Prize in Physiology or Medicine. Collaborating with Eloise Giblett (the University of Washington), he discovered genetic markers that could confirm donor matches. A successful human BMT on a disease other than cancer was conducted by Robert A. Good (the University of Minnesota) in 1968. In 1975, John Kersey (the University of Minnesota),performed the first successful BMT to cure lymphoma. There have been BMT activities reported worldwide thereafter.

The first 50,417 HSCTs worldwide were recorded in 2006, conducted by the Worldwide Network for Blood and Marrow Transplantation (WNBMT), according to a global survey of 1,327 centers in 71 countries in which 28,901 (57%) were autologous and 21,516 (43%) were allogeneic in which 11,928 from family donors and 9,588 from unrelated donors. The main indications for BMT/HSCT were lymphoproliferative disorders

(55%) and leukemias (34%). Those BMT/HSCT procedures many took place in either Europe (48%) or the Americas (36%). In December 2012, the WNBT reported the millionth BMT/HSCT to have been undertaken. In 2014, the World Marrow Donor Association (WDMA) reported the stem-cell products provided for unrelated transplantation worldwide had increased to 20,604 (4,149 bone-marrow donations, 12,506 peripheral blood stem-cell donations, and 3,949 cord-blood units).

In Indonesia, BMT procedures started in 1987, in which the first BMT was reported in Semarang, followed by Yogyakarta in 1988, Jakarta in 1989 and Surabaya in 2014. (a) The first BMT was reported in Semarang, Central Java, when the Pediatric Hematologists performed BMT in kids supported the Australian BMT team. After several years vacuumed, in 2012 Adult Hematologists in Semarang resumed the BMT activities with the support from the Singapore and Adelaide BMT teams and in 2020 Semarang BMT team reported 14 autologous BMT and 2 allogeneic BMT procedures which were performed during that period. The BMT program in Semaang has been reported in in BMT Journal in 2020

(b) BMT procedure was firstly conducted by Adult Hematologists in Yogyakarta. However, there was no more report thereafter.

(c) In 1989, Jakarta BMT team performed the first BMT procedures in Dr Cipto Mangunkusumo Hospital (CMH) in some patients, which include a patient with chronic myeloid leukemia (CML) who underwent allogeneic BMT who survived until more than 20 years later, as well as some other patients with acute leukemias (AML and ALL) with the favorable outcome in ALL patient, but unfavorable outcome in AML patient. However, since then the CMH BMT Jakarta team just performed BM stem cell rescue for patients who received a high dose chemotherapy regimen, mostly non Hodgkin lymphoma, due to financial barrier.

The BMT CMH Jakarta program in that era was initiated with the prior training of the BMT team in Paris, France and Leiden, the Netherland. Several years later, in 1996, autologous peripheral blood stem cell transplantation (PBSCT) was firstly performed in the Dharmais Cancer Hospital (DCH) – Jakarta, in AML patients followed by autologous PBSC rescue for patients with a high dose chemotherapy, mostly for non Hodgkin lymphomas and other solid tumor patients who developed a long term neutropenia with or without febrile neutropenia. The DCH BMT – Jakarta team had a short training in Perth, Australia and visited some BMT centers in the USA which include Fred Hutchinson-Seatle, MD-Anderson Cancer Center-Houston, and Cedar Sinai Hospital, Los Angeles for comparing and learning the standard operating procedure (SOP) of BMT in those hospitals. In the following years junior staff of the CMH and DCH had the training of BMT in some other BMT centers, which include Singapore, Tokyo and Seoul.

The BMT activities in Jakarta (CMH and DCH) were vacuumed for some years due to financial barriers as well as the constraints of the hospital management in the upgrading and updating all facilities required in the BMT/HSCT and PBSCT procedures. However, since 2018 the activities of BMT in the DCH Jakarta was resumed. Meanwhile, in the CMH Jakarta the renovation of the positive pressure rooms for the allogeneic BMT/ HSCT or PBSC was finished. However, the CMH BMT program has been postponed due to the COVID 19 Pandemic. After the President of the Republic of Indonesia declared the status conversion for Pandemic to Endemic, both BMT Teams in 2 hospitals in Jakarta re-start the BMT/HSCT and PBSCT activities.

In Jakarta , beside in the CMH and the DCH, BMT activities have been also performed some other hospitals including in the Medistra Hospitals and the Mochtar Ryadi Cancer Center, mostly autologous PBSCT in MM and NHLs.
(d) In Surabaya the BMT procedures were performed by the Adult Hematologists from 2014 until 2017 in 11 patients with MM and 3 patients with AML.

Barriers in the BMT program sustainability in Indonesia

Despite the BMT program was initiated in 1987 in Indonesia, there have been several points which have become the barriers of the BMT program sustainability in Indonesia, which include:

a) the access to the national health insurance system (NHIS), in which the NHIS provides an inadequate reimbursement
b) the updating and upgrading of the BMT facilities, particularly the positive pressure rooms, in which this program depends on the hospital budget availability with no special support from the official government regulation, except if they are specifically proposed to the authority which needs years to be accepted
c) the updating and upgrading of the laboratories and stem cell banking which are mostly supporting the successful of the BMT procedures
d) the sustainability recruitment of new staff in the multidisciplinary hospital BMT team, which include various departments staff, i.e. pre clinical, clinical and supporting departments, in which some senior expert staff have been retired
e) the patients and families preference to have the BMT as an in internationally recommended procedures in some diseases to achieve the curative treatment