International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Paediatric Hematopoietic Stem Cell Transplantation (Matched Unrelated Donor Stem Cell Transplantation in a Case of Hemoglobin E/B-Thalassemia): A Caregiver's Challenges

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Abstract

A 5-year-old girl born to non-consanguineous parents was diagnosed with hemoglobin E/β-thalassemia at 14 months of age. Genetic evaluation revealed that her mother was a carrier of the hemoglobin E gene and her father had β-thalassemia trait. She required 36 blood transfusions before undergoing a haplo identical hematopoietic stem cell transplantation (HSCT), which subsequently resulted in graft rejection. She was referred to Apollo Multispeciality Hospitals, Kolkata, for further management. Following urgent re-evaluation, a fully matched unrelated donor was identified through the DATRI registry, and a second HSCT was successfully performed after an appropriate conditioning regimen. Despite developing severe post-transplant complications, including profound neutropenia, septic shock, acute respiratory distress syndrome (ARDS), and cardiac arrest requiring cardiopulmonary resuscitation, the child was successfully managed with intensive multidisciplinary care. Comprehensive nursing interventions included reverse barrier nursing, strict aseptic line care, ventilatory support, prone positioning, hemodynamic stabilization, nutritional support, blood component therapy, and continuous monitoring for infection and organ dysfunction. Timely recognition of complications, evidence-based antimicrobial therapy, and specialized nursing care contributed significantly to the patient's recovery. This case highlights that repeat matched unrelated donor HSCT can be a successful curative option after graft failure in paediatric hemoglobin E/β-thalassemia and emphasizes the pivotal role of multidisciplinary collaboration and expert nursing care in improving clinical outcomes.

Introduction

Thalassemia comprises a heterogeneous group of inherited hemoglobin disorders characterized by reduced or absent synthesis of the α- or β-globin chains, resulting in chronic anemia and ineffective erythropoiesis. Hemoglobin E (HbE) is an abnormal hemoglobin with a single point mutation in the β chain. At position 26 there is a change in the amino acid, from glutamic acid to lysine (E26K), is one of the most common

structural hemoglobin variants worldwide and is highly prevalent in Southeast Asia, Northeast India, Bangladesh, and Sri Lanka. Inheritance of one HbE gene from one parent and a β-thalassemia gene from the other results in HbE/β-thalassemia, a clinically diverse disorder ranging from mild anemia to severe transfusion-dependent disease.

Patients with transfusion-dependent HbE/β-thalassemia require lifelong red blood cell transfusions and iron chelation therapy to maintain adequate hemoglobin levels and prevent iron overload. However, repeated transfusions are associated with significant complications, including iron overload, alloimmunization, and transfusion-transmitted infections, all of which adversely affect quality of life and long-term survival. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the only established curative treatment for transfusion-dependent thalassemia, with the best outcomes achieved when performed early in life using a suitably matched donor.

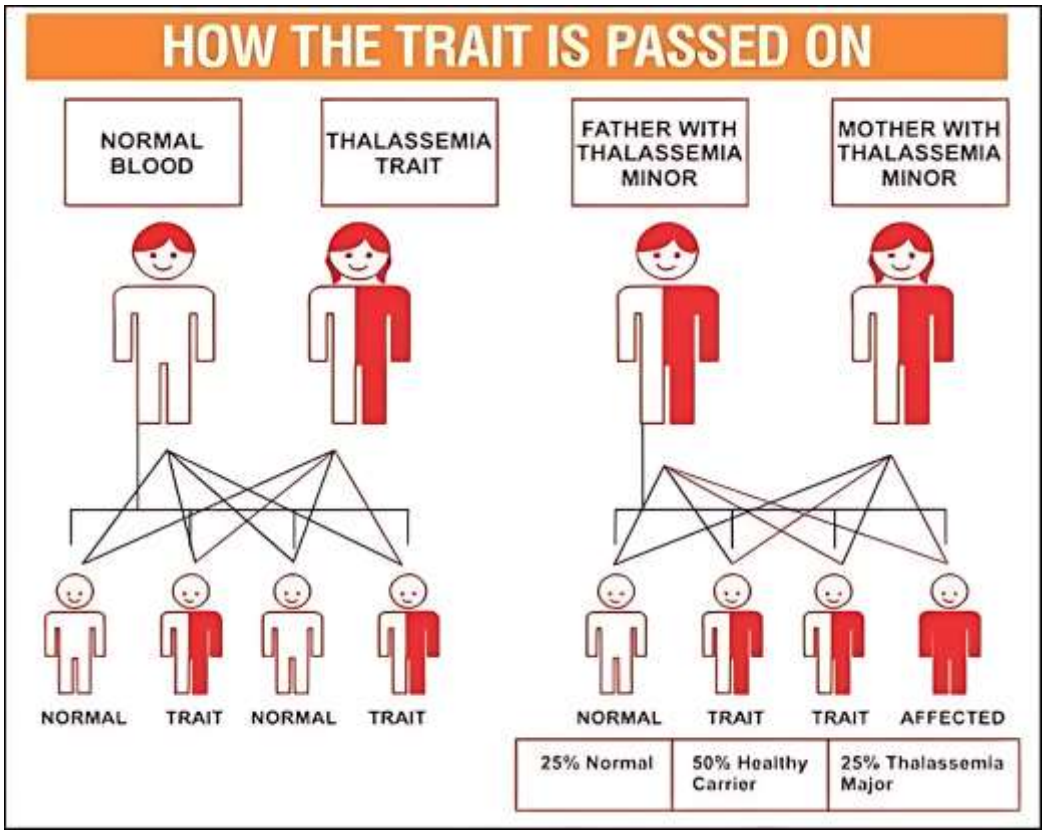
Despite advances in transplant techniques and supportive care, graft rejection, graft-versus-host disease (GVHD), severe infections, and organ dysfunction continue to pose significant challenges following HSCT, particularly in patients undergoing a second transplantation after graft failure. Successful management of these patients requires a coordinated multidisciplinary approach involving transplant physicians, intensivists, microbiologists, rehabilitation specialists, and highly skilled nursing professionals.

Nurses play a pivotal role throughout the transplant journey by providing continuous assessment, infection prevention, hemodynamic monitoring, medication administration, central venous catheter care, nutritional support, family education, and early recognition of life-threatening complications such as septic shock and acute respiratory distress syndrome (ARDS). Timely nursing interventions and evidence-based supportive care are critical in improving patient outcomes and reducing transplant-related morbidity and mortality.

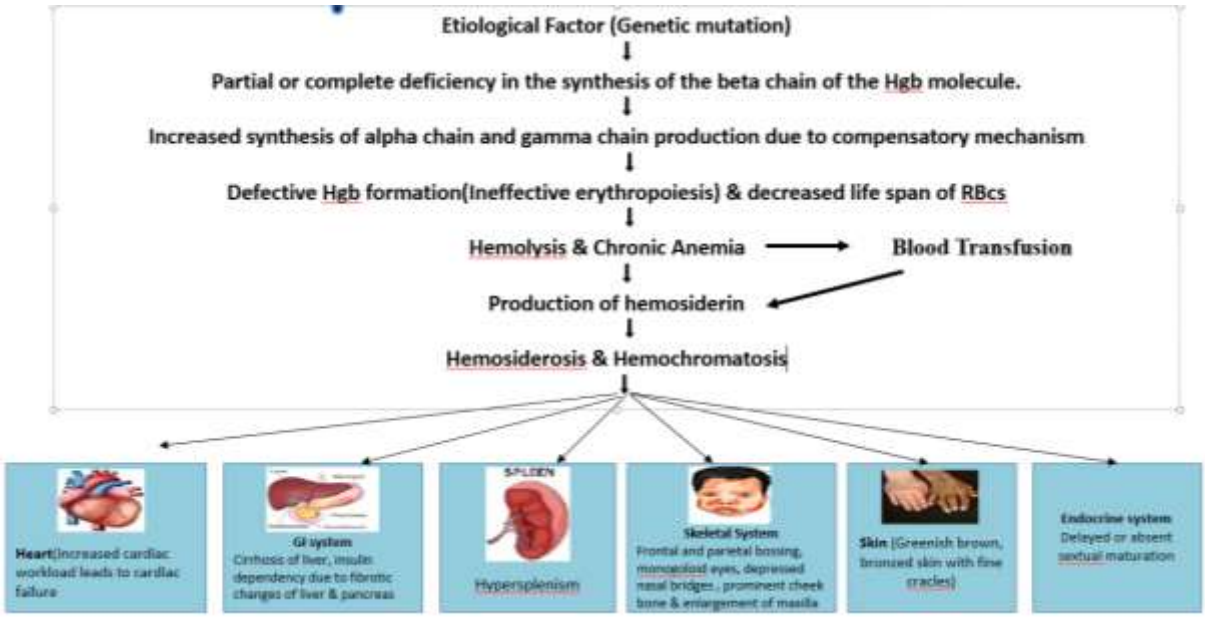
This case report describes the successful management of a 5-year-old girl with transfusion-dependent HbE/β-thalassemia who underwent a repeat matched unrelated donor HSCT following graft rejection after a previous haploidentical transplant. The report highlights the complexity of post-transplant critical care and emphasizes the indispensable role of specialized nursing interventions and multidisciplinary collaboration in achieving a successful clinical outcome.

Etiology: Thalassemia can be inherited from one or both parents. If both parents carry thalassemia genes, their child has a higher risk of developing thalassemia.

This child inherited beta thalassemia gene from the father and Hb E gene from the mother.



Pathophysiology



Medical Management

- Blood Transfusion(Baseline Hb- 9.5-10.5 gm/dl)-Leucodepleted, microbiologically checked
- Extended red cell phenotype matched packed red blood cell
- Iron Chelation- Deferasirox, Desferrioxamine, Deferiprone

Surgical Management

- Bone Marrow transplant

Eligibility criteria for Bone marrow Transplant

- Thalassemia major(Hb<7g/dl)
- Preferable age <8years
- No hepatomegaly(liver<2cm)
- Lab values (creatinine, bilirubin and transaminase) to be within normal value.
- Chest X ray and Echocardiography should be normal

Case Details

A 5years old female child, born to non-consanguineous parents was diagnosed with hemoglobin E/β-thalassemia at 14 months of age, whose mother was a carrier of the HbE gene, while the father had β-thalassemia trait, received 36 blood transfusions since 3.5 years of age and before his first transplant. Thereafter, she underwent a haploidentical hematopoietic stem cell transplantation (HSCT-8/10) where donor was her mother. But over the period of time child became very cytopaenic and Chimerism analysis confirmed graft failure so they came here for further management. Urgent repeat evaluation was done. Donor was searched and fully matched donor was identified through DATRI registration and planned for second HSCT. She was treated with blood and platelet transfusions as necessary. On clinical examination, child was found hemodynamically stable and only found dental carries, healed sore on occiput and perianal ulcer. ECG, Echo and X ray revealed within normal range. In the pre transplant phase she had Influenza A/AH3 treated with Oseltamivir followed by transaminitis and in view of her severe iron overload with very high ferritin she was treated with IV Desferrioxamine infusion 500mg/ night overnight for 4 weeks prior to transplant. Her pre-transplant ferritin was 4200. Pre-transplant discussion was done regarding the urgency transplant, survival rate and complications. After taking informed consent transplant was planned and peripheral blood stem cells were collected and cryopreserved.

Pre transplant Workup

HLA match = 10/10

Donor

- Gender: Male
- Blood group : O Positive
- Serology - CMV IgG : Positive

Recipient

- Blood group : O positive
- Serology - CMV IgG : Positive,
- EBV IgG : Positive

Phases of Transplant

Phase	Drugs
Conditioning	1. **TLI**- 5 Gy single fraction D-8

	2. **Fludarabine**- 40mg/m2/ day X 4 days D-7, D-6, D-5, D-4 3. **Treosulfan**- 10 gram/m2/day X 3 days D-7, D-6, D-5 4. **Thiotepa** – 3.5mg/kg BD on D-4 (total 7mg/kg) 5. **ATLG** (GRAFALON, Total 35 mg/kg)- D-3, D-2 and D-1
Stem cell infusion	Peripheral Blood Stem cell apheresis product was transported to Apollo Hospital Kolkata and cryopreserved on 02/05/25 in to 3 different bags. On the day of infusion CD34 and CD3 count was done from the defrosted bag number 2 and rest of the 2 bags have been kept in reserve. Total CD34 cells in product: 39 x 10^6/ kg Total viable CD 34 CELLS: 2968/ micro L % CD 34+ cell viability: 78.2% CD3 cells: 24027/ micro L CD4 cells: 8061/ micro L CD8 cells: 13968/ micro L After proper premedication with Injection Avil and Injection Paracetamol, 1st bag of stem cells containing 150 ml were transfused on 21/05/25. DMSO volume 10ml. No infusional toxicities were seen. CD34 cell dose- 16 million/kg CD3 cell dose- 134 million/kg. CD4 cell dose- 47.4 million/kg. CD8 cell dose- 82 million/kg

Post-operative Management

Indications	**Drugs and Doses**	**Start time**	**Stop time**
Passive immunity	Immunoglobulin (10gram) IV0.5 g/kg/dose	Monitor post transplant. Give when IgG<400 Mg/dl	
Antifungal Antiviral prophylaxis	Micafungin- 50mg once a day during conditioning Posaconazole suspension PO 4 mg/kg dose TDS when able to tolerate orally after transplant Acyclovir IV 250 mg/dose QSH or PO 40 mg/kg/dose BD PO Letermovir Ursodeorycholic acid (150	Start on D-10, 240 mg OD Start D+1till D+90	Until D+100, absence of GVHD and immune recovery Until I year post HSCT and off immunosuppression
Indications	**Drugs and Doses**	**Start time**	**Stop time**
VOD prophylaxis VOD prophylaxis Defibrotide	Ursodeorycholic acid (150 mg) PO 10 mg/kg/dose BD	D-10 D-7	D+28 Until D+14

	Defibrotide IV 50 mg QDS (2 hours infusion)		
Antiemetic prophylaxis	Ondansetron (3 mg) IV 0.15 mg/kg/dose 8hrly &SOS Fosaprepitant (100 mg) IV 5 mg/kg x I dose	D-10 D-8	CINV resolves Single dose
GVHD Prophylaxis	Tacrolimus Aim trough level 5- 15 MMF (Cell Cept) PO 15 mg/kg/dose TDS Methotrexate IV Push 15 mg/m2 on D+l and 10 mg/m2 D+1, D+3 and D+6 , on D+3 and D+6 (With folinic acid rescue)	D-3 D+1 D+1, D+3 and D+6	D+ 120 in the absence of GVHD D+35 and then taper
PJP prophylaxis Supplementation	Cotrimoxazole, PO2.5mg TMP /Kg/dose BD on Sat/Sunday Every week start after Engraftments Vitamin K IV 0.3 mg/kg/dose once a week Maxium dose 5mg /dose	Stop on D-2 Restart upon Engraftments Start from Day+1	Until 6 months post HSCT absence of GVHD off IST therapy & CD4> 200cells Until diet established
Pneumococcal Prophylaxis	Penicillin PO 250 mg BD	Strat from D+100 in patients with GVHD or levels or on immuno suppressive therapy	Proof of protective titre post vaccination

Nursing Management

Nursing Diagnosis	**Intervention**
Pre-operative Hyperthermia related to neutropenia	Tepid sponging was performed to reduce fever. Injection Piptaz was started
Post-operative(Day5-7) Ineffective breathing pattern related to ARDS Post transplant	Propped up position given. Oxygen given by nasal cannula with 4 lit o2. Shifted child to PICU and **cohered in view of reverse barrier** **HFNO** started with FIO2- 50 %, Flow -30% Injection. Clindamycin started
Impaired gas exchange related to septic shock (HR-155b/min, RR-52br/min, spo2-82%) Hb-8.3 g/dl, **TLC**- 60cells/µL, **Platelet count-6000/cumm**, CRP-18.8, Procalcitonin-43.9	The neurological status was assessed using the Glasgow Coma Scale. (**GCS-7)** Monitored the respiratory pattern & effort

	Respiratory effort, including the presence of **chest retractions,** was closely monitored. The child was transitioned from HFNO to invasive mechanical ventilation (Mode: PC Fio2-100%, PEEP-14, RR-35/min, PC above PEEP-20) Inj. Zavicefta, Aztreonam, Teicoplanin, Metrogyl started along with Inj Micafungin, acyclovir, Letermovir Strict reverse barrier nursing followed
Ineffective cardiac tissue perfusion related to septic shock(**cardiac arrest during intubation)**	Vital signs were monitored regularly. **PALS** initiated as per protocol. **ROSC achieved after1 cycle CPR.** Checked for distal pulse, CRT, cyanosis **Ongoing immunosupresants(Tacrolimus, L-glutamine, MMF, folinic acid, udiliv) stopped i/v/o sepsis**. IV **GCSF** (Neukine) started.
Anemia	Vital signs were monitored regularly. **1 unit PRBC** (leucodepleted & irradiated) transfused. She was closely monitored for clinical signs of bleeding.
Risk for bleeding(platelet-6000cu/mm)	4 units RDP transfused. Checked for any adverse reaction.
Hypotension related to septic shock(BP-80/50 mm of hg)	Vital signs were monitored regularly Injection. Noradrenaline 0.1mcg/kg/min started Echocardiography demonstrated a left ventricular ejection fraction of 60%. (LVEF-60%)

Impaired gastrointestinal tissue perfusion (brown coloured aspiration, albumin 2.2 and raised bilirubin 4.2)	Assessed the colour and amount of gastric content. The child was kept nil by mouth (NPM) because of gastrointestinal compromise. Started Injection. Pantoprazole BD
POD -Day 8	Assessed the respiratory pattern.

Impaired gaseous exchange related to ARDS Impaired renal tissue perfusion related to **AKI**(oliguria, Urine output-<0.5ml/kg/hr	Regular endotracheal suctioning was performed to maintain airway patency. **Prone ventilation done** Assessed the urine output. **Injection. Albumin with injection. Lasix started.**
POD Day 9-35 Blood stream infection related to CTX-M, Oxa 48 Klebsiella Hypertension(BP-134/80 mm of hg) Ineffective airway clearance	Monitored the Temperature, HR Assess the **central line site, backflow was checked** **CLABSI bundle** maintained. Injection Tigeccycline was added Injection Ceftazidime was started Injection. Labetolol started, then tapered to oral hydralazine and Amlodipine. The child was monitored for stridor, breath sounds, and respiratory distress. **Extubation** done followed **by NIV support** then nasal canula Udiliv, Letermovir and Aciclovir was restarted Checked for skin condition.
Impaired skin integrity related perineal abcess (swelling of perineal area)	Pressure injury prevention measures including regular repositioning, back care and skin care were implemented. Assess the perineal area. **Perineal care & sitz bath given**. oral Linezolid was added.
Day 36-43 Pneumonia related to Acinetobacter Baumanii, CTX-M, NDM, VIM(intermittent low grade fever)	Assessed the signs for infection. Assessed the respiratory pattern. Oral Augmentin was started
Impaired daily living activities	Assessed the activities of daily living. Physiotherapy was initiated from the beginning. Age-appropriate physical activity was encouraged as tolerated.
Impaired swallowing	Assessed for swallowing status. Swallowing rehabilitation was initiated under the guidance of a speech and language therapist.

Imbalanced nutrition less than body requirement	Assessed the appetite. Body weight and nutritional status were monitored regularly. **TPN administered followed by soft neutropenic diet.**
Risk for DVT	Assessed the signs for DVT **TEDS** stocking applied **Physiotherapy** was ongoing

Complications:

- GVHD(Graft-versus-host disease)
- Infection
- Mucositis

This patient developed-

- CTX-M, Oxa 48 Klebsiella blood stream infection
- ARDS
- AKI
- Septic shock
- CTX-M, NDM, VIM Acinetobacter Baumanii from Broncho alveolar lavage

Infection control

- Reverse barrier nursing
- CLABSI bundle implementation
- Strict hand hygiene
- Central line care

Family education and support

Comprehensive education and counselling were provided to the child's caregivers throughout hospitalization and before discharge to ensure safe transition to home care and long-term recovery. Educated the care givers regarding,

- Neutropenic diet (Avoid raw, uncooked or steamed food, pickles and whole fruits)
- Physical Activity: Encourage physical activity, plan for physiotherapy for 1 week
- Continue speech and language therapy.
- Infection prevention at home: Emphasized strict hand hygiene and personal hygiene practices. Instructed caregivers to monitor for warning signs of infection, including fever, cough, breathlessness, skin lesions, oral ulcers, diarrhea, and urinary symptoms, and to seek immediate medical attention if these occurred.
- Medication regimen : Educated caregivers on the importance of strict adherence to prescribed immunosuppressants and supportive medications.
- Follow up: Stressed the importance of regular outpatient follow-up for clinical assessment, laboratory investigations, monitoring of graft function, and early detection of graft-versus-host disease (GVHD),

infections, or disease recurrence.

- Vaccination schedule: Explained the importance of maintaining an updated immunization schedule during long-term follow-up about vaccination (not to vaccinate without consulting doctor)
- Psychosocial Support
- Provided emotional support to the child and caregivers to reduce anxiety and enhance coping during the prolonged treatment journey.
- Encouraged open communication regarding concerns related to treatment, recovery, and social reintegration.
- Informed the family about available psychological counselling and support services when required.

Comprehensive caregiver education and active family participation were integral components of post-transplant care, contributing to treatment adherence, early recognition of complications, successful home-based management, and improved long-term clinical outcomes.

Discussion

Hemoglobin E/β-thalassemia is one of the most common forms of severe β-thalassemia in South and Southeast Asia and remains a major cause of transfusion-dependent anemia in children. Regular blood transfusions and iron chelation therapy improve survival but are associated with complications such as iron overload, alloimmunization, endocrine dysfunction, and impaired quality of life. Consequently, allogeneic hematopoietic stem cell transplantation (HSCT) is considered the only established curative treatment for eligible patients, particularly when performed early in childhood before the development of irreversible organ damage[1].

The present case is clinically significant because the child underwent a successful matched unrelated donor (MUD) HSCT after graft rejection following a previous haploidentical transplant. Primary graft failure remains an uncommon but serious complication of HSCT and is associated with substantial morbidity and mortality. Repeat transplantation offers the best chance of cure in selected patients; however, it carries a higher risk of infectious complications, prolonged immunosuppression, graft-versus-host disease (GVHD), and transplant-related mortality. Successful outcomes require careful patient selection, timely donor identification, meticulous transplant planning, and comprehensive supportive care.

One of the most remarkable aspects of this case was the development of life-threatening complications during the early post-transplant period, including profound neutropenia, septic shock[2], acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), cardiac arrest, and multidrug-resistant bloodstream infection[3]. Such complications are well recognized among pediatric HSCT recipients and remain major contributors to transplant-related mortality. Published studies have shown that early recognition of sepsis, prompt initiation of broad-spectrum antimicrobial therapy, aggressive organ support, and multidisciplinary intensive care significantly improve survival in critically ill transplant patients[2].

The successful recovery of this patient highlights the importance of coordinated multidisciplinary management involving pediatric hematologists, intensivists, infectious disease specialists, microbiologists, transfusion medicine experts, physiotherapists, nutritionists, and nursing professionals. Early microbiological diagnosis, culture-directed antimicrobial therapy, ventilatory support, hemodynamic stabilization, blood component therapy, nutritional rehabilitation, and rehabilitation services collectively contributed to the favorable clinical outcome despite the severity of illness.

From a nursing perspective, this case emphasizes the indispensable role of specialized pediatric transplant nursing throughout the continuum of care. Nurses were central to maintaining reverse barrier precautions,

implementing strict infection prevention practices, monitoring central venous access devices, administering complex medication regimens, performing continuous hemodynamic and respiratory assessments, recognizing early clinical deterioration, and initiating timely escalation of care[4]. Evidence indicates that adherence to standardized infection prevention bundles, meticulous central line care, and continuous clinical surveillance significantly reduce healthcare-associated infections and improve outcomes in immunocompromised patients undergoing HSCT.

Family-centered nursing care also played a crucial role in the patient's recovery. Education regarding neutropenic precautions, medication adherence, nutritional management, early recognition of infection and GVHD, vaccination, rehabilitation, and psychological support enhanced caregiver confidence and preparedness for long-term post-transplant care. Active involvement of caregivers is recognized as an essential component of successful pediatric transplant programs and contributes to improved treatment adherence and quality of life[5].

This case adds to the limited literature on successful repeat matched unrelated donor HSCT following graft failure in pediatric HbE/β-thalassemia. It highlights how timely multidisciplinary intervention, evidence-based infection management, and specialized nursing care can successfully overcome severe transplant-related complications and improve survival in critically ill pediatric HSCT recipients. that successful repeat matched unrelated donor HSCT is achievable even after previous graft rejection when supported by timely multidisciplinary intervention and comprehensive evidence-based nursing care. It reinforces the critical contribution of nursing professionals in the prevention, early identification, and management of transplant-related complications and underscores the value of coordinated teamwork in improving survival and long-term outcomes in pediatric HSCT recipients.

Learning Points

- Repeat matched unrelated donor HSCT can be a successful curative option after graft rejection in selected pediatric patients with HbE/β-thalassemia.
- Early recognition and aggressive management of septic shock and transplant-related complications are critical to improving survival.
- Strict infection prevention practices, central line care, and continuous nursing surveillance are essential components of post-HSCT management.
- Multidisciplinary collaboration among transplant physicians, intensivists, microbiologists, rehabilitation specialists, and nursing professionals is fundamental to successful outcomes.
- Family education and long-term follow-up play a vital role in recovery, treatment adherence, and quality of life.

Conclusion

This case demonstrates that repeat matched unrelated donor hematopoietic stem cell transplantation (HSCT) can be a successful curative option for children with transfusion-dependent HbE/β-thalassemia following graft failure after a previous haploidentical transplant. Despite the occurrence of life-threatening complications, including septic shock, acute respiratory distress syndrome (ARDS), acute kidney injury, cardiac arrest, and multidrug-resistant bloodstream infections, the patient achieved a favourable clinical outcome through timely multidisciplinary intervention and comprehensive evidence-based supportive care.

Specialized nursing care played a pivotal role throughout the transplant journey by facilitating early recognition of clinical deterioration, implementing stringent infection prevention measures, providing meticulous central venous catheter and ventilatory care, ensuring hemodynamic monitoring, supporting nutritional rehabilitation, and delivering comprehensive caregiver education. This case underscores the importance of coordinated multidisciplinary collaboration and highlights the indispensable contribution of transplant nurses in preventing, identifying, and managing complex post-transplant complications. Sharing such experiences may help guide clinicians and nursing professionals in optimizing the care of paediatric HSCT recipients with severe post-transplant complications.

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