CASE REPORT

Unveiling success: determinants of a successful haematopoietic stem cell transplant: a case report

Tariq Mahmood Satti[1], Rimsha Jafar[2], Zoya Habib[3], Koukab Ejaz[4], Zulqarnain Arif[5], Fahad Haider Shah[6]

Abstract

Patients with beta thalassemia major can make an uneventful and miraculous recovery after bone marrow transplantation despite lacking a sibling donor. The once widely accepted belief that only a transplant received from a sibling or mother would lead to a successful outcome has been challenged by the advent of new approaches and drugs. We present the case of a 15-year-old girl who received stem cells from her father and, despite suffering an attack of acute graft versus host disease (aGVHD) and depression, still managed to achieve a 100% success rate. This report highlights the importance of factors other than the source of stem cells in evaluating the patient's outcome and the lack of awareness about this disease even among the literate population in our country.

Keywords: Haematopoietic stem cell transplantation, Beta thalassemia, GVHD.

DOI: https://doi.org/10.47391/JPMA.21537

Introduction

Thalassemia, a genetic disorder affecting haemoglobin production, is one of the most widespread haemoglobinopathies globally. The cause of these defects is gene mutations leading to low levels and/or malfunctioning α and β globin proteins, respectively. Genes for beta chains are seen on chromosome 11.

The severity of disease depends on the extent of mutation. The mildest form of the disease, thalassemia minor, also known as thalassemia trait, is usually asymptomatic with an increase in Red blood cell count. Beta-thalassemia major is the severe form of disease in which both beta genes are mutated. Growth retardation, skeletal abnormalities, hepatosplenomegaly, jaundice, and severe anaemia are common clinical presentations. Secondary or transfusional haemochromatosis develops due to recurrent transfusions in patients. According to a study, hereditary haemochromatosis might also be associated with beta-thalassemia major.[1]

To ensure the timely diagnosis and management of this life-threatening illness, it is critical to enhance the general population's knowledge about the disease. A study was conducted by Shahzad A et al. to assess the knowledge, attitude and practices (KAP) of the parents of β-thalassemia children of Rawalpindi-Islamabad. Majority of the respondents (70%) had no information about thalassemia before marriage.[2] This case report is presented to highlight the successful outcome of paternal haploidentical Haematopoietic stem cell transplant, despite initial rejection concerns and to emphasize the role of non-donor factors (e.g. iron control, preventive measures, paternal literacy) in transplant success. It also underscores the urgent need for nationwide awareness programmes to reduce thalassemia prevalence.

Case report

On 26 September 2008, a three-month-old girl presented to the outpatient department of Pakistan Ordnance Factory Hospital, Wah Cantt with the complaint of acute diarrhoea for three days. Among the baseline investigations, Haemoglobin was 6.6g\dL (normal for infants: 11.5-15.5 g/dL), MCV was 64.93fL(normal: 70-90fL), and MCH 16.8pg(normal: 25-35pg). Remarkably, within a mere 24-hour interval, her Hb had dropped to 6g/dL indicating a rapid and concerning decline. Further workup, including serum ferritin and Hb electrophoresis, confirmed it to be a case of beta thalassemia major (BTM). Initially, blood was transfused to build the patient's Hb.

The patient continued to receive blood transfusions until the age of 12, maintaining her haemoglobin levels consistently above 9 g/dL. Additionally, her ferritin levels remained within the normal range, managed by Deferoxamine, which was initiated six months after starting the transfusions. Her Hb and ferritin levels were regularly monitored every three weeks. At seven years of age, her parents had sought Haematopoietic stem cell transplantation (HSCT). For this purpose, HLA testing was performed but Human leukocyte antigens (HLA) did not match with her mother and her only five-year-old brother,

[1]Department of Haematology, Shifa International Hospital, Islamabad, Pakistan. [2-6]Final Year MBBS Student, Wah Medical College, Wah Cantt, Pakistan.

Correspondence: Zoya Habib **Email:** xoyahabib11@gmail.com

ORCID ID: 0009-0005-4122-3926

Submission complete: 28-07-2024 **First Revision received:** 11-10-2024

Acceptance: 29-03-2025 **Last Revision received:** 28-03-2025

Figure-1: Image showing the caring and compassionate behaviour of paramedic staff (pre-transplant).

Figure-2: Image showing the patient's condition after an attack of acute GVHD — Post transplant (Day 33).

but it completely matched with her father. Medical professionals initially declined to proceed with the transplant due to concerns about a high rejection rate.

At 12 years of age, Allo-antibodies formation to transfused red cells made it difficult to find compatible blood for transfusions. Moreover, her ferritin levels increased to 1328.54ng/mL. Keeping this in view, doctors reconsidered their opinion and opted for transplant at Shifa International Hospital, Islamabad using stem cells harvested from her father. She was optimised for HSCT with a chemotherapy plan at home for 40 days and was admitted on August 30, 2021, to a specialised transplant centre.

On admission she was active, alert, with normal vitals, and no lymphadenopathy. Spirometry suggested mild restriction (probably due to lack of understanding to perform the test), normal diffusion, and normal chest X-ray. Cardiovascular and liver Magnetic Resonance Imaging for iron quantification showed normal study with ejection fraction of 61%. There was no significant myocardial or hepatic iron deposition. ECOG (Eastern Cooperative Oncology Group) score was zero (indicating full activity without symptoms), while KPS (Karnofsky Performance Status) scale was greater than 90% (able to perform normal activity with minor symptoms). A 45-day protocol was initiated. She was started on chemo regimen (BU – 14mg/kg, cyclo – 120mg/kg and ATG 15mg/kg). Stem cells were transfused on September 8, 2021.

After 28 days, she developed hypertensive fits. She was immediately shifted to an Intensive Care Unit and emergency management was initiated. Computerized Tomography scan was done, and the report was unremarkable. Two months after the transplant she had an attack of grade 2 aGVHD (abdominal pain, loose stools, and mouth ulcers). She also went through a phase of depression. On December 14, 2021, the patient's Fluorescence in situ hybridisation (FISH) analysis showed karyotype 400/400 (100%) XY donor cells. The patient is now healthy, receives no transfusion, Haemoglobin is maintained on 9 g/dl, and is getting vaccinated according to the schedule.

Discussion

Beta thalassemia major, one of the most prevalent inherited haemoglobinopathies in Pakistan, has a carrier rate of about 9.8 million in general population.[3] In developing countries like Pakistan, mortality following Hematopoietic stem cell transplantation is much lower than that in developed nations where it reaches almost 82% from match-related donors.[4] However, it can be much reduced following the consideration of factors participating in its success and failure. This case study highlights the determinants of a successful haematopoietic stem cell transplant in a Bone Marrow transplant. In this case, multiple factors contributed to its success; the most important ones are: 1) fully matched paternal transplant, 2) preferred age group, 3) good iron control, 4) no signs of haemochromatosis, 5) literate parents, 6) financial stability, 7) accessibility to medical facilities, 8) empathic and supportive attitude of doctors dealing with the case, 9) strict precautionary measures taken to prevent the development of any infections. In countries like Pakistan, where literacy rate is very low and insurance policies are not available, the major problem that one has to face is the inability to bear the finances and poor compliance on iron chelation therapy.

Infections following HSCT are the most common cause of morbidity and mortality but establishing preventive measures from the very beginning proved to be a positive factor why this patient did not develop infections. The success rate of HSCT from father according to a study is only 14 percent,[5] yet the successful outcome of this patient was due to the above-mentioned factors. It is important to bring to light the complications such as acute GVHD which develops in about 35 to 50 percent of HSCT recipients.[6] Although the initial regimen given to our patient consisted of ATG which is thought to have a prophylactic role in preventing aGVHD, here its efficacy remained questionable. New studies have revealed that prophylactic application of Ruxolitinib is effective in preventing aGVHD,[7] though clinical trials need to be conducted. There are 2.06 times more chances that hypertension will occur in patients receiving allogenic transplant than healthy siblings.[8] The risk factors of hypertension include younger age, GVHD and the use of Cyclophosphamide.[8] Another notable effect it had on the patient in this case was depression, which was effectively managed through counselling and psychological support. According to the studies, depression occurs in approximately 30% of the patients following HSCT.[9] Regular monitoring and early diagnosis are key factors to prevent adverse outcomes.

This case also highlights the lack of awareness of pre-marital screening for beta thalassemia minor. The parents came to know about their carrier status after the diagnosis of their child's BTM, although both the parents were literate. This highlights the significance of creating awareness and educating the general population via seminars, print media, mass education, etc. After the diagnosis of this child, extended family screening was done and thus many new cases were prevented. Many countries including Thailand, Taiwan, Saudi Arabia have significantly reduced the cases of BTM following pre-marital and pre-natal screening programmes.[10] Thus, considering these factors will result in the reduction of new cases and better utilisation of resources in already present cases in this resource limited country.

Conclusion

In conclusion, this case report draws attention to the critical factors that contribute to the successful haematopoietic stem cell transplantation (HSCT) in beta thalassemia major (BTM). Additionally, it emphasises the need for increased public awareness and implementation of pre-marital and pre-natal screening programmes to reduce the prevalence of BTM in our resource-limited setup.

Acknowledgement: We are thankful to the patient and her parents for granting us the consent to publish this case report and the images.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Sharif Y, Irshad S, Tariq A, Rasheed S, Tariq MH. Association of frequency of hereditary haemochromatosis HFE gene mutations (H63D and C282Y) with iron overload in beta-thalassemia major patients in Pakistan. Saudi Med J. 2019; 40:887-92. doi: 10.15537/smj.2019.9.24482.
2. Shahzad A, Rafiq N, Ullah I, Asad MJ, Ahmad MS, Waheed U. Knowledge, attitude and practices (KAP) of the families of b-thalassaemia children in thalassaemia centres of Rawalpindi and Islamabad, Pakistan. J Pak Med Assoc. 2017; 67:1434-7.
3. Ehsan H, Wahab A, Anwer F, Iftikhar R, Yousaf MN. Prevalence of Transfusion Transmissible Infections in Beta-Thalassemia Major Patients in Pakistan: A Systematic Review. Cureus. 2020; 12:e10070. doi: 10.7759/cureus.10070.
4. Lucarelli G, Isgrò A, Sodani P, Gaziev J. Hematopoietic stem cell transplantation in thalassemia and sickle cell anaemia. Cold Spring Harb Perspect Med. 2012; 2:a011825. doi: 10.1101/cshperspect.a011825.
5. Ramprakash S, Agarwal RK, Dhanya R, Sedai A, Kumari A, Parmar L, et al. Rejection of paternal vs maternal fully matched bone marrow grafts in children with thalassemia. Bone Marrow Transplant. 2017; 52:1585-6. doi: 10.1038/bmt.2017.199.
6. Jacobsohn DA, Vogelsang GB. Acute graft versus host disease. Orphanet J Rare Dis. 2007; 2:35. doi: 10.1186/1750-1172-2-35.
7. Zhao Y, Shi J, Luo Y, Gao F, Tan Y, Lai X, et al. Calcineurin inhibitors replacement by Ruxolitinib as graft-versus-host disease prophylaxis for patients after allogeneic stem cell transplantation. Biol Blood Marrow Transplant. 2020; 26:e128-33.doi: 10.1016/j.bbmt.2020.01.012.
8. Kwon DH, Jung S, Lee EJ, Lee JY, Moon S, Lee JW, et al. Incidence and risk factors for early-onset hypertension after allogeneic haematopoietic stem cell transplantation in children. Korean Circ J. 2013; 43:804-10. doi: 10.4070/kcj.2013.43.12.804.
9. Mumby P, Adams W, Smith S, Rao M, Stiff P. Pharmacotherapy for the Prevention of Depression and Behavioural Side Effects in Haematopoietic Stem Cell Transplantation Patients. Transplantation and Cellular Therapy. 2024; 30:320.e1-. e11. doi: 10.1016/j.jtct.2023.12.014.
10. Kattamis A, Forni GL, Aydinok Y, Viprakasit V. Changing patterns in the epidemiology of β-thalassemia. Eur J Haematol. 2020; 105:692-703. doi: 10.1111/ejh.13512.

AUTHOR'S CONTRIBUTION:
TMS: Agreement to be accountable for all aspects of the work.
RJ & ZH: Concept and design.
KE & ZA: Final approval.
FHS: Drafting and revision.