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Case Report

Comprehensive management of a child with X-linked lymphoproliferative disease undergoing stem cell transplantation: a case report

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ABSTRACT

An uncommon immunodeficiency disease known as X-linked lymphoproliferative disease (XLP) has been associated with severe immunological dysfunction and a high susceptibility to Epstein-Barr virus (EBV) infections. This case report describes a four-year-old boy who had X-linked lymphoproliferative illness and died from multiple system organ failure (MSOF) after receiving treatment with a haploidentical hematopoietic stem cell transplant (halo-HSCT). While providing care in such circumstances, rational-based care, prompt identification, primary nursing care, health education, and emotional assistance for parents of individuals with X-linked lymphoproliferative diseases are vital.

Keywords: Children, X-linked lymphoproliferative disease, Haploidentical stem cell transplant, Allogenic stem cell transplant

INTRODUCTION

X-linked lymphoproliferative illness (XLP), is a rare genetic condition that results in primary immunodeficiency resulting in fever, immune dysregulation, tissue damage, and hepatosplenomegaly that leads to multiorgan failure.[1,2] XLP1 and XLP2/XIAP are the two categories of X-linked lymphoproliferative disorders. An estimated one out of every one million boys has XLP1. XLP2 is even rare, affecting about one in five million boys.[3,4] The majority of conservative therapies for managing XLP symptoms, such as interferon, steroids, intravenous immunoglobulins (IVIG), antiviral medications, chemotherapy, and IVIG, may work for a short while. The only curative treatment is allogeneic stem cell transplantation.[5-9]

CASE REPORT

We reported a four years-old male child who was brought to the emergency department with a chief complaint of non-remitting fever (temperature >38 °C) for 3 weeks, a history of jaundice, dark-coloured urine, petechial skin rash, and oral bleeding for one day. On clinical evaluation, the child was found to have hepatomegaly and transaminitis with lymphocytic leucocytosis with positive Epstein Barr virus-viral capsid antigen (EBV VCA) IgM. Given the significant history of unexplained death of several male individuals on the maternal side, the possibility of X-linked primary immunodeficiency was raised (Figure 1). Based on the revealed deletion spanning genomic location and two-generation pedigree analysis a diagnosis of XLP1 was confirmed.

The child was started on monthly IVIG replacement @ 2 g/kg and methylprednisolone @ 30 mg/kg/day for 3 days followed by oral steroids in a tapering course for significant cytopenia and elevated inflammatory markers. EBV copies by polymerase chain reaction (PCR) were monitored monthly along with hemophagocytic lymphohistiocytosis (HLH) markers which showed resolving trends and clinically child had no fever and

hepatomegaly. So, he was referred to the bone marrow transplant department. Before transplantation, the child underwent testing for donor-specific anti-HLA antibodies which were found to be negative after that myeloablative conditioning regimen was given that consisted of rabbit anti-thymocyte globulin 2.5 mg/kg IV over days −8 to −6, busulfan (BU) 1 mg/kg IV q 6 h for 16 doses on days −5 to −2. Bone marrow (BM) stem cells were freshly harvested from his father. Graft-versus-host disease (GVHD) prophylaxis included post-transplant cyclophosphamide (PT-CY) 50 mg/kg IV on days +3 and +4 followed by initiation of mycophenolate mofetil (MMF) 15 mg/kg and cyclosporin 30 mg iv on days +5. Standard bacterial prophylaxis was used (Levofloxacin) when absolute neutrophil count (ANC) dropped below 0.5×109/l. Acyclovir was also started on admission time itself for herpes simplex and varicella virus prophylaxis. Bi-weekly PCR monitoring for cytomegalovirus (CMV) and weekly for adenovirus, Epstein–Barr virus (EBV), and human herpes virus-6 (HHV-6) were performed. Granulocyte-colony stimulating factor (G-CSF) was started on day +5 at 5 mcg/kg/day.

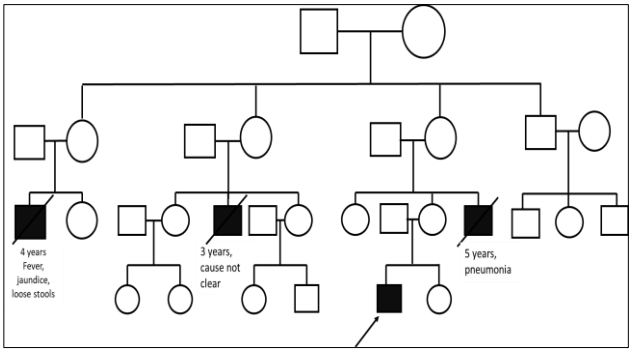

Figure 1: Pedigree of four years-old male child with X-linked lymphoproliferative disease.

Health education regarding care of the Hickman line, early signs of infection and isolation maintenance was given to parents. Through this comprehensive approach, the patient was managed successfully and discharged on day +21. Based on the primary nurse's care model, focusing on asepsis, and nutritional requirements for the child through clinical evaluation with a daily physical examination and implemented for the child (Figure 2).

Follow-up and outcomes

The child was doing well till one week following the discharge. On day +29 child had acute respiratory worsening and was brought to our emergency department of the hospital. He was intubated and shifted to the paediatric intensive care unit (PICU). Chest X-ray showed bilateral acute respiratory distress syndrome with pulmonary oedema. Coagulopathy (hematemesis and malena) was also present. Day +33 urine output was nil. He was treated with vancomycin, meropenem and IVIG and improved clinically. On day +39 child was extubated and was on high-flow nasal cannula (HFNC). Day + 40 urine was positive for BK virus. On hematologic examination, ANC dropped to zero and platelet count was 26 k with gross bleeding. Chest CT scan showed bilateral widely diffuse pulmonary infiltrates that indicate severe infection. IVIG and acyclovir were administered but the child did not respond to treatment. He showed encephalitic symptoms (convulsions and coma) and symptoms of HLH on day +64 and died with multiple system organ failure (MSOF) on +67 days.

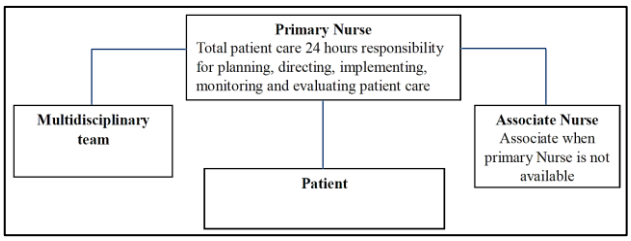

Figure 2: Primary nurse care model.

DISCUSSION

XLP patients have severe immune dysregulation often after viral infection (typically EBV).[10] The present case presents typical clinical features of HLH, including fever, hepatosplenomegaly, pancytopenia, and coagulopathy with hypofibrinogenemia after bone marrow transplant.[11] In a study from India, rabbit ATG and thiotepa 10 mg/kg were added to the Baltimore regimen of CY, FLU, and total body irradiation (TBI) resulting in engraftment following PBSC(Peripheral blood stem cells) haplo-transplant without acute or chronic GvHD.[16] However, in this study, a high rate of mixed chimerism and infections (death attributed to infectious complications) is noted.

There is a scarcity of research shreds of evidence to guide the management of children with XLP. The nursing care provided to the child in the PICU and bone marrow transplant unit was based on maintaining a thermo-neutral environment, providing ventilator support, protecting the child from infection, ensuring optimal nutrition, and electrolyte balance, maintaining skin integrity, and providing psychological support to the parents. Although allogeneic SCT is considered only curative treatment for XLP, only a limited number of cases have been reported in the literature.[11]

Counselling

The mother of the child had a lot of psychological stress due to the prolonged stay of the child and his poor prognosis. The bone marrow transplant team tried to give emotional, psychosocial and spiritual support especially mothers to discuss openly about fears, feelings of guilt, hopes and expectations because of maternal history. The role and empathic attitude of the clinician is crucial in this process.

CONCLUSION

Overall, the outcomes in patients with XLP1 have been improving substantially during the last 30 years, especially as a result of better management of clinical manifestations such as HLH. Survival after bone marrow transplantation has also improved, but mortality related to active disease at the time of transplantation and mismatched donor parameters remains significant.

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