CORRESPONDENCE

Haplo-identical Hematopoietic Stem Cell Transplant is a Possible Cure in a Patient with Relapsed Hemophagocytic Lymphohistiocytosis Syndrome

Jyotsna Kapoor¹ · Rayaz Ahmed¹ · Narendra Agrawal¹ · Mukul Aggarwal¹ · Pallavi Mehta¹ · Priyanka Verma¹ · Niharika Bhatia¹ · Pragya Bhandari¹ · Dinesh Bhurani¹

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Dear Editor,

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome of uncontrolled immune responses resulting in hypercytokinemia because of underlying primary or acquired immune defect. Currently, the only cure for primary or relapsed HLH is allogeneic stem cell transplantation (AlloSCT) [1]. Our report concerns a 13-year-old boy with a relapsed distinctively blurred HLH [2], who achieved prolonged complete remission (CR) after haplo-identical stem cell transplant (Haplo-SCT) following salvage chemotherapy.

A previously healthy 11-year-old boy, the youngest son of a healthy nonconsanguineous parents without family history of HLH/similar disorders in first/second-degree relatives was hospitalised at a local hospital with complaints of 106 °F fever and hepatosplenomegaly and found to have *Brucella* infection and histiocyte proliferation in bone marrow (BM). On further investigations, he had raised serum triglyceride, serum ferritin, and low fibrinogen levels, on the basis of which he was diagnosed with HLH. Cerebrospinal fluid was normal. The genetic mutations of HLH were not tested for parents did not give consent for same. He received chemotherapy using HLH-2004 protocol and achieved CR.

On routine follow up, he was found to have relapse of HLH without any underlying infective stimulus, after 25 months of initial therapy for which he received etoposide-based salvage chemotherapy and attained a second

complete remission. Thereafter he was referred to us for alloSCT. He had no HLA matched donor in the family, but had 3/6 HLA match with his mother with negative donor specific anti-HLA antibodies screen.

Considering the relapsed nature of HLH and in need of alloSCT lacking a matched HLA donor from family, he received a Haplo-SCT using T cell replete peripheral blood stem cell (PBSC) from his mother with a CD34 cell dose of 6.06×10^6 cells/kg after Fludarabine, cyclophosphamide and TBI (FluCyTBI) conditioning. For GvHD prophylaxis, cyclophosphamide at day + 3 and + 4 post SCT was employed. ANC and Platelet Engraftment was achieved at day + 16 and + 21 of SCT respectively, and was further confirmed by 100% donor karyotype on FISH for XX analysis of peripheral blood at day + 30. Acute GvHD (aGvHD), overall grade II with skin and gut involvement, became apparent at day + 16 which was managed with corticosteroids. By day + 120, he developed aGvHD of liver, which progressed to grade IV despite being on corticosteroids, etanercept and basiliximab and was controlled after Anti thymocyte globulin (ATG) therapy. He had no major infections except for chronic otitis media and UTI with *Enterococcus fecalis*. Currently, he has mild chronic GvHD involving oral mucosa and eyes requiring minimal immunosuppression and is disease free with maintenance of complete chimerism at day + 840 of Haplo-SCT.

Use of alloSCT for HLH has remarkably improved the survival and prognosis of patients. Henter et al. [3] demonstrated 62% survival rate at 3 years and 10% of graft failure (GF) among 65 HLH patients treated with alloSCT. Ouachée-Chardin et al. [4] reported a series of 48 primary HLH patients who received alloSCT out of which 60% received haplo-SCT, was found associated with increased treatment related toxicity, poor prognosis and 22% GF rate. Uppuluri et al. [5] reported a case of 2 young children with

✉ Rayaz Ahmed
rayazhemat@gmail.com

¹ Department of Hemato-Oncology, Rajiv Gandhi Cancer Institute and Research Centre, Sector-5, Rohini, New Delhi, Delhi 110085, India

primary HLH who underwent Haplo-SCT using PTCy remained disease free after 6 months of Haplo-SCT with manageable aGvHD and CMV viremia as the major complication. It has been noted that GvHD is the common complication post alloSCT while late complications post alloSCT are infrequent in patients with durable engraftment who remained in remission indefinitely.

In conclusion, patients with infective etiology associated HLH after treatment with induction therapy should be closely monitored for relapse. Haplo-SCT is potentially a curative treatment.

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Compliance with Ethical Standards

Conflict of interest The Authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by our Institutional Review Board.

Informed Consent The informed consent was obtained from the individual participant included in the study.

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