

# The Successful Treatment of Severe Aplastic Anemia with Autologous Cord Blood Transplantation

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## ABSTRACT

Cord blood transplantation has been used extensively in the allogeneic setting for acquired and genetic disorders of hematopoiesis. There is less experience in the utility of autologous cord blood transplantation, and there is great controversy about the role of autologous cord blood collection and storage. We report on the successful use of autologous cord blood transplantation for the treatment of severe aplastic anemia following fulminant hepatic failure and living related liver transplantation.

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## KEY WORDS

Anemia • Aplastic • Autologous • Transplantation • Cord blood

We report the first case of autologous cord blood transplantation for the treatment of severe aplastic anemia secondary to liver transplantation. A 20-month-old boy presented with fulminant hepatic failure of unknown etiology. Markers for viral hepatitis and congenital causes of fulminant hepatic failure were negative. A living related liver transplantation from his haploidentical father was performed. Three months later, the patient developed pancytopenia (white blood cells  $<200/\mu\text{L}$ ; platelets  $<7000/\mu\text{L}$ ). Bone marrow was empty on biopsy. Etiology for severe aplastic anemia could not be determined. He received increasing doses of cyclosporine and steroids for immunomodulation. He remained neutropenic, was dependent on transfusions of red blood cells and platelets, and had no HLA-matched siblings. The patient's parents, both physicians, had arranged for the storage of the patient's cord blood at birth. It was decided to use the stored cord blood as an autologous cord blood transplant in an attempt to restore normal hematopoiesis. A Nunc vial stored with the cord blood was thawed to confirm that it was HLA identical to the patient. The preparative regimen consisted of antithymocyte globulin 40 mg/kg/d, cyclosporine, and prednisone given for 4 days along with granulocyte colony-stimulating factor, followed by infusion of  $7.98 \times 10^7$

total nucleated cells per kilogram containing  $2.79 \times 10^5$  CD34<sup>+</sup> cells per kilogram. White blood cell engraftment ( $>1000/\mu\text{L}$ ) occurred by day 11 and platelet engraftment by day 14 ( $>20\,000/\mu\text{L}$ ). The patient's recovery was unremarkable, except for a skin biopsy positive for *Aspergillus* spp, which was treated with antifungal agents. At 3 years of follow-up, the patient remains on immunosuppressive therapy for his immunosuppressive regimen after living related liver transplantation and is in complete hematologic remission with a normal complete blood count.

Severe aplastic anemia, a life-threatening hematologic emergency requiring prompt treatment, has been reported in certain settings to occur in up to 28% of recipients of orthotopic liver transplants [1]. Marrow transplantation from an HLA-matched sibling donor has high rates of cure in children with aplastic anemia [2], but matched or compatible donors are not always available. In the absence of a matched donor, immunosuppressive therapy can restore hematologic function in some patients, but pancytopenia frequently recurs, and eventual transformation to myelodysplastic syndrome and acute leukemia is a risk.

Cord blood has been used for more than a decade as a source of stem cells for allogeneic transplantation, but reports of its use in children with aplastic anemia

**Table 1.** Cases of Hematopoietic Transplantation in Children with Severe Aplastic Anemia Post-Liver Transplantation

Patient	Liver Transplant Type	Hematopoietic Transplantation		Time to Engraftment		
		Source	Donor	WBC	Neutrophils	Platelets*
1.6-year-old boy	Living-related, HLA haploidentical father	Cord blood	Self	11 d		14d*
1-year-old boy [8]	Living-related, HLA haploidentical father	Cord blood	HLA-matched, ABO incompatible sister		12 d	45 d
8-year-old boy [5]	Orthotopic	Marrow	HLA-matched brother		20 d	
6.5-year-old boy [6]	Orthotopic	Marrow	HLA-matched sister		23 d	19d*
2.5-year-old boy [7]	Orthotopic	Marrow	HLA-matched sister, Group A identical		11 d	12 d

\*Indicates recovery defined as platelets  $> 20,000/\text{mm}^3$ . In other cases, recovery defined as platelets  $> 50,000/\text{mm}^3$ .

secondary to liver transplantation are rare. In the non-liver transplant setting, 2 cases of hematopoietic transplantation with allogeneic cord blood and bone marrow from HLA-matched siblings have been reported: one in a 7-year-old boy with acquired severe aplastic anemia [3] and the other in a 9-year-old girl with myelodysplastic syndrome due to hepatitis-associated aplastic anemia [4]. In both cases, engraftment was prompt ( $< 1$  month) and successful.

Three cases of severe aplastic anemia after orthotopic liver transplantation have been reported (Table 1). In all cases, prompt hematopoietic recovery was successfully achieved by using marrow from HLA-matched siblings [5-7]. Umeda et al. [8] described a case of a 1-year-old boy who developed aplastic anemia after a living related liver transplantation from his HLA-haploidentical father (Table 1). The patient was platelet transfusion dependent and developed 2 episodes of life-threatening intracranial hemorrhage while receiving immunosuppressive therapy. Marrow engraftment was achieved by using stem cell transplantation with related allogeneic cord blood and bone marrow from an HLA-matched sibling.

To our knowledge, our case is the first report of the successful treatment of severe aplastic anemia by using only autologous cord blood. Of note, because T cells derived from the cord will develop in the setting of exposure to the HLA-disparate liver graft, there is also the possibility of inducing HLA-disparate tolerance; thus, the recipient may not require chronic immunosuppression.

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