Letter to the Editor

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Successful Treatment of Autoimmune Hemolytic Anemia with Steroid, IVIg, and Plasmapheresis in a Haploidentical Transplant Recipient

Haploidentik Transplant Alıcısında Otoimmün Hemolitik Aneminin Steroid, IVIg ve Plazmaferez ile Başarılı Tedavisi

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To the Editor,

Autoimmune hemolytic anemia (AIHA) is a rare, but clinically significant complication following hematopoietic stem cell transplantation (HSCT). It is characterized by hemolysis due to antibodies produced by the donor's immune system against donor red cell antigens. The 3-year cumulative incidence of AIHA is 4.44% in adults; however, 75% of patients develop AIHA during the first post-HSCT year [1]. AIHA after allogeneic HSCT has been associated with a variety of conditions, including chronic graft-versus-host disease (GVHD) [2], T-cell depletion [3], and unrelated donor transplants [4]. HSCT from unrelated donors and the development of chronic extensive GVHD were the only independent factors associated with AIHA [1]; however, the incidence of and risk factors for AIHA, as well as its prognosis and response to treatment remain unclear.

A 56-year-old male was diagnosed with high-risk acute myelogenous leukemia in April 2008. He was administered 8 cycles of chemotherapy, including idarubicin, cytosine arabinoside (ara-C), and sorafenib, and achieved complete remission. He remained in remission for 17 months, and then relapsed. He was treated with ara-C, and clofarabine, and achieved complete remission for the second time. He received a haploidentical (70% matched) bone marrow transplant (BMT) from his son on 03 March 2010, following conditioning with fludarabine, melphalan, and thiotepa, at the MD Anderson Cancer Center. GVHD prophylaxis was tacrolimus 1 mg p.o. twice daily and mycophenolate mofetil 1000 mg p.o. daily.

Stem cell infusion was uneventful, except for mild hypotension. The patient had mild veno-occlusive disease of the liver that eventually resolved, and several (4-5) episodes of CMV viremia, but no evident GVHD throughout his course. His blood type was A–, but the donor (son) was A+. The patient underwent bone marrow biopsy 3 months after transplantation, which showed 1% blasts and no flow cytometric evidence of relapse. Post-transplant microsatellite polymorphism was compatible with successful engraftment. No chimerism was observed. On post-transplant day 208 he presented with septic/hypotensive shock, and was supported with broad-spectrum antibiotics and intravenous fluids. He did not require mechanical ventilation or vasopressor therapy; however, deep anemia was noted (Hb: 3.8 g dL^{-1}) and most of the RBC units cross-matched for transfusion appeared to be incompatible. It was noted that the patient's blood group had converted to A+, suggesting full erythroid donor chimerism. AIHA was diag-

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Table 1: The patient's laboratory results upon admission, after each plasmapheresis, and upon discharge.

	Normal range	Upon admission	After 1st plasmapheresis	After 2nd plasmapheresis	After 3rd plasmapheresis	After 4th plasmapheresis	Upon discharge
Hb (g dL^{-1})	13.6-17.2	**3.8**	**3.2**	**9.4**	**8.3**	**8.4**	**8.5**
WBC (x 10^3 μL^{-1})	4.3-10.3	**14.8**	**18**	**13,9**	9,9	**12.6**	**11**
Plt (x 10^3 μL^{-1})	156-373	192	229	**148**	**97**	**112**	**120**
Ret (%)	0.6-2.6	**4.3**	N/A	N/A	N/A	**4.97**	N/A
LDH (U L^{-1})	240-480	**489**	N/A	**916**	**652**	**630**	471
I. Bil (g dL^{-1})	0.1-0.9	**1.54**	N/A	**1,22**	**1,05**	0.75	0.50
Haptoglobin (mg mL^{-1})	36-195	**<5.83**	N/A	N/A	N/A	16.5	17.6
DAT	negative	**positive**	**positive**	**positive**	**positive**	N/A	N/A
IAT	negative	negative	negative	negative	negative	N/A	N/A

***Hb:** hemoglobin; **WBC:** white blood cell; **Plt:** platelet; **Ret:** reticulocyte; **LDH:** lactate dehydrogenase; **I. Bil:** indirect bilirubin; **N/A:** not available; **DAT:** direct antiglobulin test; **IAT:** indirect antiglobulin test.*

nosed, based on fulfillment of all of the following criteria: positive direct antiglobulin test (DAT), negative indirect antiglobulin test (IAT), clinical and laboratory evidence of hemolysis (Table 1), and exclusion of other causes of immune hemolytic anemia.

Methylprednisolone 1 mg kg^{-1} (60 mg d^{-1}) IV was initiated. Plasmapheresis with fresh frozen plasma (FFP) was performed (median exchange volume: 3014 mL) for 4 days. After the 1st, 2nd, and 3rd plasmapheresis, DAT was positive and IAT was negative (Table 1). The reactives for the DAT test were polyspesific for IgG and C3d. Unfortunately, the patient's Hb value fell to 3.2 g dL^{-1} at that time (Table 1). IV immunoglobulin (IVIg) 25 g d^{-1} was administered the same day as the 2nd and 3rd plasmapheresis (after apheresis). Methylprednisolone was tapered to 40 mg d^{-1} on the fifth treatment day. As a result, the patient received 17 units of RBC, plasmapheresis 4 times, and IVIg twice during the course of treatment. Two weeks later AIHA was in control without RBC transfusion and the patient was discharged with an Hb value of 8.5 g dL^{-1} (Table 1). Methylprednisolone was tapered off within a month. Written informed consent was obtained from the patient.

Sanz et al. reported that most patients receive steroids as a primary treatment for AIHA and that the majority of cases do not respond [1]. Based on the response in the presented patient, plasmapheresis in addition to IVIg and corticosteroid should be considered a viable alternative treatment option in patients with AIHA that develops during the post-transplant period.

Conflict of Interest Statement

The authors have no conflicts of interest, including specific financial interests, relationships, and/or affiliations, relevant to the subject matter or materials included.

References

1. Sanz J, Arriaga F, Montesinos P, Orti G, Lorenzo I, Cantero S, Puig N, Moscardó F, de la Rubia J, Sanz G, Sanz MA: Autoimmune hemolytic anemia following allogeneic hematopoietic stem cell transplantation in adult patients. Bone Marrow Transplant 2007; 39: 555-561
2. Graze PR, Gale RP: Chronic graft versus host disease: A syndrome of disordered immunity. Am J Med 1979; 66: 611-620
3. Drobyski WR, Potluri J, Sauer D, Gottschall JL: Autoimmune hemolytic anemia following T cell-depleted allogeneic bone marrow transplantation. Bone Marrow Transplant 1996; 17: 1093-1099
4. O'Brien TA, Eastlund T, Peters Ch, Neglia JP, Defor T, Ramsay NK, Scott Baker K: Autoimmune haemolytic anaemia complicating haematopoietic cell transplantation in paediatric patients: High incidente and significant mortality in unrelated donor transplants for non-malignant diseases. Br J Haematol 2004; 127: 67-75