To the Editor:

Minor ABO incompatibility, in which donor-derived antibodies are directed against antigens on the recipient’s erythrocytes, may cause delayed hemolysis of recipient erythrocytes 1 to 2 weeks after allogeneic bone marrow transplantation (BMT). This phenomenon is caused by transient antibody production from passenger immunocompetent donor lymphocytes and not due to passive transfer of antibodies during marrow transfusion. Passenger lymphocyte-mediated hemolysis has been described in solid organ transplant recipients treated by cyclosporine. The donor origin of the antibodies has been confirmed by studies of Ig allotypes. We describe the first case of donor-derived immune hemolysis occurring after allogeneic peripheral blood stem cell transplantation (PBSCT).
A 12-year-old boy, blood group A+, with Philadelphia-positive acute lymphoblastic leukemia in first complete remission was referred to us for allogeneic PBSCT from his HLA-matched MLC nonreactive sister, blood group O+. After conditioning, he received 100 mL of washed buffy coat containing \(5.4 \times 10^8\) viable non-T-cell–depleted cells/kg, harvested by CS-3000 plus (Baxter, Deerfield, IL) from his donor who was treated with recombinant human granulocyte colony-stimulating factor (rhG-CSF) at 10 \(\mu\)g/kg/d for 5 days (harvesting was performed on day 5). Cyclosporine A was administered as graft-versus-host disease (GVHD) prophylaxis. On day 8 posttransplantation, he developed fever, abdominal and bilateral flanks pain, and severe intravascular hemolysis, with a decrease in his hemoglobin level to 5.4 g/dL. Maximal bilirubin level reached 1,050 \(\mu\)mol/L (N < 17), a lactate dehydrogenase level of 6,800 IU/L (N = 300 to 620), a free hemoglobin level of 20 mg%, a haptoglobin level of less than 50 mg%, a urea level that increased to 21.5 mmol/L (N = 4.1), the creatinine level was normal, and free hemoglobin was detected in the urine. The direct Coombs’ test was positive, further characterized by a complement-specific antiglobin serum as C3d. A maximal titer of 1:8,000 IgM and IgG anti-A antibodies were found in the patient’s serum. The anti-A titer in the donor’s serum was 1:32. The child was treated with solumedrol at 4 mg/kg. He received exchange transfusion of 1 blood volume, 6 U of packed cells, fluids, and diuretics. He recovered from this hemolytic reaction after 7 days, with normalization of all deranged laboratory values.

The incidence of intravascular hemolysis due to passenger B lymphocytes after allogeneic PBSCT may be higher than after allogeneic BMT. Almost 95% of donor lymphocytes of minor ABO-mismatched bone marrow allografts, in particular O+-A+, produce antibodies against recipient red blood cells; however, only 10% to 15% of patients develop clinically significant hemolysis. This may not be the case in allogeneic PBSCT, because the CD19+ and CD20+ lymphoid cell yields of PBSC harvests exceed those of bone marrow allografts by 11-fold.4,5 This life-threatening transfusion reaction may occur in increasing frequencies after allogeneic PBSCT, especially when the donor is O+ and the recipient A+. Because immediate diagnosis and aggressive treatment is essential in these cases, transplanters should be especially alert to these complications because the number of allogeneic PBSCT are increasing. One should also consider purging of B cells if more cases will be reported.

Amos Toren
The Institute of Hematology
The Chaim-Sheba Medical Center
Tel-Hashomer, Israel

Yehudit Dacosta
Noga Manny
Blood Bank
Gabor Varadi
Reuven Or
Arnon Nagler
Department of Bone Marrow Transplantation
Hadassah University Hospital
The Hebrew University
Jerusalem, Israel

REFERENCES


Passenger B-lymphocyte-induced severe hemolytic disease after allogeneic peripheral blood stem cell transplantation [letter]

A Toren, Y Dacosta, N Manny, G Varadi, R Or and A Nagler