Donor origin Rh antibodies as a cause of significant hemolysis following ABO-identical orthotopic liver transplantation

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A group A, D-positive patient underwent orthotopic liver transplantation from a group A, D-negative (*cde/cde*) donor. Anti-D and -E were eluted from the recipient's red cells and were found in the recipient's serum 13 days later, at which time significant hemolysis developed. These Rh antibodies appear to be secondary to passive transfer of sensitized donor lymphocytes, a rare finding following liver transplantation. ***Immunohematology*** 1992; 8:100–101.

Passively transferred donor B-lymphocytes present in a solid organ can produce red cell antibodies that may cause an immune hemolysis if the recipient's red cell antigens are viewed as "foreign."[1] While donor-origin ABO system antibodies are well recognized in renal, liver, and heart-lung transplantation, donor-origin antibodies of the Rh system are rare.[2,3,4] Here, we describe the development of anti-D and -E that caused clinically significant hemolysis in a D-positive recipient of an ABO-identical liver.

Case Report

A 53-year-old female with end-stage liver disease secondary to cirrhosis from alpha$_1$-antitrypsin deficiency was group A, D-positive (CcDEe) prior to transplantation. The liver donor was group A, D-negative (*cde/cde*). Donor history was not available. The transplant proceeded without complications, and seven units of A, D-positive, packed red blood cells (PRBCs) were administered perioperatively and cyclosporine was started. Postoperatively, the hematocrit was 27.6%, the bilirubin was 18.8 µmol/L, and no spherocytes were noted on the peripheral blood smear.

The patient became weak due to progressive anemia without evidence of bleeding. Bilirubin was 205.2 µol/L on posttransplant day 7. On posttransplant day 13 (see Fig. 1), the hematocrit was 21.2% and indirect bilirubin was 97.5 µmol/L. Serum haptoglobin levels were < .05 g/L, and spherocytes were noted on peripheral blood smear. Anti-D and -E were identified in the patient's serum and in an eluate from the patient's red cells. She received a total of nine group A, D-negative (*cde/cde*) compatible PRBCs and was discharged from the hospital on day 24 without further evidence of hemolytic anemia. Four months post-transplantation, the patient is asymptomatic, hematocrit is > 35% and there is no further transfusion requirement.

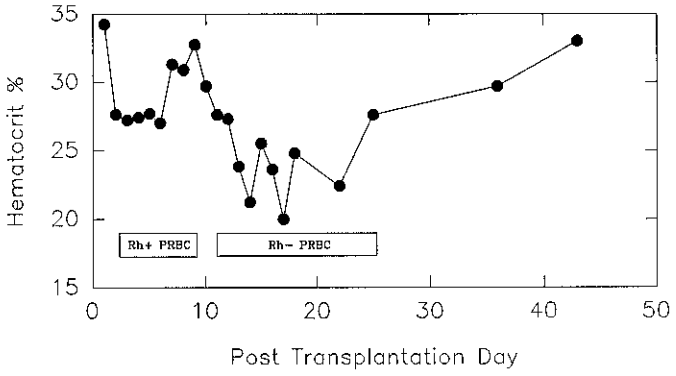

Fig. 1. Significant hemolysis noted by decreasing hematocrit following ABO-identical liver transplantation in a D-positive recipient. D-positive and D-negative (*cde/cde*) PRBC transfusions are indicated by boxes.

Materials and Methods

Red cell ABO group and Rh type, antibody screen and identification, and direct antiglobulin test (DAT) were performed using standard methods[5] and commercially available reagents (Immucor, Norcross, GA; Ortho Diagnostic Systems, Raritan, NJ). An eluate was prepared using EluKit-II (Gamma Biologicals, Inc., Houston, TX).

Results

On admission, the patient was found to be group A, D-positive. The Rh phenotype was CcDEe. Screening for unexpected antibodies was negative, as was a DAT.

On posttransplant day 13, because of progressive anemia, another sample was sent to the blood bank. The patient's red cells were again noted to be group A, but typing for the D antigen was invalid due to 3+ agglutination of her cells in Rh control media. Further investigation revealed a positive DAT (2+ with anti-IgG and weak agglutination with anti-C3). The patient's antibody screen was positive and the results of tests with a panel of red cells revealed agglutination consistent with anti-D and -E. An acid eluate made from the patient's red cells also revealed the presence of anti-D and -E. A total of nine crossmatch-compatible D-negative (*cde/cde*) PRBCs were transfused over the next 9 days.

Discussion

This is a case of clinically significant immune hemolysis due to donor-derived anti-D and -E following liver transplantation. Immune-mediated hemolysis following solid organ transplantation is not uncommon and is due to B-lymphocytes in the graft that may produce antibodies against host antigens.[1] The sensitized B-lymphocyte response represents a secondary immune response, while a primary response is blocked by immunosuppressive agents. These responses are in contrast to preformed antibodies that are passively transferred with the transplant and therefore would be detectable immediately and quickly disappear.

Ramsey et al.[1] reported that isohemagglutinins were detectable in 28 percent of ABO-incompatible orthotopic liver transplant recipients 8 to 16 days posttransplantation. Five of eight recipients who had donor-derived isohemagglutinins developed hemolysis lasting from 7 to 19 days. Although donor- derived isohemagglutinins are well recognized in solid organ transplantation, Rh antibodies are rare.[2] These have been reported exclusively in kidney transplant recipients, except for an abstract that described one patient who developed severe hemolysis due to anti-D following liver transplantation while on the immunosuppressive agent FK506.[6] Of the nine cases of Rh antibodies in kidney transplant recipients,[2] seven patients had hemolysis in a median of 17.5 days postoperatively. DATs continued to be reactive for 69 to 179 days after transplantation.

The case reported here highlights a D-positive individual who developed significant hemolysis due to anti-D and -E produced by donor B-lymphocytes residing in the D-negative (*cde/cde*) donor's liver. This hemolysis can be confused with a delayed hemolytic transfusion reaction. Therefore, it is important to recognize this unusual complication of liver transplantation so that antigen-negative blood can be administered.

References

1. Ramsey G, Nusbacher J, Starzl TE, Lindsay GD. Isohemagglutinins of graft origin after ABO-unmatched liver transplantation. N Eng J Med 1984;311:1,167–70.
2. Ramsey G. Red cell antibodies arising from solid organ transplants. Transfusion 1991;31:76–86.
3. Shanwell A, Eleborg L, Blomqvist BI, Wiechel B, Ericzon BG. Hemolysis in ABO-compatible liver transplantation—only after O grafts? Transplant Proc 1989;21:3,532.
4. Angstadt J, Jarrell B, Maddrey W, et al. Hemolysis in ABO-incompatible liver transplantation. Transplant Proc 1987;19:4,595–7.
5. Walker RH, ed. Technical manual. 10th ed. Arlington, VA: American Association of Blood Banks, 1990.
6. Ramsey G, Kiss JE, Sacher RA, Fernandez C, Starzl TE. Rh antibodies in two patients receiving liver and kidney-pancreas grafts from the same Rh-sensitized donor (abstract). Joint Congress of the American Association of Blood Banks and the International Society of Blood Transfusion, Los Angeles, 1990:S791.

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