TRANSFUSION MEDICINE
Official Journal of the British Blood Transfusion Society
Transfusion Medicine | LETTER TO THE EDITOR

Successful liver and lung transplantation in patients with severe IgA deficiency, high anti-IgA concentration and a history of anaphylactic transfusion reaction

Dear Sir,

Patients with immunoglobulin A (IgA) deficiency and a high concentration of anti-IgA antibodies (anti-IgA) are at risk for anaphylaxis when IgA-containing regular blood products are transfused (Leikola *et al.*, 1973; Sandler *et al.*, 1995). This case report describes successful liver and lung transplantation in patients with severe IgA deficiency and a history of anaphylactic transfusion reaction due to a high anti-IgA concentration.

Concentrations of IgA and anti-IgA were assayed with in-house enzyme immunoassays (EIA) with a detection limit of 0.05 mg L^{-1} for IgA and 7 AU L^{-1} for anti-IgA (Hirvonen *et al.*, 1993; Koskinen *et al.*, 1995a). On the basis of a known anti-IgA antibody titre in the haemagglutination assay, a value of 12 000 AU L^{-1} was assigned as a standard in the EIA. This enabled direct comparison of EIA values with the reciprocal value obtained with the hemagglutination assay (e.g. anti-IgA value 12 000 AU L^{-1} corresponds to anti-IgA titre 1/12 000).

The transplantations were performed at Helsinki University Central Hospital, Helsinki, Finland. Fresh frozen plasma (FFP) from donors with severe IgA deficiency (IgA <0.05 mg L^{-1}) and leukocyte-depleted red blood cell (RBC) and platelet components washed three times were used for transfusion support. Each platelet component was derived from four whole blood donations. Both components fulfilled the criteria for washed RBC components defined by the Council of Europe (protein content <0.5 mg $unit^{-1}$; European Directorate for the Quality of Medicines & HealthCare, 2013).

The first patient was a 62-year-old woman with idiopathic pulmonary fibrosis. The patient suffered an anaphylactic reaction after the infusion of a small amount of regular RBC component, and a severe IgA deficiency with a high anti-IgA concentration was discovered (Table 1). Lung transplantation was performed in August 2010. Donor lungs were thoroughly perfused. During the procedure, three RBC, four platelet and two FFP components (2100 mL) were transfused without adverse effects. In addition, 5000 mL of other intravenous solutions were infused.

In samples taken 15 and 30 days after transplantation, low IgA concentrations were detected, with no anti-IgA (Table 1). Two years later, due to infections, treatment with a gamma-globulin preparation containing a small amount of IgA (<3 μg mL^{-1}) was initiated. In samples 2.5 and 3 years after transplantation, the severe IgA deficiency had reappeared and a low anti-IgA concentration was detectable (Table 1).

Table 1. Changes in serum IgA and anti-IgA concentration in relation to transplantation (day 0 = transplantation)

	Lung transplantation	
Time interval	IgA (mg L^{-1})	Anti-IgA (AU L^{-1})
Patient 1		
−12 years	<0.05	1290
−1 years	<0.05	1150
+15 days	21	<7
+30 days	16	<7
+2.5 years	<0.05	65
+3 years	<0.05	50
Patient 2		
−7 years	<0.05	11 750
−1 months	<0.05	7800
+9 days	0.21	<7
+15 days	0.42	<7
+43 days	<0.05	2180
+3 months	<0.05	1610

The second patient was a 56-year-old woman with cryptogenic hepatic cirrhosis and hepatocellular carcinoma. She had suffered an anaphylactic transfusion reaction after the infusion of regular FFP, and a severe IgA deficiency with a very high anti-IgA concentration was discovered (Table 1). Later, she tolerated transfusion of two washed platelet components. In January 2013, the patient received a liver transplant. The donor liver was thoroughly perfused. At the beginning of anaesthesia, 4% albumin was infused to compensate 6 L of removed ascites. After the first 100 mL, the patient developed decreased oxygen saturation (85%) and hypotension (65/30 mmHg), which were resolved with the administration of noradrenalin, corticosteroids, ranitidine and promethazine to enable the continuation of 2000 mL infusion. Three RBCs and platelets and two FFP components (1900 mL) were transfused without adverse effects. In addition, 2000 mL of other intravenous solutions was infused.

A low IgA concentration without anti-IgA was detected on the 9th and 15th post-operative days. On samples taken 43 days and

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doi: 10.1111/tme.12136

3 months post-operatively, the severe IgA deficiency and a high anti-IgA concentration had reappeared (Table 1).

Washed RBC and platelet components proved safe for severely IgA-deficient patients with a high anti-IgA concentration and a history of anaphylactic transfusion reaction. Albumin preparation and washed cell components may contain some IgA, yet microgram quantities of IgA are usually tolerated (Lashinger *et al.*, 1984; Hirvonen *et al.*, 1993). Two previous reports describe the use of washed cell components in liver transplantation in four patients with anti-IgA, two with undetectable IgA and two with a decreased IgA concentration (Davenport *et al.*, 1992; Win *et al.*, 1997). Due to a history of anaphylactic transfusion reaction, one of these patients received platelets collected by apheresis from IgA-deficient donors (Win *et al.*, 1997). However, due to short platelet shelf life, this policy may reduce the availability of platelet components for IgA-deficient patients, which decreases their chance of receiving an organ transplant. In previous reports, the criteria for IgA deficiency were not as strict as in this report, and anti-IgA levels were reported only on one patient with a detectable IgA level. Based on over 40 years of experience from our laboratory, specific anti-IgA antibodies are found only in patients with undetectable IgA (Koskinen *et al.*, 1995b). With respect to an anaphylactic transfusion reaction caused by IgA, the reported anti-IgA concentrations have been high, over 1000 AU L^{-1} in nearly all the cases (Leikola *et al.*, 1973).

In post-transplantation samples, low concentrations of IgA appeared, while anti-IgA was undetectable. Similar observations have been made earlier (Davenport *et al.*, 1992; Win *et al.*, 1997). Despite careful perfusion, small amounts of IgA may remain in the transplanted organ. IgA-secreting plasma cells have also been demonstrated in post-transplantation liver biopsies (Lashinger *et al.*, 1984), which explains the prolonged production of IgA in transplant recipients. During the transplantation procedure, dilution caused by infused blood components and other solutions causes a marked reduction in anti-IgA (Davenport *et al.*, 1992), whereas strong immunosuppressive therapy may decrease further anti-IgA production. In addition, IgA produced by the transplanted plasma cells may form complexes with the transplant recipient's anti-IgA, resulting in the disappearance of anti-IgA detected with EIA; in this case, anti-IgA activity would still be demonstrated in the complex-containing fractions in serum fraction analysis (Sundin *et al.*, 1998).

The severe IgA deficiency and anti-IgA had reappeared by 43 days after liver transplantation. The anti-IgA concentration was markedly lower than in the pre-transplant sample. This may be a consequence of decreasing IgA production by transplanted plasma cells and concurrent immunosuppressive therapy. A similar phenomenon has been observed when immunoglobulin therapy was switched to a preparation containing less IgA (Koskinen *et al.*, 1995b). In the lung transplantation patient, the follow-up samples were obtained as late as 2.5 and 3 years after transplantation. In these samples, IgA was undetectable and a very low level of anti-IgA was measured. This decrease in anti-IgA may be due to treatment with an immunoglobulin preparation containing a low level of IgA and continuing immunosuppressive therapy.

In conclusion, solid organ transplantation can be performed successfully in severely IgA-deficient patients with a high level of anti-IgA and a history of anaphylactic transfusion reaction. Washed RBC and platelet components proved safe for transfusion support in these patients. Transplantation may result in a short transitory period of low-level IgA production and disappearance of detectable anti-IgA reactivity. The small residue of IgA in the transplant and the IgA produced by plasma cells in the transplanted organ did not seem to pose a risk for adverse reactions in the transplant recipient, possibly due to the strong immunosuppressive therapy that these patients receive.

ACKNOWLEDGMENTS

S. B. analysed patient data and wrote the paper. K. J. designed the analyses, analysed patient data and critically revised the manuscript in preparation. A.-M. K. collected patient data and critically revised the manuscript in preparation. H. I. collected patient data and critically revised the manuscript in preparation. M. H. collected patient data and critically revised the manuscript in preparation. P. H. collected patient data and critically revised the manuscript in preparation. S. K. designed the analyses, analysed patient data and wrote the paper.

CONFLICT OF INTEREST

The authors have no competing interests.

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