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Transfusion Management of Patients with IgA Deficiency and Anti-IgA during Liver Transplantation

Abstract

Severe anaphylactic or allergic reactions may occur during blood transfusion to patients who are IgA-deficient and have anti-IgA in their blood, particularly those with class-specific antibodies. These patients are a particular challenge to the hospital transfusion service when large volumes of blood components are required for transfusion support, as in liver transplantation. We have successfully provided blood components for 3 such patients undergoing liver transplantation. Red cells were washed manually or by automated technique. Platelets were washed manually. All plasma was from IgA-deficient donors. One patient's entire plasma requirements were supplied by autologous plasmapheresis. Serial determinations of IgA levels and anti-IgA titers in 1 patient demonstrated an abrupt fall in anti-IgA with the appearance of barely detectable amounts of IgA during the surgery. IgA-containing plasma cells were demonstrated in the biopsies of liver homografts of 2 patients following transplantation. IgA deficiency with anti-IgA can be successfully managed during liver transplantation with advance planning.

Allergic reactions to blood transfusion are relatively common, occurring in approximately 2–3% of recipients [1]. Most of these are relatively minor; however, severe allergic reactions, including anaphylaxis, occur with an estimated frequency of 1:20,000–1:47,000 transfusions [2]. One group of patients who appear to be at significantly increased risk of severe reactions are those with antibody to IgA. Such antibodies are considered as class-specific when they react with all human IgA myeloma proteins and are defined as limited specificity when they react with some, but not all, examples of IgA [3]. Most serious transfusion reactions in this setting have been associated with class-specific antibodies, although reactions may occur with limited specificity antibodies as well [2, 4].

Liver transplantation often requires large volumes of plasma containing blood components for patient support. When patients who are IgA-deficient, with anti-IgA, become candidates for liver transplantation, the hospital transfusion service is faced with a significant challenge to provide safe blood components in a timely fashion. There are currently no published guidelines on how to approach the transfusion management of such patients. We have successfully supported 3 patients with IgA deficiency and anti-IgA during liver transplantation.

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Table 1. Clinical patient data prior to transplant

Patient	Age/ sex	Prior transfusions			IgA level	Anti-Iga specificity	Diagnosis
		RBC	plasma	reactions			
1	48/F	none	none	none	0.015 g/l	limited	primary biliary cirrhosis
2	16/F	none	2 units	none	<0.01 g/l	class	autoimmune hepatitis
3	32/M	5 units	2 units	yes[1]	0.05 g/l	class	hepatitis C

[1] Nausea, vomiting, diarrhea, later fever and chills.

Materials and Methods

IgA levels were determined by passive hemagglutination. Anti-IgA levels were determined by hemagglutination inhibition as described [5]. Red blood cells (RBC) and platelets were washed by manual or automated technique using Cobe 2991 Cell Washers.

Case Reports

The patients were (1) a 48-year-old woman with primary biliary cirrhosis, (2) a 16-year-old woman with autoimmune chronic active hepatitis, and (3) a 32-year-old man with chronic hepatitis C. Patients 1 and 2 were transplanted at University Hospital, London, Ontario. Patient 3 was transplanted at The University of Michigan Hospitals, Ann Arbor, Mich.

The transfusion history and IgA status of each patient is shown in table 1. All were IgA-deficient. The first 2 were identified by quantitative immunoglobulin determination during pretransplantation evaluation. Patient 1 had not been transfused but had been pregnant and had an antibody of limited specificity. The antibody in patient 2 was discovered after transfusion of plasma without any clinical reaction, which was most likely the mode of sensitization. Patient 3 had been transfused with 5 units of RBC 3 years before without experiencing any transfusion reaction. However, during pretransplant evaluation he received plasma and experienced a prompt allergic reaction. A class-specific antibody was then detected in his serum

The perioperative transfusion management of each patient is summarized in table 2. Patient 1 had coagulation parameters in the normal range. Six 500-ml units of autologous plasma were collected by apheresis and frozen. This patient received 8 units of washed RBC, and 10 units of autologous fresh frozen plasma (FFP, expressed as 200-ml equivalents). Patient 2 received 6 units of washed RBC and a pool of 6 random donor platelets, washed by manual technique, as well as 12 units of FFP from IgA deficient donors. Patient 3 received 7 units of RBC 5 weeks before transplant because of gastrointestinal hemorrhage. These were washed by automated technique. Intraoperatively, he received 24 units of RBC, washed by automated technique, 4 pools of 6 random donor platelet concentrates, washed by manual technique, and 32 units of IgA-defencient FFP. At the end of the operation, he also received 2 units of red blood cells, adenine-saline added (AS-1) that were not washed, as the supply of washed RBC was exhausted. Postoperatively, he received 2 additional units washed RBC.

Table 2. Perioperative transfusion management

Patient	Number of units transfused		
	1	2	3
Preoperative			
RBC	0	0	7[b]
Intraoperative			
RBC	6[b]	6[b]	26[c]
FFP	6[a]	8[d]	32[d]
Platelets	0	6[b]	24[b]
Postoperative			
RBC	2[b]	0	2[b]
FFP	4[a]	4[d]	0

[a] Autologous, expressed as FFP equivalents (200 ml).
[b] Washed.
[c] Twenty-four units washed, manual of automated, last 2 units AS-1 and not washed.
[d] IgA-deficient.

The results of successive IgA levels and anti-IgA titer in the perioperative period of patient 3 are shown in figure 1. Before the transplant procedure, the patient had a high titer of anti-IgA that dropped precipitously during the operation to undetectable levels, as the result of dilution by crystalloid solutions and non-IgA-containing blood components. At the end of the procedure, both IgA (0.06 g/l) and anti-IgA (titer: 1:10) were present in the serum at the lowest limit of detectability, and persisted over the subsequent 2 weeks. The patient also received 65 g of intravenous immunoglobulin (Sandoglobulin) postoperatively as passive immunotherapy for cytomegalovirus prophylaxis, and another 30-gram dose as an outpatient. Ten months after transplantation, this patient had no detectable IgA and anti-IgA titer of 1:1,280. He had not received blood products in the interim.

All 3 patients were successfully transplanted without any evidence of adverse reactions to transfusion. Patient 1 died of heart disease unrelated to any transfusion sequelae 5 years after transplantation. Patients 2 and 3 were alive 11 and 13 months posttransplant, respectively. Posttransplant liver biopsies from patients 2 and 3 were available for review. In order to determine if there was evidence of donor lymphocyte engraftment and IgA production, sections were stained by immunoperoxidase technique for IgA. In both cases, IgA-containing plasma cells were readily identified in portal tracts.

Discussion

The experience gained from these 3 cases demonstrates that, with advance planning, a history of IgA deficiency with anti-IgA is not a contraindication to elective surgical procedures requiring large-volume blood product support, such as liver transplantation, even if the patient has manifested previous severe allergic reactions to blood transfusion. As serial determinations of antibody titer in patient 3 demonstrates, there is a progressive and marked reduction in anti-IgA levels as the volume of transfused blood components increases. In this case, the antibody reached undetectable levels after approximately a 2 blood volume transfusion. Subsequently, the transfusion of routinely collected RBC, or other plasma-containing components, appears to be of little risk during the period when the anti-IgA levels are very low. In addition, since Sandoglobulin contains a relatively large amount of IgA compared to other immunoglobulin concentrates (562±53 μg/ml) [6] it appears that subsequent challenge with IgA while the titer of antibody is low poses no additional risk of reaction.

Clearly, autologous blood transfusion is preferable for these patients, if possible. When this is not an option, IgA-deficient FFP and cellular blood components are preferable, but the latter is not practical in liver transplantation as the availability of a suitable organ donor cannot be predicted. However, our experience indicates that routinely washed red blood cells and platelets can be safely used for transfusion support. All of the units we processed by either manual or automated technique were washed in unbuffered saline. Recently, a technique for washing platelets, which removes a greater proportion of IgA, using citrate-buffered saline, has been published [7]. While such a technique has theoretical advantages, it may not be necessary in all cases.

As part of the transplantation immunosuppression protocol, all of our patients received preoperative steroids, which may have ameliorated any potential allergic reactions. Although there is no incontrovertible evidence

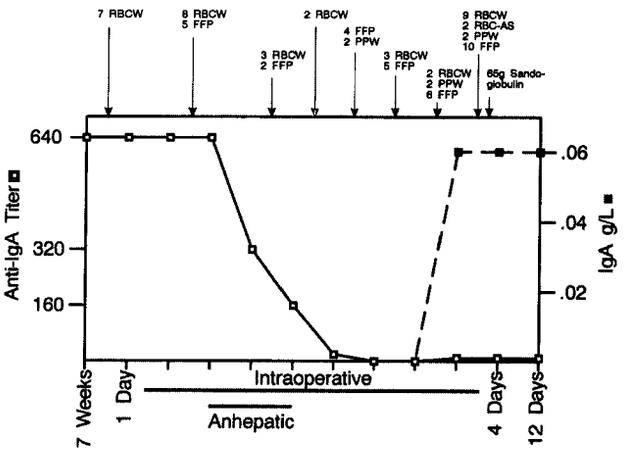

Fig. 1. Perioperative changes in IgA levels (■) and anti-IgA titer (□) in patient 3. RBCW = washed RBC; PPW = washed platelet pool; FFP = IgA-deficient fresh frozen plasma; RBC-AS = AS-1 red blood cells.

that pretransfusion steroid administration will prevent anaphylaxis, it seems prudent that prophylactic steroids should be considered when non-IgA-deficient components are transfused.

Finally, the presence of IgA in the graft poses little, if any, risk to the patient. IgA-secreting plasma cells can be demonstrated in homografts after transplantation. Their presence may serve as a marker of donor lymphocyte engraftment.

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