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Acute Hemolytic Transfusion Reactions due to Multiple Alloantibodies Including Anti-E, Anti-c and Anti-Jk^b

We report a case of two consecutive episodes of acute hemolytic transfusion reactions (HTRs) due to multiple alloantibodies in a 34-yr-old man who suffered from avascular necrosis of left femoral head. He received five units of packed red blood cells (RBCs) during surgery. Then the transfusion of packed RBCs was required nine days after the surgery because of the unexplained drop in hemoglobin level. The transfusion of the first two units resulted in fever and brown-colored urine, but he received the transfusion of another packed RBCs the next day. He experienced even more severe symptoms during the transfusion of the first unit. We performed antibody screening test, and it showed positive results. Multiple alloantibodies including anti-E, anti-c and anti-Jk^b were detected by antibody identification study. Acute HTRs due to multiple alloantibodies were diagnosed, and the supportive cares were done for 6 days. We suggest the antibody screening test should be included in the panel of pretransfusion tests for safer transfusion, and it is particularly mandatory for the patients with multiple transfusions, pregnant women, and preoperative patients.

Key Words : *Blood Transfusion; Blood Grouping and Cross Matching; Blood Group Incompatibility; Isoantibodies*

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INTRODUCTION

The most severe acute hemolytic transfusion reactions (HTRs) occur when transfused packed red blood cells (RBCs) are incompatible with serum ABO blood group of the recipient (1). Such HTRs with severity also are associated with unexpected antibodies (1, 2). We report a case of two consecutive episodes of acute HTRs due to multiple alloantibodies including anti-E, anti-c and anti-Jk^b in a 34-yr-old man who received repeated transfusions after total hip replacement.

CASE REPORT

A 34-yr-old man who suffered from hematuria and fever was admitted to the Emergency Department of Pusan National University Hospital on 7 December 2002, after repeated transfusions of packed RBCs. Total hip replacement was performed at a local orthopedic clinic on 26 November 2002 for treatment of avascular necrosis of left femoral head. He received five units of packed RBCs during the surgery. An unexplained drop in hemoglobin level was observed nine days after the surgery. He was transfused with packed RBCs; however, during the transfusion of the first two units, fever and brown-colored urine were resulted, and the transfusion was discontinued. Transfusion of RBCs was performed again the next day. He experienced even more severe symptoms during the transfusion of the first unit, and therefore the transfusion was stopped and the patient was transferred to Pusan National University Hospital. Vital signs were as follows: blood pressure 110/70 mmHg, pulse rate 80/min, temperature 36℃, and respiration rate 20/min. Physical examination revealed no remarkable abnormal findings except icteric sclera. Complete blood cell count showed leukocyte count of 6,400/μL, hemoglobin level of 8.8 g/dL, and platelet count of 22,000/μL. Blood chemistries yielded abnormal results: total bilirubin 2.46 mg/dL (reference range 0.3-1.3 mg/dL), direct bilirubin 1.16 mg/dL (reference range 0.05-0.40 mg/dL), aspartate aminotransferase 44 IU/L (reference range 15-40 IU/L), alanine aminotransferase 34 IU/L (reference range 6-40 IU/L), alkaline phosphatase 146 IU/L (reference range 95-280 IU/L), BUN 14 mg/dL (reference range 6-26 mg/dL), creatinine 1.2 mg/dL (reference range 0.4-1.5 mg/dL), and lactate dehydrogenase 1,251 IU/L (reference range 218-472 IU/L). The results of ABO and RhD blood grouping showed group O and RhD positive. The antibody screening test (DiaMed AG, Cressier, Morat, Switzerland) produced positive results. Anti-E, anti-c and anti-Jk^b were detected by antibody identification study (Table 1); however, the result was negative on repeated direct antiglobulin tests. Kidd and Rhesus antigenic phenotyping

Table 1. The results of antibody screening and identification test (DiaMed AG, Screening cell Lot No. Set I+II 45151.16.x and 05980.85.x: Panel cell Lot No. SetID-Diapanel 45161.17.x)

	Rh-hr						Rh-hr						Duffy		Kidd		Lewis		P	MNS				Lutheran		Xg	Lewis	
	D	C	E	c	e	C^w	K	k	Kp^a	Kb^b	Js^a	Js^a	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P$_1$	M	N	S	s	Lu^a	Lu^b	Xg^a	LISS*/ Combs	Enzyme phase
I	+	+	0	0	+	0	0	+	0	+	nt	+	+	0	0	+	+	0	+	+	+	+	+	0	+	+	2+	nt
II	+	0	+	+	0	0	+	+	0	+	nt	+	+	+	+	0	0	+	+	+	0	+	0	0	+	0	4+	nt
Di^{a+}	+	0	+	+	0	0	0	+	0	+	0	+	+	0	+	0	0	+	+	+	+	+	+	0	+	0	4+	nt
1	+	+	0	0	+	+	0	+	0	+	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	1+	2+
2	+	+	0	0	+	0	0	+	+	+	0	+	+	+	+	0	+	0	+	+	0	0	+	0	+	+	-	-
3	+	0	+	+	0	0	0	+	0	+	0	+	0	+	+	0	0	+	+	+	0	+	0	0	+	0	4+	4+
4	0	+	0	+	+	0	0	+	0	+	0	+	+	+	+	+	+	0	0	+	0	0	+	0	+	nt	+/-	2+
5	0	0	+	+	+	0	0	+	0	+	0	+	+	0	+	+	0	+	+	+	0	0	+	+	+	+	0	4+	4+
6	0	0	0	+	+	0	+	+	0	+	0	+	0	+	0	+	0	+	+	+	0	+	0	0	+	0	2+	4+
7	0	0	0	+	+	0	0	+	0	+	0	+	+	0	0	+	0	+	+	0	+	0	+	0	+	0	2+	4+
8	+	0	0	+	+	0	0	+	0	+	0	+	0	0	+	+	0	0	0	0	+	+	+	0	+	+	+/-	4+
9	0	0	0	+	+	0	+	+	0	+	0	+	+	+	+	0	0	+	+	0	+	0	+	0	+	0	-	4+
10	+	+	0	+	+	0	+	0	0	+	0	+	+	+	+	+	+	0	+	+	0	+	0	0	+	+	-	3+
11	+	+	0	+	+	0	0	+	0	+	0	+	+	+	+	+	0	0	+	+	0	+	+	0	+	+	-	3+

*LISS, low ionic strength salt solution; nt, not tested.

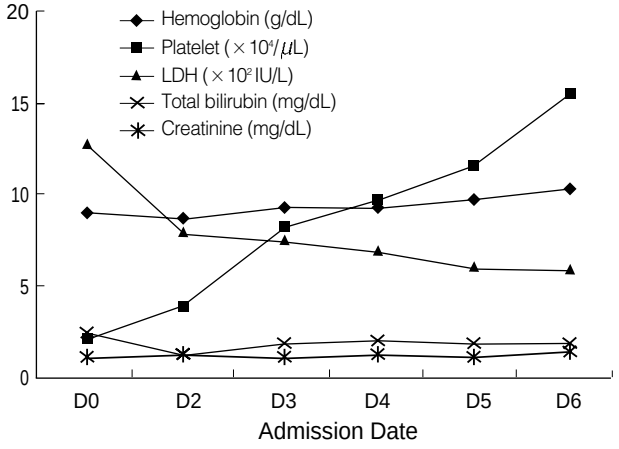

Fig. 1. The changes of laboratory results after acute hemolytic transfusion reactions.

(DiaMed AG) were conducted; it showed Jk^a positive, Jk^b negative on Kidd antigenic phenotyping, and Rhesus subgroup was CDe. The haptoglobin level was below the detection limit (<10.0 mg/dL).

He was diagnosed as having acute HTRs due to multiple alloantibodies including anti-E, anti-c and anti-Jk^b. No more transfusions were requested, and he was under the supportive care for 6 days. He returned to the previous hospital with relief of symptom, and his condition gradually improved thereafter (Fig. 1).

DISCUSSION

Acute HTRs are most severe when these occur in ABO incompatibility (1). They also are associated with unexpected antibodies to the other blood group antigens (1, 2). The binding of antibody to blood group antigens may activate complement and intrinsic clotting cascade of coagulation system and causes intravasucular hemolysis, or may be phagocytozed by macrophages in reticuloendothelial system, which results in extravascular hemolysis (2). Also, the role of cytokines in acute HTRs is increasingly recognized (1, 2). The symptoms and signs produced by acute HTRs include fever, hematuria, jaundice, renal failure, and even the state of shock. The reports of acute HTRs related to unexpected antibodies including antibodies against Rhesus, Kidd, Diego, P antigens, and others have been introduced in the literature (3-8).

The patient reported having received the transfusion of packed RBCs during the surgery of right knee twelve years before. Thus, we think that the delayed HTR might have occurred mainly due to anti-E, known as the most common

causative antibody in delayed HTRs, with or without the other unexpected antibodies, after receiving the transfusion of the five units of packed RBCs during the operation; however, no antibody screening test was performed for detection of unexpected antibodies. First acute HTR was noticed when the patient was transfused with the two units of packed RBCs nine days after the replacement surgery, and he complained of fever and brown-colored urine concomitantly. Unfortunately, no further evaluation was done for hemolytic reaction, and he was transfused again with one unit of packed RBCs the day after. Then the second acute hemolytic episode with even more severe symptoms and signs such as fever, hematuria, and jaundice occurred. In addition, severe thrombocytopenia was observed immediately upon admission, probably accompanied by the activation of coagulation system during the acute HTR. However, no further evaluation was done for any other particular coagulopathies.

Anti-E, anti-c and anti-Jk^b were detected by a series of antibody identification tests (DiaMed AG), such as antiglobulin and enzyme phase. In general, direct antiglobulin test reveals positive in HTR, but the result in this case was negative probably due to immediate and aggressive destruction of transfused red cells by multiple alloantibodies. In Korea, pretransfusion tests including ABO, RhD blood grouping and crossmatching test for safe transfusion have been performed for many years. The primary purpose of the crossmatching is to detect ABO incompatibility, and the secondary purpose of this test is to exclude incompatible donor cells with patient serum (i.e. detection of unexpected antibodies). Antibodies reactive at 37℃ or in the antiglobulin test are more likely to be clinically significant than cold reactive antibodies (2). Unfortunately, antiglobulin phase of crossmatching in order to rule out the unexpected antibodies have not been conducted by many hospitals other than university-affiliated medical centers in Korea. Hence, the clinically significant unexpected antibodies such as antibodies against Rhesus, Kidd, Duffy, Diego antigens, and others cannot be detected by saline phase of crossmatching alone.

The antibody screening test is used as a part of routine pretransfusion studies for the purpose of detection of unexpected antibodies; however, in Korea it has not received as much attention as such a tool prior to transfusion. According to the annual reports by *The Korean Association of Quality Assurance for Clinical Laboratory* published in 2002, hospitals with ability to perform antibody screening tests have been gradually increasing in number for the past 3 or 4 yr as column agglutination method was introduced, presenting up to 42.1% of the laboratories participated (9). However, the number of hospitals that actually perform this test as part of their routine pretransfusion study is quite limited. For preventing HTRs due to unexpected antibodies, antiglobulin phase of crossmatching or antibody screening test must be conducted in all patients who receive transfusion. Thus, we suggest the antibody screening test should be included in the panel of pretransfusion tests for safer transfusion, which is already a part of routine pretransfusion procedure in other countries. In addition, it is needed to make it mandatory for patients with multiple transfusion and pregnant women as well as preoperative patients.

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