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Unravelling the complexities of compatibility testing in multiple alloantibodies: A case report exploring challenges and solutions

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Abstract

Multiple transfusions pose a risk of alloimmunization resulting in delayed hemolysis in recipients. This makes it difficult for blood transfusion services to find cross match compatible red cell units especially when antibodies against "Kidd" antigens are present in recipients which are clinically significant and known to cause evanescence. We present a case of a 43 years old female who presented with anaemia and required two units of packed red cells for transfusion. As per our departmental policy, antihuman globulin (AHG) cross match was performed with random red cell units of same blood group. Since no compatible units could be found, patient's antibody screening and identification was carried out and the presence of anti-Fya and anti-Jkb alloantibodies was confirmed at AHG phase. Donor red cell units were phenotyped and Fya and Jkb antigens negative units were issued to the patient. Patients with multiple alloantibodies can be managed by applying advanced immunohematological techniques for identifying those alloantibodies and providing the corresponding antigen negative PRBCs thus ensuring safe transfusion.

Keywords: Delayed hemolytic transfusion reaction; DHTR; Multiple alloantibodies; Minor blood group antigens.

Introduction/background

Providing safe blood to the recipients is the most important responsibility of blood transfusion services. Pre transfusion testing which includes compatibility testing between donor red cells and recipient's serum is a crucial step in this provision of safe blood. Despite the transfusion of crossmatch compatible red cells, sometimes the haemoglobin of the recipient declines inexplicably due to the rapid elimination of donor red cells from the recipient's circulation. Delayed hemolytic transfusion reaction (DHTR) is a delayed reaction, that occurs after 24 hours of red cell transfusion is caused due to formation of alloantibodies against minor blood group antigens, most commonly Kidd, Duffy, Kell and MNS, following pregnancy, packed red cells transfusion or transplantation [1]. The reaction is delayed as the antibody is formed after re-exposure of antigen-positive donor red cells by a process called "anamnestic response" causing a rapid increase in antibody titre. This titre may be extremely low during pre-transfusion testing giving compatible results. Delayed serological transfusion reaction (DSTR) differs from DHTR with respect to haemolysis which is may be present in DHTR but not in DSTR [2]. This complicates the process for blood transfusion services in their efforts to identify cross-match compatible packed red blood cells (PRBCs) promptly. The presence of mul-

tiple alloantibodies in recipients which are clinically significant and cause evanescence, adds further complexity, making the search for compatible PRBCs more challenging.

Here we present a case of an anemic patient with multiple alloantibodies, how the antibodies were identified and the patient was effectively managed by PRBCs transfusion.

Case presentation

A 43-year-old female presented with severe anaemia, with a history of generalized body ache, exertional dyspnea, headache, easy fatigability and dark urine at General medicine department of our tertiary care centre. The haematological parameters revealed haemoglobin level of 3.0 g/dl, WBCs 9.86/L, platelets 1,20,000, reticulocytes count 6%, BUN 3.2 mmol/L, creatinine 60 mmol/L, AST 84 U/L, ALT 20 U/L, LDH 510 IU/L, total bilirubin 16.2 mmol/L and direct bilirubin 5.8 mol/L. She was transfused with one-unit PRBC outside, three days back. She had experienced a pregnancy two years back and that time was transfused one PRBC. Blood requisition was received at our blood bank for two-units of PRBCs in view of anemia. The blood group was AB Rh(D) positive but the cross match with group specific PRBCs was found to be incompatible.

Immunohematological workup

Forward and reverse blood group, anti-human globulin (AHG) cross match, indirect coomb's test (ICT), direct coomb's test (DCT), antibody screening (AS), antibody identification (AI) and red cell antigen phenotyping was done by column agglutination technique (CAT) using gel cards (Bio-Rad Laboratories, India Pvt. Ltd.). In house prepared pooled cells were used for reverse blood grouping and ICT. Commercial 3-cell and 11-cell panels (Bio-Rad Laboratories, India Pvt. Ltd.) were used for AS and AI respectively. Commercial antisera (Bio-Rad Laboratories, India Pvt. Ltd.) were used for red cell antigen phenotype determination.

There was no blood group discrepancy and her blood group was AB Rh(D) positive.

Two units of group specific PRBC units were taken up for cross matching which were found to be incompatible. DCT was positive (1+) which suggested an ongoing hemolysis. However, autologous control was negative which ruled out the possibility of the presence of an autoantibody. AS (Table 1) and AI (Table 2) were performed. As showed positive agglutination reaction with panel cells 1 and 3 with anti-C, e, Kpa, Fya, Jkb, Lea, N, S and Lua as possible antibodies (Table 1).

On AI, positive agglutination was observed with panel cells 1,3,4,5,6,7,9 and 11 and the most probable antibodies were anti-Fya and anti-Jkb (Table 2).

Red cell antigen phenotyping for patient was done which revealed the absence of Fya and Jkb antigens.

Select cells were used from two different lots (cell no. 1 of lot no. 45161.29.x with Fya+Jkb- cells and cell no. 9 of lot no.

Table 1: Antibody screening panel using patient's serum [Lot no. 45330.35.x]

	Rh-hr	Probable Genotype	Rh-hr						Kell						Duffy		Kidd		Lewis		P	MNS				Lutheran		Xga	AHG
			D	C	E	c	e	Cw	K	k	Kpa	Kpb	Jsa	Jsb	Fya	Fyb	Jka	Jkb	Lea	Leb	P1	M	N	S	s	Lua	Lub		
I	CCD.ee	R1R1	+	+	0	0	+	0	+	+	0	+	Nt	nt	+	0	0	+	+	0	+	0	+	0	+	0	+	+	2+
II	ccD.EE	R2R2	+	0	+	+	0	0	0	+	0	+	Nt	nt	0	+	+	0	0	+	+	+	+	+	+	0	+	+	0
III	CCD.ee	R1R1	+	+	0	0	+	0	0	+	0	+	Nt	nt	+	0	+	+	0	0	0	+	+	0	+	0	+	+	2+

Table 2: Antibody identification panel using patient's serum [Lot no. 45161.69.x]

Rh-hr	Probable Genotype	Rh-hr						Kell						Duffy		Kidd		Lewis		P	MNS				Lutheran		Xga	AHG
		D	C	E	c	e	Cw	K	k	Kpa	Kpb	Jsa	Jsb	Fya	Fyb	Jka	Jkb	Lea	Leb	P1	M	N	S	s	Lua	Lub		
CCCwD.ee	R1wR1	+	+	0	0	+	+	0	+	0	+	Nt	nt	+	0	0	+	+	+	+	0	+	+	+	0	+	+	2+
CCD.ee	R1R1	+	+	0	0	+	0	+	+	0	+	Nt	nt	0	+	+	0	0	+	+	+	0	0	+	0	+	0	0
ccD.EE	R2R2	+	0	+	+	0	0	0	+	0	+	Nt	nt	+	0	+	0	0	+	+	+	+	+	+	0	+	0	2+
Ccddee	r'r	0	+	0	+	+	0	0	+	0	+	Nt	nt	0	+	+	+	0	+	0	+	0	0	+	0	0	+	2+
ccddEe	r''r	0	0	+	+	+	0	0	+	0	+	Nt	nt	0	+	0	+	0	0	+	+	0	+	0	0	0	+	2+
ccddee	rr	0	0	0	+	+	0	+	+	0	+	Nt	nt	+	+	0	+	0	+	0	+	0	+	0	0	0	+	2+
ccddee	rr	0	0	0	+	+	0	0	+	0	+	Nt	nt	+	0	+	0	0	0	0	0	+	0	+	+	0	0	2+
ccD.ee	R0r	+	0	0	+	+	0	0	+	0	+	Nt	nt	0	0	+	0	0	0	+	+	+	0	+	0	0	+	0
ccddee	rr	0	0	0	+	+	0	0	+	+	+	Nt	nt	0	+	0	+	0	+	+	+	0	0	+	0	0	nt	2+
ccddee	rr	0	0	0	+	+	0	0	+	0	+	Nt	nt	0	+	+	0	+	0	+	0	+	0	+	0	0	+	0
ccddee	rr	0	0	0	+	+	0	0	+	0	+	Nt	nt	+	0	0	+	+	0	+	0	+	+	0	0	0	+	2+

45161.35.x with Fya-Jkb+ cells) to rule out anti-Fya and anti-Jkb. The reaction of patient's serum with select cells from both the lots were positive. So, the presence of anti-Fya as well as anti-Jkb was confirmed.

Furthermore, papain enzyme treatment was performed. Strength of reaction in panel cells 1,4,5,6,9 and 11 increased to 4+ which indicated the presence of anti-Jkb and while the strength of reaction in panel cells 3 and 7 decreased to 1+ which indicated the presence of anti-Fya.

Difficulty in finding out antigen-negative PRBC units:

The challenge was to find out the antigen negative PRBC units as the blood group of the patient was among the rare blood groups found in our country. Luckily, we had an ample stock of AB Rh(D) positive PRBC units in our inventory at that time. The number of PRBC units to be phenotyped was calculated using the formula:

% Negative antigen frequency /100= n/X

(n=no.of units required for transfusion

X= no. of units to be phenotyped to find out the corresponding antigen negative PRBC units)

Since the prevalence of Fya is 85.23% & Jkb is 62.91% in India, so 14.77% population will be negative for Fya while 37.09% population will be negative for Jkb antigens [3].

Here the requested number of PRBC units was 2. So, the number of PRBC units to be phenotyped will be:

$$2/0.147 \times 0.37 = 36.7$$

Approximately 37 units were required to be phenotyped. Out of those, 2 units which were found to be Fya and Jkb negative were cross matched. They were compatible and hence issued to the patient. The patient was followed up for next 10 days. Her hemoglobin level improved and she did not require further PRBCs transfusion till her stay in the hospital. She was discharged with a hemoglobin level of 7.2 g/dl.

Discussion

There are many problems associated with blood transfusion, one of which is alloimmunization due to antigenic diversities between donors and recipients leading to hemolytic reactions and decreased survival of transfused red cells. These alloantibodies need to be identified to ensure safe transfusion which requires both resources and skilled manpower. Antibodies against antigens of minor blood group systems like Kidd and Duffy often show a transient nature making their identification a challenging task. This puts the recipients at risk of hemolysis when further transfusion is needed. There indeed has been under-reporting of DHTRs. Also, how much a blood group antibody disappears has been under-estimated and not studied much worldwide. According to few studies it has been reported that approximately 25-41% of clinically significant alloantibodies decrease to an undetectable level in recipient's serum with time [4-6].

In our patient, fall in hemoglobin level even after recent red cell transfusion raised the suspicion of DHTR. Moreover, the laboratory parameters were also suggestive of an ongoing hemolysis (increased reticulocyte count, bilirubin and LDH). Advanced immunohematological work-ups led to the identification of these antibodies responsible for DHTR. Finding out cross match compatible red cell units was also a cumbersome task as the patient had a rare blood group. However, we were able to provide compatible red cells to the patient.

Here we highlight the importance of compatibility testing and antibody identification to ensure safe and effective transfusions for patients with multiple alloantibodies. However, certain limitations such as lack of resources like special antisera and reagents, short stock of rare blood groups in blood centres and unavailability of trained manpower who can be dedicated to perform these work-ups can also be not overseen in a resource limited county like ours.

Conclusion

By employing advanced serological techniques such as phenotyping, antibodies identification, enzyme treatment, we can overcome compatibility obstacles and provide appropriate blood to meet the specific needs of patients with multiple alloantibodies.

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Conflicts of interest: None

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