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CASE REPORT

Rare Autoantibody Mimics Anti-C and Anti-e Specificity in Patient with Aplastic Anemia

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SUMMARY

Background: **Alloantibodies for the Rh blood group are the most immunogenic antibodies found in the Chinese population, typically causing acute or delayed hemolytic transfusion reactions and fetal and neonatal hemolytic diseases. Autoantibodies are generally considered nonspecific, and approximately 50% of warm antibodies are secondary to a variety of diseases, especially hematologic tumors. In this case report, a rare autoantibody that mimics anti-C and anti-e specificity was identified.**
Methods: **A 17-year-old adolescent with aplastic anemia was awaiting transfusion due to anemia. Routine laboratory testing before transfusion revealed that antibody screening was positive. Antibody identification and blood group antigen typing were performed to identify antibody specificity.**
Results: **Antibodies in the patient's plasma and red blood cell release solution were identified as anti-C and anti-e specific. The patient's proximal red blood cells were separated by capillary centrifugation to identify the Rh blood group as DCeEe. Antibodies in the patient's plasma were suspected of being autoantibodies, a rare type of antibody. Screened C and e antigen-negative blood for transfusion was effective, and the patient's anemia was relieved. The patient was discharged after transfusion.**
Conclusions: **Finding suitable blood for transfusion in patients with hemolytic anemia caused by warm autoantibodies is a challenge. Managed mimic antibodies are the same as alloantibodies, and matching-related antigen-negative blood is the first choice for transfusion in patients with mimic warm autoantibodies. However, C and e antigen-negative blood is rare among the Chinese population.**
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KEYWORDS

alloantibody, mimic antibody, aplastic anemia, transfusion, Rh blood type

INTRODUCTION

Aplastic anemia (AA) is one of the most common hematologic malignancies, which has varying degrees of anemia and infection [1]. Blood transfusion therapy is an important means of relieving the clinical symptoms of AA and improving the quality of life of patients with severe aplasia, who often require long-term and repeated transfusion therapy. Patients with AA are affected by different degrees of abnormal activation and hyperfunc-

tion of T lymphocytes, coupled with repeated blood transfusion treatment. This can in turn lead to an increased risk of autoimmunity and homoimmunity. Anti-C and anti-e antibodies are rarely detected in patients with aplastic anemia.

CASE REPORT

A 17-year-old male patient presented with severe aplastic disorder, chronic anemia, clear consciousness, pale skin, visible hemorrhagic spots in the mucous membranes, and a history of red blood cell transfusion 2 months prior. The patient's platelet count was 4 x 10^9/L with a hemoglobin level of 65 g/dL. One unit of the patient's platelets was irradiated, and phenethylamine was administered for hemostasis in the emergency department. On the second day, the patient's hemoglobin level dropped to 56 g/L and three units of red blood cells were requested. Blood analysis showed that the patient was positive for O and RhD. With a history of red blood cell transfusion two months prior, capillary centrifugation of the proximal cardiac blood indicated that the Rh typing was DCcEe. The results of both the self-control and direct erythrocyte anti-human globulin test (DAT) were negative. The antibody screening results were I (w), II (0), and III (0). The antibodies highlighted anti-C and anti-e specificities in the plasma of the patient (papain-treated antibody identification cells). Red blood cell elution identification also indicated that the patient had anti-C and anti-e antibodies. Subsequently, the C and e antigens of our patient's blood were screened against 1.5 U of C and e antigen-negative blood from 30 donors in a blood bank, resulting in the identification of a compatible match between the patient and donor blood. This indicated that PEG-enhanced blood matching was compatible. The subsequent transfusion process went smoothly, the patient's vital signs were stable, and the patient showed no signs of hyperthermia, chills, jaundice, or rashes. After blood transfusion, the patient's skin became redder, indicating that the blood transfusion was effective. The patient was discharged after transfusion with a hemoglobin level of 65 g/L.

DISCUSSION

AA is characterized by bone marrow hematopoietic failure (BMF). The annual incidence of AA is 0.74/100,000 in China across all age groups. A high incidence of AA occurs in young adults aged 15 - 25 years old and in elderly people aged 65 - 69 years old [2], with no significant difference between male and female incidence. AA can be classified into congenital and acquired forms. Bone marrow injury caused by abnormal activation and hyperfunction of T lymphocytes is currently believed to play a major role in the pathogenesis of primary acquired AA. Recent studies have shown that helper T cell subsets, Th1/Th2 differentiation deviation [3], regulatory T cells (Treg), and natural killer (NK) cells have insufficient regulatory functions in patients with AA; Th17, dendritic cells (DC cells), macrophages, and other functional abnormalities, as well as genetic background, are also involved in the pathogenesis of AA [4]. Blood transfusion is one of the most used treatments for aplastic anemia. Studies have shown that repeated blood transfusions per input 1 unit of red blood cells can increase the risk of sensitization by 1% to 2%, with multiple blood transfusions increasing the isoantibody probability by 15% to 20% [5]. Similar antibodies have the specificity of homologous antibodies and show the same reactivity as erythrocyte antigens. For example, the Rh blood group of the patient in this case report was DCcEe and the specificity of the plasma antibodies was consistent with the joint response patterns of anti-C and anti-e. The results of antibody identification and their own blood groups were contradictory, and the experimental results were consistent with the characteristics of the same-specific autoantibodies.

Alloantibodies are commonly found in patients with autoimmune hemolytic anemia. However, this is rare in patients with aplastic disease. The specificity of alloantibodies is mostly concentrated in the Rh blood group system, mimicking anti-E, anti-c, anti-Ec, and anti-D [6]. Currently, the standardized clinical blood transfusion guidelines and expert consensus in China on the treatment of patients with mimic antibodies via blood transfusion are lacking. The selection of an antigen-negative red blood cell transfusion corresponding to a mimic antibody can significantly prolong the survival time of blood cells *in vivo*. In this case, the patient's own blood group antigen should not be considered. As the blood groups of patients with AAs other than ABO and RHD are difficult to detect because of repeated transfusions, blood group identification via capillary centrifugation is necessary. The probability of finding Ce antigenic-negative blood donors in the Chinese population is 7%, and it is extremely difficult to find matching blood. Fortunately, in the present case, the patient's antibodies were clearly identified, timely treatment was provided, and transfusion reactions were avoided.

In conclusion, accurate antibody identification and matched antigen-negative blood transfusions are prerequisites for safe blood transfusions in patients with autoantibody mimics.

Source of Funds:
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Ethical Statement:
The study has obtained ethical approval of West China Second University Hospital, Sichuan University (Number: 2020051).

Table 1. Pattern of screening tests and antibody identification in plasma and eluate of the patient.

		Kell			Duffy		Kidd		Lewis		P	MNS				Luther		Xg	Experimental Results		
		Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P1	M	N	S	s	Lu^a	Lu^b	Xg^a	Plasma	Plasma (Papain)	Eluate	Eluate (Papain)
	Antibody screen																				
I		/	NT	/	0	+	+	0	0	+	+	+	0	+	0	0	/	+	w	-	w	-
II		/	NT	/	+	0	+	+	0	0	+	+	+	0	+	0	/	+	0	-	0	-
III		/	NT	/	+	0	0	+	+	0	+	+	+	0	+	0	/	+	0	-	0	-
	Antibody screen																				
1		+	/	+	+	0	0	+	0	+	+	+	0	+	+	0	+	+	0	2+	0	2+
2		+	0	+	+	0	+	0	0	+	0	0	+	0	+	0	+	+	0	2+	0	2+
3		+	/	+	0	+	+	+	+	0	+	+	+	+	0	0	+	0	0	0	0	0
4		+	/	+	+	0	+	0	0	+	+	+	+	0	+	0	+	/	0	2+	0	2+
5		+	/	+	0	+	+	+	0	+	+	+	0	+	+	0	+	0	0	2+	0	2+
6		+	/	+	+	+	+	0	0	0	+	+	0	+	+	0	+	+	0	0	0	0
7		+	/	+	0	+	+	0	+	0	0	+	0	+	+	0	+	+	0	2+	0	2+
8		+	/	+	0	+	0	+	0	+	+	0	+	0	+	0	+	/	0	2+	0	2+
9		+	/	+	+	0	+	+	0	0	+	+	+	+	0	0	0	0	w	2+	w	2+
10		+	/	+	+	+	+	0	0	0	+	0	+	0	+	0	+	/	0	2+	0	2+
11		+	/	+	0	+	0	+	+	0	+	+	0	+	+	0	+	+	0	2+	0	2+
12		+	/	+	+	0	+	+	0	+	0	+	0	+	+	0	+	+	0	w	0	w
13		+	/	+	+	+	+	0	+	0	+	+	+	+	+	0	+	/	0	2+	0	2+
14		+	/	+	0	+	+	0	0	+	0	0	+	0	+	0	+	+	0	0	0	0
15		+	0	+	+	+	0	+	+	0	+	+	0	+	0	0	+	0	0	2+	0	2+
16		+	/	+	+	0	0	+	+	0	+	+	+	0	+	0	+	+	0	2+	0	2+
PC		/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	0	0	0	0

Table 1. Pattern of screening tests and antibody identification in plasma and eluate of the patient (continued).

Kell	Kp[a]	Antibody screen	0	0	0	Antibody identification	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	/
	k		+	+	+		+	0	+	+	+	+	+	0	0	+	+	+	+	+	+	+	+	+	/
	K		+	0	0		0	+	0	0	0	0	0	+	+	0	0	0	0	0	0	0	0	0	/
Rh-Hr	e		+	0	+		+	+	0	+	+	0	+	+	+	+	+	0	+	0	+	+	+	+	+
	c		0	+	+		0	0	+	+	0	+	+	+	+	+	+	0	+	+	+	0	+	+	0
	E		0	+	0		0	0	+	0	0	+	0	0	0	0	0	+	+	0	+	0	0	0	0
	D		+	+	0		+	+	+	+	0	0	0	0	0	0	0	+	+	0	+	+	0	0	+
	C		+	0	0		+	+	0	0	+	0	0	0	0	0	0	+	w	+	0	+	0	0	+
			I	II	III		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	PC		

Declaration of Interest:
The authors have disclosed no conflicts of interest.

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