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CASE REPORT

A Rare Case of Autoimmune Hemolytic Anemia Caused by Autoantibody with Mimicking Anti-D and Anti-C Specificity

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SUMMARY

Background: **Most of the autoantibodies that cause autoimmune hemolytic anemia (AIHA) are non-specific. Autoantibodies expressing alloantibody specificity are rare.**
Methods: **We present the case of a 4-year-old boy with no history of blood transfusion or underlying medical conditions who developed AIHA caused by autoantibody with mimicking anti-D and anti-C specificity.**
Results: **Following treatment with methylprednisolone sodium succinate and transfusion of red blood cells with negative antigens for D and C, along with administration of human immunoglobulin, the patient's condition gradually improved. He was ultimately discharged with a good prognosis.**
Conclusions: **This report highlights a rare case of AIHA characterized by autoantibody with mimicking anti-D and anti-C specificity. Treatments of these patients could be antigen-negative red blood cells, glucocorticoid and immunoglobulin.**
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KEYWORDS

autoimmune hemolytic anemia, mimicking autoantibody, transfusion

INTRODUCTION

In the majority of autoimmune hemolytic anemia (AIHA) cases, red blood cell (RBC) autoantibodies exhibit a pan-reactive nature, reacting with all RBCs [1]. However, in some patients, these autoantibodies initially display apparent specificity, which is subsequently lost after adsorption with both antigen-negative and antigen-positive cells. Such autoantibodies are referred to as antibodies with mimicking specificity [2]. The literature review reveals that instances of autoantibodies with mimicking anti-D or anti-C specificity are exceedingly rare. Treatment options for these patients typically involve the selection of antigen-negative RBCs and use of glucocorticoids. In this report, we present a unique case of AIHA characterized by the presence of autoantibody with mimicking anti-D and anti-C specificity.

CASE PRESENTATION

A 4-year-old boy was transferred to our hospital after presenting with 11 days of pale complexion, skin jaundice, anemic appearance and a noticeable decrease in activity tolerance over the past 4 days. Notably, he had no history of blood transfusions or any significant underlying medical conditions. Upon admission, his hemoglobin level was measured at 46 g/L (normal range: 110 - 160 g/L), reticulocyte count at 0.4753 x 10^{12} (normal range: 0.024 - 0.084 x 10^{12}/L), lactate dehydrogenase at 659 U/L (normal range: 120 - 250 U/L), total bilirubin at 31.3 μmol/L (normal range: 5 - 23 μmol/L), and indirect bilirubin at 21.8 μmol/L (normal range: < 17 μmol/L). The patient was suspected to be AIHA at the outpatient center, and 1.5 units of compatible suspended RBCs was requested for him.

Immunological serological testing revealed that the patient's blood group was A, CCDee, with a positive direct antiglobulin test showing IgG (4+) and IgG + C3d (4+), the results of auto-erythrocyte and plasma reaction were positive. Both plasma and eluent antibody screenings were positive, with antibody screening results indicating I (2+), II (2+), and III (0). Antibody identification further confirmed the antibody specificity of anti-D and anti-C. The serological results of the patient during hospitalization are summarized in Table 1. Notably, the patient's plasma and eluate remained positive with cells treated by dithiothreitol (DTT) [3], which effectively rules out the presence of anti-LW antibody. Absorption test [4] was conducted, and the antibody was found to be adsorbed by either D, C-antigen-positive or D, C-antigen-negative RBCs, as well as individual D or C antigen-negative RBCs. On the basis of his laboratory results and clinical history, the patient was suspected to be AIHA secondary to autoantibody with mimicking anti-D and anti-C specificity.

Upon admission, the patient was administered methylprednisolone sodium succinate. In addition to the transfusion of 1.5 units of A, ccdee RBCs, intravenous immunoglobulin was concurrently administered. Subsequently, the patient's hemoglobin level increased from 46 g/L to 83 g/L. The treatment regimen was continued with the administration of intravenous immunoglobulin. After 10 days of supportive treatment, laboratory tests revealed a decrease in total bilirubin level to 22.2 μmol/L, with indirect bilirubin level at 15.7 μmol/L. The patient's hemoglobin level further improved, rising from 83 g/L to 106 g/L. As his hemolytic symptoms gradually subsided, indicating the effectiveness of the treatment, the patient was discharged with a good prognosis. He is currently under regular follow-up care.

DISCUSSION

The incidence of AIHA in the population is unknown, with an incidence of 1 - 3 in 100,000 in the Chinese population [5]. AIHA can result from the presence of autoantibodies [6]. In most cases of warm AIHA, RBC autoantibodies exhibit pan-reactivity, reacting with all RBCs. However, there are instances where these autoantibodies initially display apparent specificity, which subsequently vanishes after adsorption with antigen-negative and antigen-positive cells. Such autoantibodies are termed "mimicking antibodies", initially described as "wrong antibodies" [1]. Among these mimicking antibodies, those with specificity for the Rh blood group system are the most common, other specific autoantibodies targeting antigens such as Fya, Fyb, Jkb, Kell (K1 and Kpb), S, and U have also been reported [4-7]. Research has shown that mimicking autoantibodies can be adsorbed by RBCs regardless of their possession of the corresponding antigen [7]. The exact mechanism of their production remains unclear, and it is generally considered an autoantibody (with or without anemia), with some experts suggesting a connection to drug exposure, such as α-methyldopamine [1].

To shed light on the rarity of AHIA caused by autoantibodies with mimicking anti-D or anti-C specificity, we conducted a thorough search of PubMed databases and relevant articles were summarized in Table 2. In all cases, the patients presented with AIHA resulting in severe anemia. Of these cases, seven were successfully transfused with antigen-negative RBCs, whereas one initially received antigen-positive blood, leading to a transfusion reaction. This finding suggests that transfusing antigen-negative blood in the presence of mimicking autoantibodies is a feasible approach for these patients. Additionally, half of the patients in the reported cases received glucocorticoid treatment, which was shown to be effective.

In our patient, the mimicking specificity of autoantibody was confirmed through several key points: 1) antibody in the patient's plasma and RBC eluent both exhibited anti-D and anti-C specificity, 2) the patient's RBCs were positive for the D-antigen and C-antigen, 3) the antibody was found to be adsorbed by either D, C-antigen-negative or D, C-antigen-positive RBCs, and 4) remained positive reaction with cells treated by dithiothreitol, which ruling out anti-LW antibody. However, the precise antigenic target of the autoantibody remained unclear. Despite their relatively low frequency, mimicking autoantibodies can complicate the timely provision of compatible blood products and create challenges for laboratory and clinical staff. Adsorption of mimicking autoantibodies with both antigen-negative and antigen-positive cells serves as a valuable method for identifying them. Currently, the treatment of patients with AIHA primarily revolves around glucocorticoids. In our case, we employed glucocorticoids (methylprednisolone succinate), intravenous immunoglobulin, and transfusion of 1.5 units of D, C-antigen-negative RBCs, which were proven effective. This success is likely attributable to the established efficacy of IVIG and glucocorticoids in the treatment of warm antibody AIHA [8]. Nevertheless, it is crucial to exercise caution with blood transfusions to prevent potential alloimmunization due

Table 1. Results of screening tests and antibody identification for patient in plasma and eluate.

Cells	Rh-Hr					Kell						Duffy		Kidd	
	C	D	E	c	e	K	k	Kp [a]	Kp [b]	Js [a]	Js [b]	Fy [a]	Fy [b]	Jk [a]	Jk [b]
I	+	+	0	0	+	+	+	0	/	NT	/	0	+	+	0
II	0	+	+	+	0	0	+	0	/	NT	/	+	0	+	+
III	0	0	0	+	+	0	+	0	/	NT	/	+	0	0	+
1	+	+	0	0	+	0	+	+	+	0	+	0	+	+	0
2	+	+	0	0	+	+	+	0	+	/	+	+	0	0	+
3	0	+	+	+	0	+	+	0	+	/	+	+	+	0	+
4	0	+	0	+	+	0	+	0	+	/	+	0	0	+	+
5	+	0	0	0	+	0	+	0	+	/	+	+	0	+	0
6	0	0	+	+	0	0	+	0	+	/	+	+	+	+	+
7	0	0	0	+	+	+	0	0	+	/	+	+	+	+	+
8	0	0	0	+	+	0	+	0	+	/	+	0	+	0	+
9	0	0	0	+	+	0	+	0	+	/	+	0	+	+	+
10	0	0	0	+	+	0	+	0	+	/	+	+	0	0	+
11	+	+	+	0	+	0	+	0	+	/	+	0	+	+	+
12	W	+	+	+	0	0	+	0	+	/	+	0	+	+	+
13	+	0	0	+	+	+	+	0	+	/	+	+	0	+	0
14	0	+	+	+	0	0	+	0	+	/	+	+	0	+	0
15	+	0	0	+	+	0	+	0	+	/	+	+	+	+	0
16	0	0	0	+	+	0	+	0	+	/	+	0	+	+	+
PC	+	+	0	0	+	/	/	/	/	/	/	/	/	/	/

Cells	Lewis		P	MNS				Luther		Xg	Experimental results			
	Le [a]	Le [b]	P1	M	N	S	s	Lu [a]	Lu [b]	Xg [a]	Plasma	Eluate	Plasma (DTT)	Eluate (DTT)
I	0	+	+	+	0	+	0	0	/	+	2+	4+	2+	4+
II	0	0	+	0	+	0	+	0	/	+	2+	4+	2+	4+
III	+	0	+	+	+	0	+	0	/	+	0	0	0	0
1	0	+	+	0	+	+	+	0	+	+	2+	4+	2+	4+
2	0	0	+	+	0	0	+	0	+	+	2+	4+	2+	4+
3	+	0	+	0	+	0	+	0	+	0	2+	4+	2+	4+
4	0	0	+	+	+	0	+	0	+	/	2+	4+	2+	4+
5	+	0	+	+	0	0	+	0	+	0	2+	4+	2+	4+
6	0	+	+	+	+	0	+	0	+	+	0	0	0	0
7	0	+	+	+	0	+	0	0	+	+	0	0	0	0
8	+	0	0	0	+	0	+	0	+	/	0	0	0	0
9	0	+	+	+	0	0	+	+	0	0	0	0	0	0
10	0	+	+	0	+	0	+	0	+	/	0	0	0	0
11	0	+	0	+	+	+	0	0	+	+	2+	4+	2+	4+
12	+	0	+	0	+	+	+	0	+	+	2+	4+	2+	4+
13	0	0	+	+	+	+	+	0	+	/	2+	4+	2+	4+
14	0	+	+	+	0	+	0	0	+	+	2+	4+	2+	4+
15	+	0	+	+	+	+	0	0	+	0	2+	4+	2+	4+
16	W	+	0	+	0	0	+	0	+	+	0	0	0	0
PC	/	/	/	/	/	/	/	/	/	/	4+	4+	4+	4+

PC - patient's cell, NT - not tested, W - weak.

Table 2. Review of published AIHA caused by autoantibodies mimicking anti-D or anti-C.

Case	Clinical diagnosis	TF-history	Hb	Antibody specificity	Therapy	Outcome
1 [8]	AIHA	no	2.1 g/dL	anti-D	prednisone, D antigen-negative RBC transfusion	good prognosis
2 [9]	AIHA and EBV infection	no	2.4 g/dL	anti-D	D antigen-positive RBC transfusion and D antigen-negative RBC transfusion	transfusion reaction good prognosis
3 [10]	burkitt lymphoma and AIHA	no	5.5 g/dL	anti-D	prednisone, D antigen-negative RBC transfusion	good prognosis
4 [11]	kidney transplant and AIHA	no	5.9 g/dL	anti-D	basiliximab, prednisone, D antigen-negative RBC transfusion	good prognosis
5 [12]	primary sclerosing cholangitis and AIHA	no	NM	anti-C	C antigen-negative RBC transfusion	good prognosis
6 [13]	AIHA and SLE	no	7.5 g/dL	anti-C	prednisolone	good prognosis
7 [14]	AIHA	no	3.9 g/dL	anti-D	NM	NM
8 [15]	AIHA	no	5.4 g/dL	anti-D	NM	NM
10 [16]	refractory anemia and AIHA	no	5.2 g/dL	anti-D	prednisone and D antigen-negative RBC transfusion	good prognosis
11 [17]	AIHA	no	7.4 g/dL	anti-C and anti-e	conservative treatment, no blood transfusion	good prognosis

Hb - hemoglobin, RBC - red blood cell, NM - not mentioned, TF-History - transfusion history, AIHA - autoimmune hemolytic anemia, EBV - Epstein-Barr virus, SLE - systemic lupus erythematosus.

to the acceptance of different antigen phenotypic RBCs. In summary, this is the first reported case of AIHA characterized by autoantibody with mimicking anti-D and anti-C specificity. It reminds clinicians to pay more attention to such patients and choose antigen-negative red blood cells for transfusion, including treatment options that may include glucocorticoids or immunoglobulins.

Declaration of Interest:

The authors declare that they have no conflict of interest.

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