Clinically Significant Anti-E and Anti-Jka Alloantibodies Identified in a 24-year-old Female suspected of Delayed Hemolytic Anemia Requiring Emergency Transfusion

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ABSTRACT

Delayed hemolytic transfusion reactions (DHTRs) represent significant complications associated with blood transfusion, often resulting from the development of alloantibodies against specific red blood cell (RBC) antigens. We report a case of a 24-year-old female presenting with fever, generalized weakness, icterus of skin, severe anemia and a transfusion history a week before presentation. Immunohematological evaluation using the NEO-IRIS automated platform with Solid Phase Red Cell Adherence (SPRCA) technology identified anti-E and anti-Jka alloantibodies. Due to the unavailability of anti-JKa reagent, only E-antigen negative compatible blood could be provided. The patient showed significant clinical and hematologic improvement after receiving one unit of compatible blood. This case highlights the importance of comprehensive antibody screening, early referral to transfusion medicine specialists involvement, extended RBC phenotype donor registries and improving access to rare antisera are crucial to ensuring timely provision of antigen-negative units and enhancing transfusion safety.

Keywords: Alloantibodies, Immunohematology, Phenotyping, Hemolysis, Antibody Screening, Antibody Identification

Introduction

Hemolytic anemia, resulting from immune-mediated destruction of RBCs, presents notable diagnostic and therapeutic challenges. Patients who have undergone prior transfusions are particularly susceptible to the development of alloantibodies against non-self RBC antigens, which lead to delayed hemolytic transfusion reactions (DHTRs). DHTRs typically occur days to weeks after transfusion and are characterized by a drop in hemoglobin due to destruction of transfused RBCs carrying the targeted antigens.[1] Among the clinically significant red blood cell alloantibodies, anti-E (Rh blood group system) and anti-K (Kell blood group system) are commonly encountered.[2] Identifying these alloantibodies is essential for selecting compatible blood and preventing hemolytic reactions.

Advanced immunohematological platforms such as the Solid Phase Red Cell Adherence (SPRCA) based automated analyzers improve the detection of weak or low titer antibodies compared to tube or gel card methods.[3] This case underscores the challenges of managing DHTR in low-resource settings where extended phenotyping reagents may be limited, emphasizing the need for stronger infrastructure and referral systems.

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Case Report

Patient presentation:

A 24-year-old female presented with fever, generalized weakness, and icterus of skin. She had received three units of crossmatch-compatible whole blood nearly a week earlier at another hospital. Despite this intervention, her hemoglobin levels subsequently decreased to 3.9 g/dL, indicating ongoing hemolysis.

Laboratory findings:

Blood grouping revealed the patient to be A Rh (D) positive. The direct antiglobulin test (DAT) was positive but autocontrol showed a negative result suggesting that the antibodies were directed against foreign RBC antigens rather than autoantibodies. Elevated indirect bilirubin and Lactate Dehydrogenase (LDH) confirmed immune-mediated hemolysis.[4]

Immunohematological Workup:

1. Antibody Screening (Cap-R Ready-Screen 3): A sensitive technology such as SPRCA is essential to detect clinically significant antibodies that standard crossmatching alone may overlook.[5] In a positive test, the indicator red cells are unable to settle at the bottom because Anti-IgG-IgG complexes are formed on the antigen-coated surface of the immobilized red cells membrane layer. In a negative test, indicator cells can move to the bottom well easily and form a red cell button. The degree of red cell adhesion to the monolayer is the key indicator of positive and negative reactions (Figure 1).

For antibody screening, 3-cell panel was used (Figure 2) which showed positive reactions in two screening cells and the positive control was valid.

2. Antibody Identification (Cap-R Ready-ID): Due to the recent transfusion, the phenotyping of the patient's RBC will not be reliable, which led us to perform antibody identification. The primary Ready-ID plate with 14-cell panel was used for the identification (Figure 3).

The antibody screening test was Positive in this case and antibody identification panel demonstrated a reaction pattern consistent with anti-E and anti-JKa antibodies with expected dosage patterns for Kidd antibodies.[6] Providing the corresponding antigen-negative compatible blood is essential to prevent further hemolysis. To ensure the availability of antigen-negative units for alloimmunized patients, routine phenotyping for atleast Rh and Kell antigen must be performed. This will enable the rapid identification of compatible units in an emergency time. Furthermore, to reduce future alloimmunisation risks, it is important to transfuse

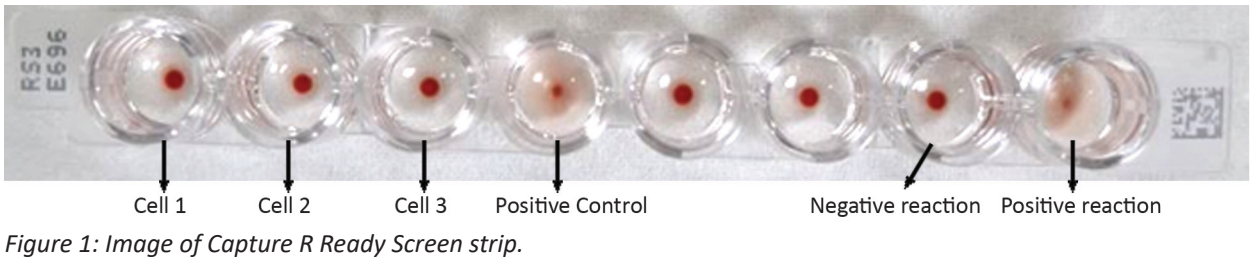

Figure 1: Image of Capture R Ready Screen strip.

CAPTURE-R READY-SCREEN (3)
Master List
417-6
E696
IMMUCOR, INC. Norcross, GA 30071 USA
US LICENSE NO: 886
LOT NO: E696
EXPIRES: 2025/08/12

CELL	Donor	Rh - Hr						Kell						Duffy		Kidd		Lewis		P	MN				Luth-eran		Xg
		D	C	c	E	e	C^w	K	k	Kp^a	Kp^b	Js^{a*}	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P_1	M	N	S	s	Lu^a	Lu^b	Xg^{a*}
I	R1wR1 B9604	+	+	0	0	+	+	0	+	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	0
II	R2R2 C5675	+	0	+	+	0	0	+	+	+	+	0	+	+	0	+	0	0	+	+	0	+	0	+	0	+	+
III	rr N3941	0	0	+	0	+	0	0	+	0	+	0	+	0	+	0	+	+	0	+	+	+	+	0	0	+	0
	Positive Control																										

CAPTURE-R READY-SCREEN

* Indicates those antigens whose presence or absence may have been determined using only a single example of a specific antibody.
An antigen designated with a 'w' represents a weakened expression of the antigen that may or may not react with all examples of the corresponding antibody.

Figure 2: Antigram of Capture-R Ready-Screen (3)

CAPTURE-R READY-ID
Master List

ID492

NAME _____
NO. _____
INSTITUTION _____
BLOOD GROUP _____
ANTIBODY IDENTITY _____
TECH _____ DATE _____

IMMUCOR, INC. Norcross, GA 30071 USA
US LICENSE NO: 886
LOT NO: ID492
EXPIRES: 2025/07/29

CELL	Special Type	Donor	Rh - Hr						Kell						Duffy		Kidd		Lewis		P	MN				Luth-eran		Xg	CELL	PATIENT'S TEST RESULTS					
			D	C	c	E	e	C^w	K	k	Kp^a	Kp^b	Js^a	Js^b	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P_1	M	N	S	s	Lu^a	Lu^b	Xg^a							
1		RzR1 A4194	+	+	0	+	+	0	0	+	0	+	0	+	0	+	+	+	0	+	+	+	0	+	+	0	+	0	1						
2		R1wR1 B7828	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	0	+	0	+	+	2						
3		R2R2 C7333	+	0	+	+	0	0	+	+	0	+	0	+	+	+	+	+	0	+	+	+	0	0	+	+	+	+	3						
4	V+*, VS+*	Ror D2052	+	0	+	0	+	0	0	+	0	+	0	+	0	0	+	0	0	0	+	0	+	0	+	0	+	+	4						
5		r'r E646	0	+	+	0	+	0	+	+	0	+	0	+	0	+	0	+	0	0	+	+	+	+	0	0	+	+	5						
6		r''r F1038	0	0	+	+	+	0	0	+	0	+	0	+	+	+	+	0	+	0	0	+	+	+	+	0	+	+	6						
7		rr N4573	0	0	+	0	+	0	0	+	+	+	0	+	+	+	+	0	0	+	+	+	+	+	+	0	+	+	7						
8		rr G1673	0	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	0	+	0	+	+	0	+	0	+	0	8						
9		rr H2183	0	0	+	0	+	0	0	+	0	+	0	+	+	0	0	+	0	+	+	0	+	0	+	0	+	0	9						
10		rr H2116	0	0	+	0	+	0	0	+	0	+	0	+	+	0	0	+	0	+	+	0	+	0	+	0	+	+	10						
11		rr G1614	0	0	+	0	+	0	+	+	0	+	0	+	+	+	0	+	+	0	+	+	+	0	+	+	0	+	11						
12		rr N5228	0	0	+	0	+	0	0	+	0	+	0	+	0	+	0	+	0	+	+	+	0	+	0	0	+	+	12						
13	Di(a+)	rr N4966	0	0	+	0	+	0	0	+	0	+	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	0	13						
14	Mi(a+), GP.Mur	R1R2 A4554	+	+	+	+	+	0	0	+	0	+	0	+	+	0	0	+	0	+	0	+	0	0	+	0	+	+	14						
15		POSITIVE CONTROL	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	PC						
16		NEGATIVE CONTROL	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/	NC						

* Indicates those antigens whose presence or absence may have been determined using only a single example of a specific antibody.

NOTES:
An antigen designated with a 'w' represents a weakened expression of the antigen that may or may not react with all examples of the corresponding antibody.

PATIENT'S SERUM	ANTIBODY SCREEN LOT						
		I					
		II					
		III					
		IV					

426-20

Figure 3: Antigram of Capture-R Ready-ID

antigen-matched blood for at least Rh (C,c,E,e) and Kell systems. This approach will be cost-effective in the long term, as it prevents the development of additional antibodies and associated complications.[7]

Management:

To identify compatible unit, phenotyping of multiple donor blood units were performed and E-antigen negative blood with C+c+e+e+K− and C+C+e+e+K− phenotypes were selected for IgG-specific Crossmatch. Due to the unavailability of anti-Jka reagent, we could only provide E antigen-negative blood which was successfully cross-matched with the patient's serum. The patient, after receiving only one unit of E-antigen negative blood, showed a significant rise in hemoglobin level and was discharged the following day in stable condition.

Discussion

Delayed hemolytic transfusion reactions (DHTRs) occur when preformed alloantibodies in a recipient are re-stimulated by transfused red cells expressing the corresponding antigens.[8] These reactions typically present days to weeks after transfusion and are characterized by anemia, jaundice, and laboratory evidence of hemolysis. Patients with prior transfusion or pregnancy histories are particularly at risk of alloimmunization.

In this case, the patient developed anti-E and anti-Jka alloantibodies, both clinically significant and frequently implicated in DHTRs.[2,9] The detection of these antibodies was made possible using the Neo-IRIS automated system employing SPRCA technology, which offers high sensitivity and reproducibility compared to conventional tube or gel methods. The identification of anti-E and anti-Jka guided the selection of antigen-negative compatible blood, preventing further hemolysis and ensuring a favorable clinical outcome.

This case emphasizes the critical role of extended antigen typing, especially for Rh (C, c, E, e) and Kell systems, in multi-transfused patients.[1] Implementing proactive transfusion policies including pre-transfusion antibody screening, maintaining detailed transfusion records, and establishing antigen-negative blood inventories can significantly reduce the risk of alloimmunization.

Furthermore, integrating automated antibody screening platforms enhances diagnostic precision and laboratory efficiency, offering substantial benefits for transfusion services, particularly in resource-limited settings such as Nepal.

Conclusion

In patients with a history of transfusion presenting with unexplained anemia, the possibility of delayed hemolytic transfusion reaction (DHTR) due to alloantibody formation should always be considered. Comprehensive immunohematological evaluation, including antibody screening and identification using advanced platforms such as the Neo-IRIS system with Solid Phase Red Cell Adherence (SPRCA) technology, plays a pivotal role in confirming the diagnosis and guiding appropriate transfusion management.

The detection of anti-E and anti-Jka alloantibodies enabled the selection of antigen-negative compatible blood, thereby preventing further hemolysis. The patient, after receiving one unit of phenotyped matched blood, demonstrated a significant rise in hemoglobin level and was discharged the following day with clinical improvement. This case highlights the importance of maintaining detailed transfusion and antibody histories, implementing extended antigen typing, and adopting proactive blood inventory management to ensure transfusion safety. Furthermore, it underscores the value of integrating automated immunohematology systems in transfusion services to enhance diagnostic accuracy and improve patient outcomes, particularly in resource-limited settings.

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