Anti-JK-a Antibody in a Case of SLE Patient with *Plasmodium falciparum* Malaria Infection

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Abstract A 58 year old lady presented with high grade fever, pallor, abdominal pain, loss of appetite and swelling of legs. She was subsequently diagnosed with SLE along with infection of *Plasmodium falciparum* malaria. She was clinically pale and advised for two units of packed red cell transfusion. One of the two units was incompatible, so only one unit was issued. Subsequently, DAT and auto control were positive. Later antibody specificity was identified, which came out to be anti JK-a. Because of recent transfusion 2 weeks back, her antigenic phenotype could not be elicited. Though we could not make out whether this antibody was the result of pregnancy or transfusion induced allo anti-JK-a or SLE induced auto anti JK-a, this antibody is highly clinically significant from transfusion point of view.

Keywords SLE · DAT · Anti JK-a · Anti JK-b · Anti-Fy-a · Anti-Fy-b · Anti-Le-a · Anti-Le-b antibodies

Introduction

Unexpected antibody against Kidd blood group antigen is one of the most dangerous immune antibodies may develop in patient's serum [1]. We report a case of anti JK-a antibody in a 58 year old lady diagnosed as SLE with *falciparum* malaria infection. She also had history of recent blood transfusion. It is necessary to identify these atypical

antibodies in patient's serum in order to select appropriate blood for transfusion.

Case Report

A 58 year old lady, mother of two daughters was admitted to our institute presented with high grade fever, pallor, abdominal pain, loss of appetite and swelling of legs. She also had breathing discomfort for last two weeks. Prior to her referral, she had been transfused two units of packed red cells from outside. Physical examination revealed moderate pallor, mild hepato-splenomegaly, tachypnoea (20 breaths per min), tachycardia (120 beats per min) and high grade fever (39.5 °C). On admission, her hemoglobin was 6.9 gm/dl, TLC 17,000/μl, platelet 10,000/μl. Malaria antigen test revealed *Plasmodium falciparum* positive (Parabank, Zephyr Biomedical, Goa, India) with parasitic index 0.5 %. On first day of admission her creatinine was 3.4 mg/dl, urea 133 mg/dl, total bilirubin 3.4 mg/dl, direct bilirubin 2.0 mg/dl, other parameters were normal. Though she was clinically pale and had breathing discomfort, she was advised for two units of packed red cells and four units of platelets transfusion as her platelet count was very low but no active bleeding. Her blood group was A Rh D positive. One of the two group A Rh D positive packed red cell units was incompatible in IAT phase cross match, (Diamed AG, Switzerland). So, only the compatible unit was issued to the patient. Because of the patient had also observed skin abnormalities, joint pain, fever, thrombocytopenia and pallor, an autoimmune work up was performed and revealed very high ANF 14.7 (Index value Bio Rad) (<1 negative, ≥1 positive), very high dsDNA 383.6 IU/ml (normal up to 25 IU/ml) and the patient was diagnosed as SLE with *Plasmodium falciparum* infection. Subsequently,

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direct antiglobulin test (DAT) and auto control along with antibody screening test (Diamed AG, Switzerland) were performed. Both DAT and autocontrol were positive with IgG and complement, but negative for IgM. This suggested possibility of development of IgG specific autoantibody with or without complement. Antibody screening test using three cell panel revealed positive agglutination on panel cell no. I and cell III (Table 1) (Diamed ID Diacell I, II, III Lot no. 45184.41.1 Expiry: 2009.09.28). Screening cell panel result suggested the possibility of development of anti-e, anti-Duffy (Fy-a), anti-JK-a and anti-Le-b (Lewis) antibodies. Later, anti JK-a antibody was identified on eleven cell panel (Diamed ID Diacell Lot no: 45161.03.1, expiry: 2009.09.28) (Table 2). However, whether this anti-JK-a was an autoantibody or an alloantibody, could not be elicited as the patient already had previous transfusion history two weeks back. On third day of admission, patient went into renal failure and required urgent dialysis as well as two units of packed cells. We issued again one randomly identified JK-a negative and A Rh D positive IAT phase compatible unit. No adverse events were reported during and post transfusion of that unit. On the fifth day of admission, patient's clinical condition deteriorated, she developed DIC and succumbed to *falciparum* malaria infection and sepsis.

Discussion

Kidd blood group represents ninth blood group system classified by International Society for Blood Transfusion (ISBT) [1]. Antibody against Kidd antigen are known as one of the most dangerous unexpected antibodies for causing highest prevalence and incidence rate of delayed hemolytic transfusion reaction (DHTR). The fact that unexpected antibodies to Kidd antigen, when exposed to antigens, rapidly appear in blood as an anamnestic response and then fastly disappear below detectable level may account for low detection rate [2]. The antibody, whether auto-antibody or allo-antibody, shows variability in immunoglobulin class, subclass and serological characteristics. The antibody is usually IgG or a combination of IgG and IgM; pure IgM is extremely rare. It has been generally considered that major antibody component of Kidd antibody must be IgG with complement fixing ability [3]. They are usually detected by an antiglobulin test, using a polyspecific antiglobulin or complement antisera. Although, current guidelines for pre-transfusion testing indicate that antiglobulin reagents with potent anti IgG can effectively identify such antibodies, without the need of an anti complement component [4]. Anti-JK-a as an autoantibody has been rarely described. Review of literature revealed many case reports. Furthermore, similar to our

Table 1 Screening cell panel positive in cell no. 1 and 3 and was suggestive of anti-e, anti-Fya, anti-JKa and anti-Le (Diamed ID Diacell I, II, III Lot no: 45184.41.1 EXP.2009.09.28)

Cell	Rh-hr				Kell			Duffy			Kidd		Lewis		P	MNS			LUTH		Result					
	D		C		e	K	k	Kpa	Kpb	Fya	Fyb	JKa	JKb	Le ^a	Le ^b	P ₁	M	N	S	s	Lu ^a	Lu ^b	IS	37 °C	AHG	
	D	C	E	e	c	e	K	k	Kpa	Kpb	Fya	Fyb	JKa	JKb	Le ^a	Le ^b	P ₁	M	N	S	s	Lu ^a	Lu ^b	IS	37 °C	AHG
1	CCDee	R ₁ R ₁	+	+	0	0	+	0	+	+	+	+	+	0	+	+	+	0	+	0	0	+	+	-	2+	3+
2	ccDEE	R ₂ R ₂	+	0	0	+	+	0	+	0	+	0	+	+	0	+	+	+	+	+	+	+	+	-	-	-
3	ccdee	rr	+	0	0	+	+	+	0	+	+	0	+	0	0	+	+	0	+	0	+	+	+	-	2+	2+

Letter [a, b] signify subtypes of red cell antigens

Table 2 Below result shows dosage phenomenon for Kidd antigen

Cell	Rh-hr				Kell				Duffy				Kidd		Lewis		P	MNS				LUTH		Result				
	D		C		E	e	c	e	K	k	Kpa	Kpb	Fya	Fyb	JKa	JKb		Le ^a	Le ^b	M	N	S	s	Lu ^a	Lu ^b	IS	37 °C	AHG
1	CCDee	R ₁ R ₁	+	+	0	+	+	0	0	+	0	+	+	0	+	+	0	0	+	+	+	+	0	+	-	-	-	
2	CCDee	R ₁ R ₁	+	+	0	0	+	+	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	+	-	2+	2+	
3	ccDEE	R ₂ R ₂	+	0	+	0	+	0	0	0	0	+	0	0	0	+	+	0	+	0	0	0	+	+	-	-	-	
4	Ccddee	r ¹ r ¹	0	+	0	+	+	0	+	0	0	+	+	0	+	0	+	+	+	+	0	+	0	+	-	2+	2+	
5	ccddEe	r ¹ r ¹	0	0	+	+	+	0	+	0	0	+	+	0	0	+	+	+	+	+	0	+	0	+	-	-	-	
6	ccddeee	rr	0	0	0	+	+	+	+	0	0	+	0	+	+	0	0	+	0	+	0	+	0	+	-	2+	2+	
7	ccddeee	rr	0	0	0	+	+	+	0	+	+	+	0	+	0	+	+	+	+	+	+	+	+	+	-	-	-	
8	ccDee	R ₀ r	+	0	0	+	+	+	0	+	0	+	0	0	+	0	+	+	+	+	+	0	0	+	-	1+	2+	
9	ccdee	rr	0	0	0	+	+	+	0	+	0	+	0	+	+	+	0	0	0	+	+	0	0	+	-	-	-	
10	ccdee	rr	0	0	0	+	+	+	0	+	0	+	0	+	+	0	0	+	0	+	+	+	+	+	-	2+	2+	
11	ccdee	rr	0	0	0	+	+	+	0	+	0	+	0	+	0	+	0	+	+	0	+	0	0	+	-	-	-	

Anti Kidd antibody developed in the patient showed positive agglutination in panel cell no. 2, 4, 6, 8, and 10. All these panel cells are homozygous (JKa/JKa) for Kidd antigen. Cell no. 1 and 9, though contain Kidd antigen, but in heterozygous form (JKa/JKb), thus did not show any agglutination (Diamed ID cell panel (Diacell) Lot no: 45161.03.1, Exp:28.09.09 D/O/E:28.09.2009)

Letter [a, b] signify subtypes of red cell antigens

patient, in majority of patients autoimmune diseases like SLE, autoimmune thrombocytopenia, ulcerative colitis were diagnosed. In many clinical situations where auto anti JK-a has clinical significance an underlying autoimmune disease or known antibody triggering agent is responsible for anti JK-a induced clinical relevant haemolysis. However, this patient did not have any clinically significant feature of haemolysis, she had normal LDH, and her unconjugated bilirubin was 1.4 mg/dl and did not rise thereafter.

We experienced incompatibility while cross matching red cell unit. Subsequently DAT and auto-control were positive. Antibody identification on eleven cell panel showed reactivity on panel cell no. two, four, six, eight and ten. These cell panels have Kidd antigen (JK-a) expression in homozygous (JK-a/JK-a) form and no reactivity was observed in cell panel one and nine as these cell panel have Kidd antigen expression in heterozygous form (JK-a/JK-b) (Table 2). This is very typical characteristic of Kidd antigen and known as dosage effect. So, anti-JK-a present in patient sera reacts far more strongly with JK-a/JK-a than with JK-a/JK-b cells and may be undetectable with the latter [5]. As per our work up, this patient most possibly developed warm autoantibody but we could not make out with certainty whether this anti JK-a was pregnancy or transfusion induced allo-antibody or disease induced auto-antibody. This is because her antigenic phenotyping could not be done as she had recent history of blood transfusion. Moreover, the most daunting task for the transfusion medicine specialist is the detection and identification of clinically significant allo-antibodies that may be masked by existing auto antibodies [6]. In our patient, life threatening clinical condition and time constraints did not allow us to perform adsorption and elution studies for subsequent detection of any underlying allo-antibodies.

Anti JK-a and anti JK-b are both one of the notorious unexpected antibodies causing immediate or delayed hemolytic transfusion reaction. Hence, it is mandatory for the safe transfusion that any patient with detected unexpected antibodies against Kidd blood group are supplied JK-a or JK-b antigen negative through sensitive cross matching and extended antigenic phenotyping. Auto immune hemolytic anemia (AIHA) due to anti-JK-a complement binding warm autoantibodies are extremely rare. There might be an association with auto immune diseases, as in our patient, or drug-induced antibody formation and these associations should be searched for, as they can influence the treatment. Due to the rarity of the disease, specific treatment options cannot be defined. First line treatment should therefore consist of corticosteroids like in warm AIHA. In order to prevent splenectomy in slow responders intra venous immunoglobulin (IVIG) is a valuable option [7].

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