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# A case of naturally occurring anti-Di<sup>a</sup> antibody in a young man

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## Abstract:

The Diego (Di) blood group system comprises 22 antigens located on the band 3 protein, most of which are low-prevalence antigens. The majority of antibodies to Diego system antigens were of clinically insignificant; however anti-Di<sup>a</sup>, -Di<sup>b</sup>, -Wr<sup>a</sup>, -ELO and -DISK may cause hemolytic disease of the fetus and newborn (HDFN) and transfusion reaction. We reported a case of naturally occurring anti-Di<sup>a</sup> in a young man who presented to our hospital for wound debridement of fingers injury. His serological results were suggestive of anti-Di<sup>a</sup> antibody, and his molecular blood group showed he has Di (a-b+) antigen. Anti-Di<sup>a</sup> may be clinically significant. It can cause mild-to-severe HDFN, but there are only infrequent reports of it being clearly implicated in a hemolytic transfusion reaction. We suggest the need for reagent red blood cell panels to include Di<sup>a</sup> antigen-positive cells in antibody identification tests for our populations.

## Keywords:

Anti-Di<sup>a</sup>, anti-Di<sup>b</sup>, diego blood group system, naturally occurring antibody

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## Introduction

Layrisse *et al.* discovered the Diegoblood group in 1955 and was named for the first patient to produce an antibody against the new blood system's antigens. The patient, Mrs. Diego, had given birth to a child affected by hemolytic disease of the fetus and newborn (HDFN). Her serum contained an antibody (now called anti-Di<sup>a</sup>) which, during her pregnancy, had crossed the placenta to attack the red blood cells (RBCs) of her fetus (which expressed the Di<sup>a</sup> antigen).<sup>[1]</sup> The Diego blood group system currently encompasses 22 antigens, including three pairs of antithetical antigens: Di<sup>a</sup>/Di<sup>b</sup>, Wr<sup>a</sup>/Wr<sup>b</sup>, and WU/DISK. Only three antigens are of high prevalence, Di<sup>b</sup>, Wr<sup>b</sup>, and DISK, whereas the other 19 are of

low prevalence. The antigens of the Diego blood group system are carried on the erythroid band 3 protein anion exchanger 1. The gene is located on chromosome 17q21.31, and the cluster differentiation assignment is CD233.<sup>[2]</sup>

Antibodies to Diego system antigens do not seem to be of clinical significance except for anti-Di<sup>a</sup>, Di<sup>b</sup>, Wr<sup>a</sup>, ELO, and DISK, which can cause transfusion reaction and hemolytic disease of the fetus and newborn.<sup>[2]</sup>

## Case Report

An 18-year-old young male was admitted to the hospital for a right-hand injury after being stuck in a motorbike chain while trying to repair it. He was planned for wound debridement and full-thickness skin graft for his injury. He had no past medical illness or history of blood transfusion.

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A pretransfusion blood sample was sent for group screen and hold. The patient's blood type was O Rh-positive. Antibody screening was performed using 3-reagent red cell panels (BioRad ID) column agglutination technique and the result was positive. Antibody identification was performed using 11 reagent red cell panels (BioRad ID) in the saline and enzyme phases. The results showed a positive 2 + reaction in cell 5 and cell 8 in both phases [Figure 1]. The auto control was negative. The sample was further investigated by using bioCSL Phenocell™ C antibody identification panel. The result was a positive 2 + reaction on cell 4, which is suggestive of anti-Di<sup>a</sup> antibody [Figure 2]. Molecular tests for Di<sup>a</sup> and Di<sup>b</sup> antigen were performed and the results showed he was Di<sup>a</sup> antigen-negative and Di<sup>b</sup> antigen positive [Figure 3]. Crossmatching was not done because he did not require blood transfusion as he had only minimal blood loss during the procedure.

### Discussion

Most of the antigens in the Diego system are of very low prevalence. Some antigens have only been found in one family. However, although the antigens are rare, their antibodies are very common.<sup>[2]</sup> The Di<sup>a</sup> antigen is rare in Caucasian persons and is mostly found in Asian populations, including Chinese, Korean, and Japanese (5%–8%), and in South American Indians (7%–54%).<sup>[3,4]</sup> Di<sup>a</sup> antigen is found mainly in populations of Mongolian descent. It is also found in 36%, 12%, and 12% of South American Indians, Japanese, and

Chinese respectively, whereas it is rare in Caucasians individuals (0.01%).<sup>[5]</sup>

A study by Petit F *et al.* on the radial expansion of the Diego blood group system, polymorphisms in Asia, their data demonstrated large variations in frequency ranges with a hotspot in Mongolia and a significant positive correlation with geographical coordinates. Their findings suggested that DI × 01 allele carriers could have crossed into West Asia from Mongolia.<sup>[6]</sup> The Diego antigen is an anthropological marker and it is polymorphic in most Mongoloid populations.<sup>[7]</sup> Di<sup>a</sup> antigen was found with a frequency of 2.1% among Malaysian donors in three ethnic groups, namely, Malay, Chinese, and Indian. It was present among 1.25% of 401 Malay, 4.01% of Chinese, and 0.88% of 114 Indian-origin donors.<sup>[8]</sup>

Anti-Di<sup>a</sup> and anti-Di<sup>b</sup> are more commonly associated with HDFN than transfusion reactions. However, these antibodies are capable of causing immediate and delayed hemolytic transfusion reactions (HTRs).<sup>[7,9]</sup> There are reports of anti-Di<sup>a</sup> antibody causing delayed HTRs in Australia and Korea.<sup>[10,11]</sup> Anti-Di<sup>a</sup> is capable of causing moderate-to-severe HDFN, and cases have been reported in Miami, Hong Kong and Korea, and China.<sup>[12-15]</sup>

Our patient has no history of blood transfusion and naturally occurring antibody need to be considered. It has been reported that naturally occurring antibodies to low-prevalence antigens in the Diego system are common in the plasma of patients with hyperactive immune systems, for example, those with autoantibodies.

Rh-ir	Möglicher Genotyp / Possible genotype / Genotype probable / Possible genotype / Genotipo probable / Genotype probable		Rh-ir		Kell				Duffy			Kidd		Lewis		MNS		Luth		Xg		Result/Resulto/Resultado/Resultado/Resultado/Resultado	Bemerkungen / Remarques / Remarques / Remarques / Observações / Observações								
	D	C	E	c	e	C <sup>x</sup>	K	k <sup>p</sup>	k <sup>p</sup>	Jk <sup>a</sup>	Jk <sup>b</sup>	Fy <sup>a</sup>	Fy <sup>b</sup>	Jk <sup>a</sup>	Jk <sup>b</sup>	Le <sup>a</sup>	Le <sup>b</sup>	P	M	N	S			s	Lu <sup>a</sup>	Lu <sup>b</sup>	Xg <sup>a</sup>	Xg <sup>b</sup>			
1	CCC <sup>D</sup> .ee	R <sub>1</sub> R <sub>1</sub>	616095	+	+	0	0	+	+	+	nt	nt	+	0	0	+	+	+	+	+	+	+	+	+	+	+	N/A	1	0	0	
2	CCD.ee	R <sub>1</sub> R <sub>1</sub>	697261	+	+	0	0	+	+	+	nt	nt	+	0	0	+	+	+	+	+	+	+	+	+	+	+	N/A	2	0	0	
3	ccD.EE	R <sub>1</sub> R <sub>2</sub>	762904	+	+	+	0	0	0	0	+	nt	nt	+	+	+	+	+	+	+	+	+	+	+	+	+	N/A	3	0	0	
4	Ccddee	r <sup>+</sup> r	116493	0	+	+	+	+	0	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	4	0	0	
5	ccddEe	r <sup>+</sup> r	570840	0	0	+	+	+	0	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	5	2+	3+	
6	ccddeee	rr	553731	0	0	0	+	+	+	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	6	0	0	
7	ccddeee	rr	451559	0	0	0	+	+	0	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	7	0	0	
8	ccD.ee	R <sub>1</sub> R <sub>2</sub>	396149	+	+	0	0	+	+	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	+	N/A	8	2+	3+	
9	ccddeee	rr	709948	0	0	0	+	+	0	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	9	0	0	
10	ccddeee	rr	537565	0	0	0	+	+	0	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	10	0	0	
11	ccddeee	rr	056878	0	0	0	+	+	0	0	+	nt	nt	0	+	+	+	+	+	+	+	+	+	+	+	+	N/A	11	0	0	

Figure 1: Antibody identification using panels BioRad ID

Figure 2: Antibody identification using bioCSL Phenocell™

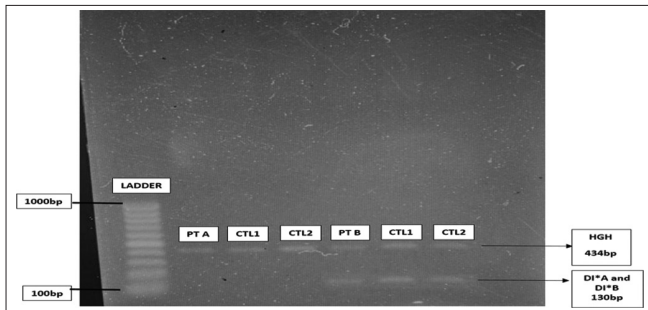


Figure 3: Molecular blood group for Di<sup>a</sup> and Di<sup>b</sup> antigen

This may be related to the exposure of the senescent cell antigen, which resides on protein residues in band 3.<sup>[2]</sup> Agglutinins with anti-Di<sup>a</sup> specificity have been reported in individuals with no known RBC exposure. Anti-Di<sup>a</sup> has been shown to activate complement, and they have demonstrated the capability of causing *in vitro* hemolysis and severe immediate or delayed transfusion reactions.<sup>[3]</sup>

### Conclusion

In the context of transfusion, anti-Di<sup>a</sup> may be clinically significant. It can cause mild-to-severe HDFN, but there are only infrequent reports of it being clearly implicated in an HTR. Given the general rarity of Di<sup>a</sup> antigen, RBC units that are cross-matched compatible in the indirect antiglobulin testing phase at 37°C should be selected for transfusion. Routine donor red cell antigen phenotyping at our center does not include Di<sup>a</sup> typing; therefore, a request for Di<sup>a</sup>-negative RBC units results in additional manual phenotyping and/or genotyping. We suggest the need for reagent RBC panels to include Di<sup>a</sup> antigen-positive cells in antibody identification tests for Malaysian populations.

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### Conflicts of interest

There are no conflicts of interest.

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