

Anti-f in a 24- Year Old Male: A Case Study

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ABSTRACT

This is a case study of a 24-year old male, having total knee arthroplasty, who is found to have an anti-f antibody, and denies history of previous blood product injection or blood transfusion. The anti- f antibody is produced due to exposure to the f antigen, and is one of the Rh blood group system's compound antigens expressed when the c and e alleles are in the *cis* position on the Rh chromosome. Patients with anti-f requiring transfusion could safely be transfused with units of blood lacking both the c and e antigens and units lacking only the c antigen.

INDEX TERMS: Anti-f, f antigen, blood transfusion.

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CASE PRESENTATION

A 24-year-old Hispanic male was admitted for a total left knee arthroplasty. During his pre-surgical evaluation, eleven days prior to the operation, the patient's hemoglobin and hematocrit were found to be 14.2 g/dL and 41.4%, respectively (Table 1). No pre-operative autologous units were donated; however, 350 ml of salvaged blood was reinfused during the procedure.

Table 1: Pre-surgical laboratory results of patient

Tests	Results	Reference Range
Hemoglobin	14.2 g/dL	14-18g/dL
Hematocrit	41.4 %	42-52%
ABO group type	O	
Rh	Positive	
Antibody screen	Positive	
Antibody Panel	Positive,	
Autocontrol	Negative	

The patient's 24 hour post-surgical results revealed that his hemoglobin and hematocrit were 10.1 g/dL and 28.9% respectively (Table 2). Thereafter, there was a steady decrease despite the salvaged blood reinfusion. An explanation for this decrease was attributed to post-operative blood drainage, considering the scope of the operation performed and the pre-surgical negative autocontrol result (Table 1). Day two post-surgery, the patient's hemoglobin and hematocrit dropped to 8.2 g/dL and 23.9%, which warranted transfusion per hospital protocol (Table 2).

Table 2: Post surgical results

Day	Hemoglobin	Hematocrit	Units transfused
One:	10.1 g/dL	28.9%	
Two:	8.2 g/dL	23.9%	2 c- negative PRBC units transfused
Three:	8.6 g/dL	23.8%	2 c- negative PRBC units transfused
Four:	9.6 g/dL	27.3%	
Six:	10.8 g/dL	31.2%	

The physician ordered a type and screen and four units of packed red cells. The patient's specimen was obtained and initial results indicated that the antibody screen was positive with a negative autocontrol using the gel method (Table 1). The identification panel revealed an anti-f antibody (Table 4). The American Red Cross reference laboratory was contacted to provide more information on the nature of this antibody. Then the antibody identification process was completed by antigen typing the patient's red blood cells for c and e

antigens. The cells were c-positive and e-negative as shown on Table 3.

Table 3: Antibody screen and antigen typing results of patient

Antibody Screen	
Screen cells	Results
I	0
II	0
III	2+
Autocontrol	Negative
Antigen typing results	
Antisera	Results
e	0
c	Positive

Once this antibody was confirmed, the patient's history was further investigated to determine whether the patient had been transfused, had surgery or another condition requiring the use of blood or blood products. While the patient denied receiving blood, the history revealed an earlier gunshot wound which made it likely that the patient had received a transfusion, and simply misunderstood the question or was unable to recall.

Two c-negative units were transfused on day two post-surgery with no adverse reaction. However, on day three, the patient's hemoglobin and hematocrit results remained constant with an 8.6 g/dL hemoglobin

compared to 8.2g/dL and a 23.8% hematocrit compared to 23.9% on post-surgical day two (Table 2).

The expected rise of 1 to 1.5g/dL of hemoglobin and 3 to 5% hemocrit for each transfused unit of blood did not occur. Continued blood loss was the probable explanation for this event as considerable blood loss is associated with total knee arthroplasty.¹ No additional serology was performed on the patient because the first and second set of transfusions occurred within 24 hours. Two more c-negative units were transfused on post-surgical day three, and the patient's hemoglobin and hematocrit levels increased steadily over the next few days, with a final hemoglobin value of 10.8 g/dL and hematocrit of 31.2% at discharge.

What is known about the f (ce) antigen?

The f antigen is in the Rh blood group system with the International Society of Blood Transfusion (ISBT) number 004006. It is in the Rh blood group system present in 65% Caucasians, 92% blacks and 12% Asians.³ The Rh blood group system is made up of many antigens; some of which are compound antigens.

The f antigen is one of the Rh blood group system's compound antigens. These compound antigens are the result of positional effects of the alleles on the chromosomes.³ *Cis* products of these genes are expressed

Table 4: Antibody identification panel

Cell#			Rh-hr									KELL				DUFFY		KIDD		Xg	LEWIS		MNS			P1	LUTHERAN		Results					
			D	C	E	c	e	f*	C ^w	V	K	k	Kp ^a	Kp ^b	Js ^a	Js ^b	Fy ^a	Fy ^b	Jk ^a	Jk ^b	Xg ^a	Le ^a	Le ^b	S	s	M	N	P ₁		Lu ^a	Lu ^b			
1	R1wR1	105440	+	+	0	0	+	0	+	0	0	+	0	+	0	+	0	+	+	0	0	0	+	0	+	+	0	0	+	0	0	+	0	
2	R1R1	303310	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	+	0	+	+	+	0	+	0	+	0	+	0	+	0	+	0	
3	R2R2	117496	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	+	+	0	+	0	0	+	+	0	+	s	0	+	0	+	0	
4	Ror	303105	+	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	+	+	+	0	0	+	+	+	+	+	+	0	+	0	2+	
5	r'r	303312	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	+	0	0	+	0	+	+	+	+	+	0	+	0	2+	
6	r''r	113145	0	0	+	+	+	+	0	0	0	+	0	+	0	+	+	+	+	+	+	0	0	+	0	+	+	+	0	+	0	+	2+	
7	rr	118627	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	0	+	0	+	2+	
8	rr	303070	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	0	+	0	0	+	0	+	2+	
9	rr	303297	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	+	0	+	+	+	0	+	0	+	2+	
10	rr	303311	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	0	+	+	0	+	0	+	0	+	0	2+	
11	R1R1	303301	+	+	0	0	0	0	0	0	+	+	0	+	0	+	0	+	0	+	+	+	0	0	+	0	+	+	0	+	0	+	0	0
Patient Cells																																	0	

when the alleles are on the same haplotype.³ The f antigen is believed to be expressed when the c and e alleles are in the *cis* position.^{3,4} This antigen can be found in individuals with *cde*, *cDe*, *cD^ee* genes resulting in expression of the e antigen, c antigen and f antigen (ce).⁴ This is different in individuals having the *CDe/cDE* genes in which the c and e genes are on different chromosomes. An individual having *CDe/cDE* genes will not express the compound f (ce) antigen, but will express the e and the c antigens (e+, c+).

The f antigen was identified in 1953 by absorption tests on red cells with different genotypes.⁵ It was reported that cells with the following genotypes did not react with anti-f--*CDe/CDe*, *cDE/cDE*, *CDe/cDE* and *Cde/cDE*--while red cells with the following genotypes reacted with anti-f--*cde/cde*, *cDe/cde*, *CDe/cde*, *cDE/cde*, *cDE/cde*, *CDE/cDe* and *CdE/cde*.⁵ This study confirmed the antigenic identity of the f antigen as well as its molecular basis.

An interesting finding about the f antigen is that it is also expressed when only the D and c antigens are present (cD-).^{3,6} This phenomenon can be confusing, but it has been explained that the D is dominant in this scenario with either the reduced expression of c or a qualitatively different expression of c. In this case the f antigen expression is greatly reduced^{3,7} and only approximately half the number of antigenic sites is expressed.⁷ One would expect the f antigen not to be expressed in the absence of the e antigen. The f antigen is known to be resistant to enzymes and other chemicals including Ficin, papain, trypsin, pronase, sialidase, DTT.³

Differences in Anti-f

Anti-f was first discovered in 1953 in a multiply transfused 30-year-old Caucasian male who suffered from hemophilia.^{3,7} His genotype was *CDe/cDE*, which implies that it was not possible for him to express the f antigen since the c and e antigens were in the trans position.⁴ Anti-f has been found to be qualitatively different. Anti-f is expected to react with cells containing the ce antigen but has been reported to react with cells typing cD-.⁴ Cells with the cD- phenotype have been reported to react with anti-f⁷, but failed to react with anti-e sera containing anti-f. This antibody

might have some slight differences. Qualitative differences have also been reported with anti-f produced by *Cde/cDE* individuals compared to anti-f produced by *cDe/cDE* individuals.

Just as with other antibodies, it is possible not to make anti-f if exposed to red cells expressing the f antigen.⁵ The anti-f antibody is usually IgG although there are some IgM examples. It does not bind complement and has been reported to be present in some anti-c and anti-e reagent antisera. The antibody does have clinical significance as it can cause mild hemolytic transfusion reactions and hemolytic disease of the newborn.³ Auto-anti f has also been isolated.³

Should we rely on patients to provide an accurate medical history?

Patients are often an unreliable source of information about past treatment. This can be the result of treatment given while the patient was in varying degrees of consciousness, or that caregivers did not properly explain the treatment being provided. Often, however, the problem is simply a matter of communication. For example, while a patient may give a negative reply when asked if he has had a transfusion, changing the term to "received blood" can result in a detailed explanation of how many units of each type of blood product was received. The key to receiving an accurate history is often a matter of simply asking the questions in a way the patient understands.

CONCLUSION

The patient's red cells in this case study typed cD-. Since the e antigen is absent, one would expect the reaction strength of the patient's cells with examples of anti-f to be on the weak side. In the case of this 24-year old, reaction strength of his serum with screen cells were all 2+ (Table 3). Similar reaction strengths were observed with panel cells (Table 4) which confirms the weakened expression of the antigen. Possibly there is some f antigen present in the patient's red cells that may cause production of a qualitatively different type of anti-f compared to the one produced with missing c and e antigens.

After antigen typing the patient's cells, four O positive, c-negative units were cross-matched by the gel method

and were found to be compatible. Individuals with anti-f who express only the c antigen can be safely transfused with units missing the c antigen.

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