



Immunohematology Case Studies 2016

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Clinical History



Young woman, 5th pregnancy, week 29

Ultrasound of the fetus revealed an increased middle cerebral artery peak systolic velocity

→ fetal anaemia was suspected

Percutaneous umbilical blood sampling (PUBS) was done

Clinical History



Fetal haemoglobin was 3.0 g/dL, confirming the findings of the ultrasound investigation

Blood samples of mother and fetus were sent to a laboratory specialised in diagnostics of infectious diseases in pregnancy

In addition to virus testing, a direct antiglobulin test (DAT) was done

Current Sample Presentation Data



Fetus

ABO / Rh:	B Rh pos
DAT ¹ :	4+

Mother

ABO / Rh:	B Rh pos
Antibody Screen ¹ :	non reactive
Antibody Identification ¹ :	non reactive

¹ = column agglutination technique

Challenge with the Current Presentation



Mother probably had an antibody directed against a rare antigen

Crossmatch with the father's red cells was impaired by ABO incompatibility:

Father:

ABO / Rh AB Rh pos

Tests with Maternal Serum Dilutions



Red cells	Reactivity of maternal serum									
	Titer:	2	4	8	16	32	64	128	256	512
Father	(AB)	4+	4+	4+	4+	3+	2+	2+	1+	0
Donor #1	(A ₁ B)	4+	3+	2+	1+	0	0	0	0	0
Donor #2	(A ₁ B)	4+	3+	2+	1+	0	0	0	0	0

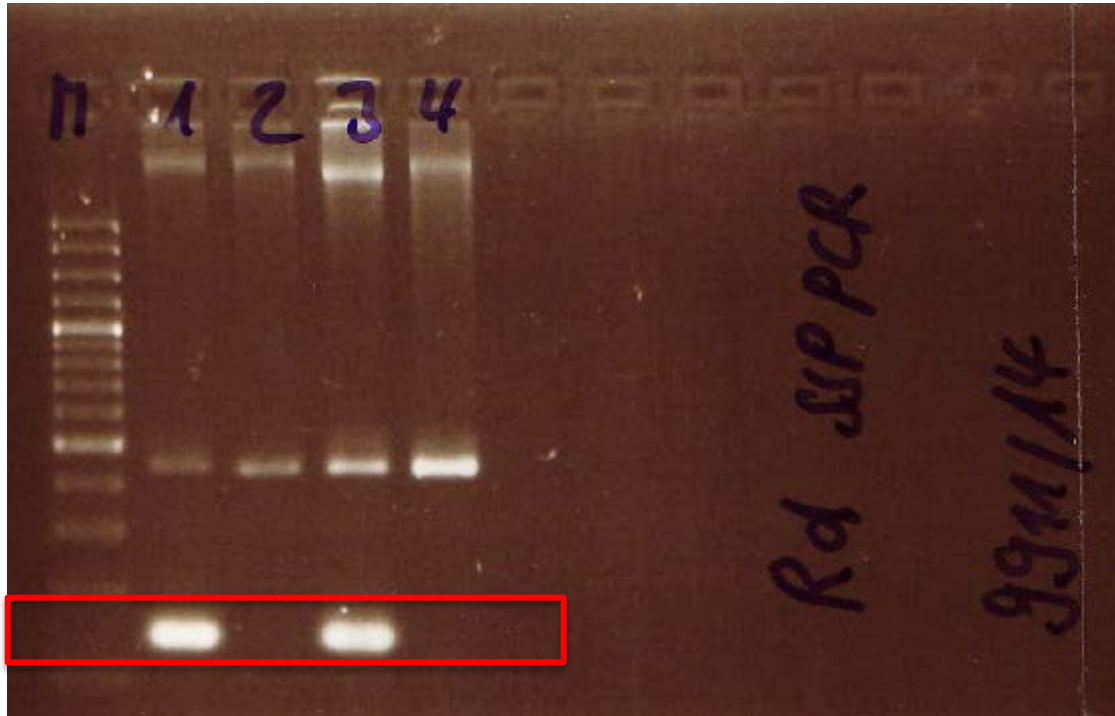
Crossmatching maternal serum with paternal red cells indicated the presence of an antibody against a rare, paternal antigen

Maternal serum was tested with cells positive for rare antigens



C^w	neg	He	neg	Mi^a	neg
Kp^a	neg	St^a	neg	Vw	neg
Js^a	neg	Tc^c	neg	C^x	neg
Lu^a	neg	Mt^a	neg	Mur	neg
Lu14	neg	Mit	neg	MINY	neg
Yt^b	neg	M^g	neg	Hil	neg
Wr^a	neg	TSEN	neg		
Di^a	neg	Ls^a	neg		
Co^b	neg	Sc2	neg		
V	neg	Rd	reactive		

Anti-Rd in group AB not available:
PCR for Radin (SC4 allele) was done



↑ ↑ ↑ ↑
neg ctrl.
pos ctrl.
pregnant woman: SC4-negative
father: SC4-positive

Interim Interpretation of the Results:

The fetal anaemia was not caused by a virus infection but by maternal blood group antibodies



Father

- carried the *SC4* allele and probably is Rd positive

Mother

- did not carry the *SC4* allele and was Rd negative
- an anti-Rd was found in the serum of the mother

Fetus

- strong reactive DAT, probably caused by maternal anti-Rd

Fetus

after PUBS, the fetus received in gestational week 29 and later in the course of the pregnancy:

1st transfusion Hb 3 → 5 g/dL

2nd transfusion Hb 5 → 8 g/dL

3rd transfusion Hb 8 → 10 g/dL

Delivery in week 37

birth weight 2,980 g (50th percentile)

Hb 8 g/dL → 1st postnatal transfusion

Further Testing Results and Interpretations



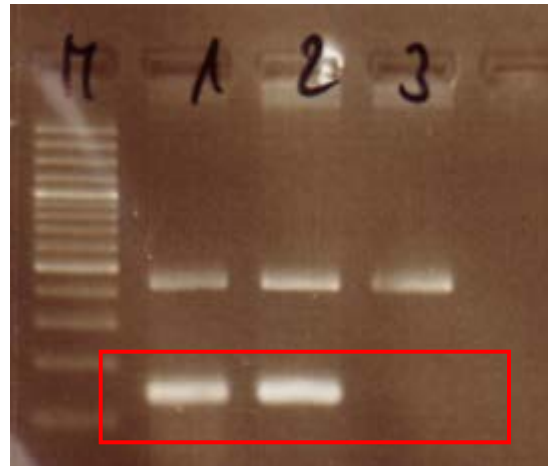
Testing newborn cord blood sample	
DAT ¹	4+
eluate antibodies (IAT ¹)	anti-Rd
serum antibodies (IAT ¹)	anti-Rd, titer 64
Flow cytometry (FITC-labeled anti-human IgG)	46 % IgG-coated RBC
Rd phenotyping	
direct typing	not possible (DAT 4+)
indirect typing	eluate contained anti-Rd

¹ = column agglutination technique

Further Testing Results and Interpretations



Newborn genotyping



↑
↑
↑
neg ctrl.
pos ctrl.
newborn: SC4-positive

Updated Clinical Information II



Day 72

Hb 7 g/dL

→ 2nd postnatal transfusion

Bilirubin

0.4 mg/dL (Ref < 1.2 g/dL)

Day 175

Hb

10 g/dL

DAT

non reactive

Physical development

normal

Lessons learned by the case



Antibodies directed against rare blood group antigens are not detected by antenatal antibody screening

In case of fetal anaemia the DAT should be included in the diagnostic workup

Lessons learned by the case



Blood group antigen Rd (Radin, Sc4)

System	Scianna
Gene	<i>ERMAP</i> ; 27,9 kbp, 12 exons
SC4	178C>G in exon 4
Protein	Erythroid membrane associated protein (ERMAP)
Function	possibly adhesion molecule or receptor
Antigen Rd	All populations “< 0.01%“ Danes 0.5 %
Anti-Rd	no transfusion reactions reported mild to severe HDFN (First reported 1967 as the cause of HDN)

References



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A „new“ infrequent red cell antigen, Rd (Radin)
Transfusion, 1967; 7(5):336-42

Reid, M.E., Lomas-Francis, C., and Olsson, M.
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Scianna antigens including Rd are expressed by ERMAP
Blood, 2003;101(2):752-57