

 THE UNIVERSITY OF KANSAS HEALTH SYSTEM

A Case of Anti-Fy3 Delayed Hemolytic Transfusion Reaction

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Patient History

- 18 Y.O. male patient with sickle-cell disease, arrives to E.D. with complaints of uncontrolled pain and SOB
- History of anti-Fy(a), anti-S, Warm Autoantibody and Cold Autoantibody. Current antibody screen Negative, 2 phenotypically matched units given on Day 1 of a 10-day admission.

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Case Study- Labs @ Admit

CHEM 12				
SODIUM	L	130	[137-147]	MMOL/L
POTASSIUM		3.8	[3.5-5.1]	MMOL/L
CHLORIDE	L	97	[98-110]	MMOL/L
GLUCOSE		95	[70-100]	MG/DL
BLD UREA NITROGEN		9	[7-20]	MG/DL
CREATININE		0.82	[0.4-1.24]	MG/DL
CALCIUM		8.8	[8.5-10.6]	MG/DL
TOTAL BILIRUBIN	H	4.0	[0.3-1.2]	MG/DL
ALBUMIN	L	3.4	[3.5-5.0]	G/DL
ALK PHOSPHATASE	H	444	[25-110]	U/L
AST	H	129	[7-40]	U/L
CO2		22	[21-30]	MMOL/L
ALT		45	[7-56]	U/L
ANION GAP		11	[3-15]	U/L
GFR NON Af- American		>60	[>60]	mL/min
GFR African American		>60	[>60]	mL/min
The eGFR is not validated for use in drug dosing adjustments. Continue to use estimated creatinine clear.				
LACTIC DEHYDROGENASE	H	744	[100-210]	U/L
CBC				
WBC COUNT	H	22.8	[4.5-11.0]	K/UL
RBC COUNT	L	3.80	[4.4-6.1]	M/UL
HEMOGLOBIN	L	6.4	[13.5-16.5]	GMV/DL
HEMATOCRIT	L	26.1	[39-50]	%
MCV		95.1	[80-100]	FL
MCH		29.9	[26-34]	PG
MCHC		32.1	[32.0-36.0]	G/DL
RDW	H	20.7	[11-15]	%
PLATELET COUNT	H	629	[150-400]	K/UL
MPV		8.0	[7-11]	FL
RETIC COUNT				
<<RET MCT>>		26.1		%
UNCORRECTED RETIC	H	19.1	[0.5-2.0]	%
Confirmed by smear				
CORRECTED RETIC		11.1		%
ABSOLUTE RETIC CT	H	534.2	[30-94]	K/UL

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Hgb Electrophoresis @ Admit

HGB A	L	10.0	[94.5-98.5]	%
HGB A2		3.3	[1.5-3.5]	%
HGB S	H	73.1	[0]	%
HGB C		<<DO NOT REPORT>>	[0]	%
HGB OTHER		<<DO NOT REPORT>>	[0]	%
HGB F	H	13.6	[0-2]	%
HGB E		<<DO NOT REPORT>>	[0]	%

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Case Study- Hospital Day 3

- Patient not getting any better. New Acute Chest Syndrome symptoms and continued uncontrolled pain despite aggressive medication and fluid regimen.
- “Acute chest syndrome (ACS) is a leading cause of death for patients with sickle cell disease (SCD). Defined as a new radiodensity on chest radiograph accompanied by fever and/or respiratory symptoms, ACS in adults with SCD requires prompt management to prevent clinical deterioration and death. The cause is vaso-occlusion within the lung vasculature.”

Source: UpToDate 2020

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Case Study- Hospital Day 5

- An exchange transfusion of 9 RBCs is requested. A new XM is performed, the screen is now positive in gel. All allo antibodies are ruled out, Cold Auto is re-identified.
- C, E, K, Fy(a), and S negative units are LISS compatible. Exchange transfusion is performed, and patient has stabilized.

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Case Study- Hospital Day 7

- Patient is clinically deteriorating again, with worsening ACS and pain.

CHEM 12			
SODIUM	L	132	[137-147]
POTASSIUM		4.9	[3.5-5.1]
CHLORIDE	L	93	[98-110]
GLUCOSE	H	150	[70-100]
BLD UREA NITROGEN		15	[7-25]
CREATININE		0.76	[0.4-1.24]
CALCIUM		9.7	[8.5-10.6]
TOTAL BILIRUBIN	H	10.0	[0.3-1.2]
ALBUMIN	L	3.2	[3.7-5.0]
ALP PHOSPHATASE	H	236	[125-310]
AST	H	116	[7-40]
CO2		22	[21-30]
ALT		38	[7-56]
ANION GAP		7	[3-12]
GFR NON African American		>60	[>60]
GFR African American		>60	[>60]
MAGNESIUM		1.8	[1.6-2.6]
PHOSPHORUS		3.4	[2.0-4.5]
TROPONIN I	H	2.00	[0.0-0.05]
CBC			
WBC COUNT	H	25.4	[4.5-11.0]
RBC COUNT	L	3.2	[4.5-5.4]
HEMOGLOBIN	L	11.5	[12.5-16.5]
HEMATOCRIT	L	33.4	[40-50]
HCV		97.9	[99-100]
MCH		35.8	[26-34]
MCHC		34.4	[32-36.8]
RDW	H	15.5	[11-15]
PLATELET COUNT	†	207	[150-400]
MPV		8.3	[7-11]

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Post-Exchange Hgb Electrophoresis

HGB A	L	80.7	[94.5-98.5]	%
HGB A2		2.5	[1.5-3.5]	%
HGB S	H	14.5	[0]	%
HGB C		<<DO NOT REPORT>>	[0]	%
HGB OTHER		<<DO NOT REPORT>>	[0]	%
HGB F	H	2.3	[0-2]	%
HGB E		<<DO NOT REPORT>>	[0]	%

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Hospital Day 9- New XM Drawn

- Screen is pan-reactive in Gel and Solid-Phase
 - LISS panel is pan-reactive at AHG
- DAT is newly positive for both IgG and C3, 2+
 - Eluate is weakly pan-reactive, which I called a Warm Autoantibody per our procedure
- Sample is severely hemolyzed
- Clinicians want to transfuse another RBC. I am not confident in this workup, so I send it to CBC.

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Meanwhile...

- I get a call from hematology because the patient failed a delta-check on his Hgb

CHEM 12			
SODIUM	L	129	[137-147]
POTASSIUM		4.0	[3.5-5.1]
CHLORIDE		98	[98-110]
GLUCOSE	H	107	[70-100]
BLD UREA NITROGEN		11	[7-25]
CREATININE		0.45	[0.4-1.24]
CALCIUM		8.5	[8.5-10.6]
TOTAL PROTEIN		5.1	[6.0-8.0]
TOTAL BILIRUBIN	H	3.0	[0.3-1.2]
ALBUMIN	L	2.5	[3.5-5.0]
ALP PHOSPHATASE	H	433	[25-110]
AST	H	60	[7-40]
CD2		26	[21-30]
ALT		15	[7-56]
ANION GAP		5	[3-12]
GFR NON Afr. American		>60	[>60]
GFR African American			The eGFR is not validated for use in drug dosing adjustments. Continue to >60 [1-60]
LACTIC DEHYDROGENASE	H	2876	[100-210]
TSH	H	5.880	[0.35-5.00]
CBC			
WBC COUNT	H	27.4	[4.5-11.0]
RBC COUNT	L	7.15	[4.5-6.5]
HEMOGLOBIN	L	7.4	[13.5-16.5]
HEMATOCRIT	L	22.3	[40-50]
HCV	I	24.8	[60-100]
MCH		31.4	[28-34]
MCHC		33.1	[32.0-36.0]
RDW	H	17.1	[11-15]
PLATELET COUNT		225	[150-400]
MPV		0.5	[7-11]

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Day 9 into Day 10

- Of course, it's a Friday night so CBC called in a tech to do this workup. I send the sample ~1900, and I get the report back ~0400 the next morning...

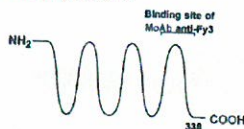
Types		Prevalence	Direct Antiglobulin Test		Complement
Fcs		Positive	Anti-Sensitizing	Positive	Positive
Identification					
Previous Serologic Findings					
Antibody	Subclass/Significance	Result	Antibody	Subclass/Significance	
Warm autoantibody	See Below	Plasma & Eluate	Anti-Fy3	See Below	
Anti-Fy ^a	Significant	Plasma	Cold autoantibody	See Below	
Anti-S	Significant	Plasma	Rouleaux	See Below	
Cold autoantibody	See Below				
Transfusion Recommendation					
Fy(b-)			S-		
Units Provided					
Additional Comments					
Transfusion of patients with warm autoantibodies carries a greater than normal risk. Cold autoantibodies are not usually clinically significant. Prewarmed testing may be required to circumvent the cold autoantibody in pretransfusion testing.					
The patient's plasma and an eluate prepared from the patient's cells contained anti-Fy3. This is an unexpected finding as the patient has the GATA mutation and would not be predicted to make anti-Fy ^a or anti-Fy3.					
Rouleaux was detected at 22 C and was dispersed by saline replacement.					
Reported By					

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Anti-Fy3 Facts

Molecular basis associated with antigen

The Fy(a-b-) phenotype in Blacks is due to a single nucleotide substitution (T to C) at position -46 in the Duffy (Fy^b) gene. This mutation impairs the promoter activity in erythroid cells by disrupting a binding site for the GATA1 erythroid transcription factor. Thus, Black Fy(a-b-) RBCs lack the Duffy protein^{1,2}. This also explains why anti-Fy3 is rarely made by Black Fy(a-b-) individuals. The molecular basis of four Caucasian Fy(a-b-) has been determined³. The third extracellular loop contains sequences necessary for binding of monoclonal anti-Fy3⁴.



Effect of enzymes and chemicals on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
Protase	Resistant
Stalidase	Resistant
DTT 200 mM	Resistant
Chloroquine (RT)	Resistant
Acid	Resistant

In vitro characteristics of alloantibody	Immunoglobulin class	IgG
	Optimal technique for detection	LAT, enzymes
	Complement binding	Rare
	Clinical significance of alloantibody	Transfusion reaction
HDN		Mild (rare)
Comments	Formation of anti-Fy3 is usually preceded by formation of anti-Fy ^a (see FY1). In spite of the high percentage of the Fy(-3) phenotype among Blacks, anti-Fy3 is a rare specificity. To date, no Black Fy(a-b-) individual has made anti-Fy ^a (see FY2), which is probably due to the presence of an Fy ^a gene that is silent only in the erythroid lineage.	
	Fy(-3) [Fy(a-b-)]RBCs resist invasion by <i>P. vivax</i> and <i>P. knowlesi</i> malarial parasites. Fy3 is expressed on RBCs from chimpanzees, gorilla, gibbon, rhesus, cynomolgus, baboon, dourocol ¹ .	

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So, What Happened?

- This was considered a delayed, severe hemolytic transfusion reaction.
- The patient was transferred to a pediatric facility that allowed for more diverse pain treatment options.
- He survived- but now requires Fy(a), Fy(b), S, C, E, K negative units- very rare. He will be increasingly difficult to transfuse.

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Questions?

Thank you very much for your time and attention!

Please feel free to email me (efiore@kumc.edu) with any general questions you have later!

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