FATAL HEMOLYSIS 13 DAYS AFTER CAESARIAN SECTION

Case study by Jim Perkins M.D. and Elizabeth Clay MT(ASCP)SBB (©2010)

A 30 year old woman underwent caesarian section. Prior to admission she was taking cephalothin orally. There were 2 previous uncomplicated term pregnancies; she had never been transfused and her prenatal antibody screen was negative. During the hospitalization she received 2 doses of intravenous (iv) cefotetan and went home on the second post-operative day, apparently without complications. A CBC before discharge documented a hgb/hct of 11.4/32.9.

On the 7th post-operative day a nurse visiting her at home did not note any obvious problems.

The patient did well until 11 days post-op. when she felt faint. She reported this by telephone to her physician who entertained hypoglycemia as a cause.

The following day she noted vaginal bleeding, fatigue, malaise and jaundice, and again reported to her physician. A CBC revealed a hgb/hct 5.1/14.6, WBCs 22,000, and platelets 524,000. She was admitted to the hospital at 12:30 pm for transfusion.

Two units of RBCs were ordered. Her antibody detection test ("antibody screen") was negative, as were crossmatches using the indirect anti-globulin test, but the autocontrol was 2+. Transfusion was delayed pending further workup which included a non-reactive eluate. These findings were confirmed by a reference laboratory during the evening prior to transfusion. Other laboratory data included a normal total bilirubin (1.4, ULN 1.5), and a normal LDH level. A sonogram showed a 9 x 8 x 4 cm hematoma anterior to the uterus. Oral ampicillin was administered at 16:00 and 20:00.

After discussion between the blood bank, a pathologist, and the attending physician, RBCs were made available. At approximately 22:30 the temperature had increased to 102.2^{o}f, and 2 grams of cefotetan were administered iv. At 23:00 an "in vivo crossmatch" - administration of 50 cc of RBCs followed by testing - was started. Soon thereafter the patient was noted to be restless and anxious with nausea, vomiting and complaints of abdominal pain. Transfusion was stopped and Benadryl was administered. The *in vivo* crossmatch sample did not show hemoglobinemia, although the DAT had increased from 2+ to 3+, and the urine specimen was noted to contain "blood". Thereafter the entire unit of RBCs was administered. A CBC at 23:30 revealed a hgb/hct of 4.2/11.8.

The patient was transferred to the ICU where blood pressure instability was noted. The transfusion was completed at 01:00, but the patient was noted to be lethargic and was oozing blood. A 2nd unit of RBCs was started but was stopped after 50 cc were administered. Multiple blood samples were found to have hemolysis. A 3rd unit of RBCs was started at 01:45 but stopped after 15 minutes. A CBC at 01:50 demonstrated a hgb/hct of 3/7.6. Vital signs included pulse rates of 150-160, respiratory rates of 30-40, and blood pressures of 130-150/50-60. Repeat crossmatches of all of the units with the original specimen were negative, but crossmatches with blood specimens drawn at 01:15 and 01:50 reacted 4+ with all RBCs tested. At this time the DAT was 4+ with anti-IgG and vw+ with complement, and the antibody screen was 4+ positive with all cells as well.

At 03:25 the hgb/hct was 1.8/3.5 and FDP were >40 (nml <10). The patient died at 04:36.

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IMMUNOHEMATOLOGIC TEST RESULTS

Tests Performed at the Hospital

ABO and Rh Typing

Specimen	Anti-			Test Cells		Anti-			Interp.	
	A	B	AB	A1	B	D	Du	Cont	ABO	Rh
Initial	4+	0	4+	0	4+	4+		0	A	Pos
Post-Cefotetan	4+	0	4+	0	4+	4+		0	A	Pos

Antibody Screen

	Initial Specimen				Eluate		Post-Cefotetan			
	IS	30'37^{o}	AHG	CC	AHG	CC	IS	30'37^{o}	AHG	CC
OI	0	0	0	2+	0	2+	0	0	4+	
OII	0	0	0	2+	0	2+	0	0	4+	
OIII	0	0	0	2+	0	2+	0	0	4+	
Autocontrol	0	0	2+				0	0	4+	

Direct Antiglobulin Test

Specimen	Polyspecific AHG	anti-IgG	anti-C'3	CC
Initial	2+	2+		
Post-Cefotetan		3+		

Crossmatches

	Initial Specimen				Post-Cefotetan			
Unit	IS	30'37^{o}	AHG	CC	IS	30'37^{o}	AHG	CC
1	0	0	0	2+	0	0	4+	
2	0	0	0	2+	0	0	4+	
3	0	0	0	2+	0	0	4+	
4	0	0	0	2+	0	0	4+	
5	0	0	0	2+	0	0	4+	
6	0	0	0	2+	0	0	4+	

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Tests Performed at the Reference Laboratory

		Initial Sample	Post-Cefotetan
ABO		A	A
Rh phenotype		DEce	DEce, mixed field
DAT	anti-IgG	2+	4+
	anti-C'3	w+	vw+
Antibody Screen		Negative	3+ @ AHG, all cells

Drug Studies: Initial Sample

	Patient Serum			Eluate		
	IS	60', 37^{o}	AHG	IS	60', 37^{o}	AHG
Drug coated RBCs	4+		4+	0		4+
Control RBCs	0		0	0		0
Drug + RBCs		3+, H	3+		0	3+
Drug + RBCs + C'*		4+, H	4+		0	3+
PBS + RBCs		0	0		0	0
PBS + RBCs + C'		0	0		0	0
Controls without serum or eluate						
Drug + RBCs		0	0			
Drug + RBCs + C'		0	0			

* C' indicates fresh serum added as a complement source

QUESTIONS:

1. What antibody(ies) are present? What is the diagnosis?

2. Why was auto-control, performed with the antibody detection test, positive? Transfusion was delayed because of concern over this finding. Would your laboratory have delayed transfusion because of this result and the positive DAT with a negative eluate? Does your laboratory perform an autocontrol with the antibody screen?

3. The patient first noted symptoms 11 days after treatment with cefotetan, in spite of the fact that the plasma half-life of cefotetan is 3 to 5 hours. How could this happen?

4. Why did the antibody detection test and crossmatch results change from negative to positive after the patient received cefotetan?

5. What was the root cause of this patient's death?