AIHA CASE #8 Case Study by Jim Perkins MD (©, 2009)

History: The patient was a 62 year old man who was referred to a hematologist for evaluation of anemia and an IgM mono-clonal gammopathy.

One year earlier he noted red urine after working in a cold warehouse all day. He went to an emergency room where anemia (hemoglobin 11.6 gm/dL) and hyperbilirubinemia (total bilirubin 3.1 mg/dL) were noted. The reticulocyte count was normal (2.5%). Urine microscopic examination revealed 5-10 RBCs but the urine sample for dipstick testing was lost. His past history was remarkable for kidney stones many years before. Mild anemia and elevations of bilirubin had also been noticed; the latter were ascribed to Gilbert's syndrome. Urologic workup, including cystoscopy, revealed only a renal cyst on CT scan; there was no lymphadenopathy or spenomegaley on review of the scan.

One month before the evaluation, and 11 months after the first episode, he had a second incident of "maroon, brown" urine after a significant cold exposure; urine dipstick analysis showed "large" blood, but the microscopic exam revealed only 0-1 RBCs. For the past year or two he had noted that his fingers became blue when he went out into the cold, but he denied the pain or other skin color changes of Raynaud's phenomenon. His wife also related that his earlobes would become blue when he went out into the cold. Over the year since the first episode of red urine his hemoglobin had fluctuated around 12 gm/dL Laboratory results included an IgM level of 800 mg/dL (nml 46-304), and a 600 mg/dL paraprotein. Overall the patient felt well and denied fever and weight loss.

Physical examination was essentially normal.

Notable laboratory findings included:
Hgb/hct = 11.7/32.6, rdw = 13 (nml 11.6-14.8)
WBC = 5,800
plts = 284,000
total bilirubin = 1.9
LDH = 372 (1/28/05)

A cold agglutinin evaluation was ordered. The sample was collected in the cancer care center and transported in a tube wrapped in a heel warmer to the blood bank where it was allowed to clot in a 37°C waterbath before the serum was separated.

ABO and Rh Typing

<A	<B	A1 cells	B cells	6% alb	<D	<D/AHG	CCC	Interp
0	0	4+	4+		4+			O, pos

Antibody Screen

	Gel
OI	0
OII	0

Direct Antiglobulin Test

	Poly	IgG	<C3
AHG	0		
CCC	2+		

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Cold panel				
	IS	RT	18ºC	4ºC
OI	2+	2+	3+	4+
OII	2+	2+	3+	4+
AC	0	1+	2+	4+
Oi	0	0	0	4+
Oi	0	0	0	4+

Thermal amplitude study				
		37º	30º	RT
Saline susp. RBCs	OI	0	0	1+
	OII	0	0	1+
Albumin susp. RBCs	OI	0	0	2+
	OII	0	0	2+

Titration at 4ºC												
	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1024	1:2048
OI	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	2+	0
OII	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	1+	w+

Because the findings above were inconsistent with a clinically significant cold autoantibody, repeat testing was scheduled. The sample was drawn in the blood bank donor room and immediately placed in the 37ºC water bath prior to separation of the serum and RBCs. The new test results were as follows.

ABO and Rh Typing

<A	<B	A1 cells	B cells	6% alb	<D	<D/AHG	CCC	Interp
0	0	4+	4+		4+			O, pos

Antibody Screen

	Gel
OI	0
OII	0

Direct Antiglobulin Test

	Poly	IgG	<C3
AHG	1+	0	1+
CCC		2+	

Thermal amplitude study				
		37º	30º	RT
Saline susp. RBCs	OI	0	w+	4+
	OII	0	0	4+
Albumin susp. RBCs	OI	0	4+	4+
	OII	0	4+	4+

Titration at 4ºC												
	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1024	1:2048
OI	4+	4+	4+	4+	4+	4+	4+	4+	4+	2+	1+	1+
OII	4+	4+	4+	4+	4+	4+	4+	4+	4+	4+	2+	1+

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1. What is the significance of reactivity of a cold autoantibody at 30°C? (See Garratty and Petz, Immune Hemolytic Anemias, pg. 182-190)

2. Why was there a difference between the first and second thermal amplitude test? Was the difference in titration results consistant with your hypothesis?

3. What is the specificity of the antibody in this case?

4. Discuss the features of cold autoimmune hemolysis as exemplified by the case. Is this likely a polyclonal or a monoclonal cold autoantibody? Why was the reticulocyte count normal at the time of the first episode of hemoglobinuria?