AIHA CASE #7, ANSWERS

Case study by Jim Perkins, M.D. (© 2009)

Indian Immunohematology Initiative

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

Reactivity at 30°C, with or without albumin enhancement, is regarded as an indication of the clinical significance of cold agglutinins. Patients with cold autoantibody-related hemolysis (cold agglutinin disease) are described (and we have experienced multiple times) who have cold autoantibodies with relatively low, or even normal, titers, but whose serum reacts with RBCs at 30°.

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

To accurately determine the thermal amplitude in borderline cases, the specimen must be collected properly, that is, into a pre-warmed tube that is continuously maintained at 37°C until it is clotted and the serum is separated. That is a major take-home point of this case. If the specimen is allowed to cool, the cold-autoantibody can adsorb to the RBCs, decreasing its concentration in the serum as seen in the titration results. In cases in which the autoantibody is polyclonal, it is precisely the clones that are active at the highest temperatures that will be selectively removed.

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

The antibody reacts at room temperature and 18°C with normal adult group O cells but not with I negative ("i") cells, indicating that it has anti-I specificity. Cord blood cells would also be expected to be non-reactive at those temperatures. Note that all cells react at 4oC, showing that the specificity is only relative, and this is typical.

4. Discuss the features of cold autoimmune hemolysis as exemplified by the case. What is the pathogenesis of the patient's blue fingers? 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?

This patient has classic cold agglutinin disease associated with monoclonal gammopathy. Cold autoantibodies may cause symptoms not only by fixing complement and lysing the RBCs, but also by agglutinating RBCs in the microvasculature causing cyanosis and even ischemic pain or ulceration.

Delay in diagnosis of AIHA, both warm and cold, is common. At the time of the patient's first hemolytic episode his red urine was assumed to represent hematuria. The history of kidney stones was an important "red herring" (misleading fact). The normal reticulocyte count is not strong evidence against hemolysis since the latter was acute related to a cold exposure. Even in warm autoimmune hemolysis, which tends to be less episodic, the reticulocyte count is normal 30% of the time, either because onset is resent or the patient's marrow is unable to respond. Immune hemolytic anemias are uncommon and frequently missed by clinicians. Typical is the patient who presents to the ER with anemia in whom the diagnosis is only made when a type-and-screen is ordered in anticipation of transfusion. We need to be alert to such cases, and communicate with the clinicians promptly.