A SIX MONTH OLD GIRL WITH HEMOLYTIC ANEMIA

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

QUESTIONS:

1. Why wasn't an autoadsorption done in this case?

   Autoadsorption is preferred to alloadsorption in patients with autoantibodies who have not been transfused recently. However, the patient's RBCs proved too fragile to withstand chemical treatment with reagents such as chloroquine, and presumably ZZAP, that are used to remove antibody from the patient's cells and otherwise render them suitable for autoadsorption. This is an occasional finding in patients with severe autoimmune hemolytic anemia and complicates the investigation. Note that a large number of adsorptions were needed in order to remove the autoantibody. Had both of these conditions been absent, it would still have been a problem to obtain from this small infant enough RBCs to perform autoadsorption.

2. Why were the parental phenotypes useful?

   Obtaining a valid phenotype for patients with warm autoantibodies allows the laboratory to predict what alloantibodies the patient might be able to make and to select cells of an appropriate phenotype to rule those antibodies out by alloadsorbtion. In addition, if the patient requires transfusion donor RBCs of a similar phenotype to the patient's can be chosen in order to decrease the incidence of alloimmunization. In this case the infant's RBCs were too fragile to survive chemical treatment to remove the bound autoantibody, and at the time this case was investigated, few monoclonal typing sera were available which could type DAT positive RBCs. Therefore the parent's phenotypes were determined in an effort to predict the infant's phenotype. The laboratory was lucky in that the parent's phenotypes were such that almost the complete phenotype could be predicted. Of note, the mother appeared to be homozygous E/E, so the infant was likely to be E positive as well. This result was at odds with the E typing result obtained with "saline" antisera. The predicted E phenotype was judged to be the more accurate of the two results since false negative typing results are know to occur when large amounts of antibody are bound to the RBCs. This result proved to be very important in answering the following question.

3. What allo- and/or autoantibodies are present in this case?

   The patient appeared to have a warm autoantibody of broad specificity, as well as an underlying allo-anti-M. The latter was unexpected since the patient had not been transfused, but anti-M is well known as a "naturally-occurring" antibody. Since the anti-M reacted at 37°C and in the antiglobulin test, most laboratories would choose to provide M-negative donor RBCs for transfusion. The alloadsorbed serum also contained anti-E, as shown by the two reactions with E-positive enzyme-treated RBC samples. Since the patient was E-positive, this was interpreted to represent auto-anti-E specificity among some of the clones of warm autoantibody that was revealed by adsorption of the rest of the autoantibody onto the E-negative alloadsorbing cell. Because of this antibody specificity, E-negative RBCs were selected for transfusion in the hope that their survival might be prolonged relative to E-positive RBCs.

4. Comment on the patient's clinical presentation, treatment, and course.

   This case illustrates a number of important features of WAIHA by example and contrast. The diagnosis was readily apparent from the presence IgG antibody bound to the patient's RBCs in concert with evidence of hemolysis in the form of anemia with reticulocytosis, microspherocytes, and poikylocytes. A drug-related antibody of the methyldopa (drug-independent) type was readily ruled out by the history. WAIHA is uncommon in children and even more so in infants. In the series of Habibi 93 of 767 cases of AIHA (12%) occurred in children, and 78% of those with IgG on their RBCs followed a chronic course as illustrated by this infant.*

Although many cases of acute AIHA are preceded by a non-specific upper respiratory infection, her symptoms began only 4 days before she was found to be severely anemic, and a reticulocytosis was already apparent by then. Since it takes more than 4 days for reticulocytosis to appear, the respiratory infection was presumably NOT the precipitating event, although it may have exacerbated the AIHA.

Therapy was begun with steroids to which IVIG was added with little success. In an adult patient the next step might have been splenectomy. However, carries high long-term risks in children, so cyclosporine, another immunosuppressive agent, was tried. Although this agent was effective in treating the autoimmune hemolytic anemia, it is a difficult agent to use, doubly so in a growing infant.

* *Habibi B, Homberg JC, Schaison G, Salmon C. Autoimmune hemolytic anemia in children; A review of 80 cases. Amer J Med, 1974;56:61-9.*