A PATIENT WITH A HIGH RETICULOCYTE COUNT

ANSWERS:

1. Comment on the clinical findings in the case. (E.G. diagnosis, laboratory findings, response to therapy, clinical course).

   This patient presents a classic case of severe warm autoimmune hemolytic anemia (WAIHA). Criteria for that diagnosis include evidence of autoantibody directed against the RBCs as well as classic evidence of hemolysis. The former is evident in the form of a positive DAT due to IgG and complement coating of the RBCs. Reactivity with all cells in the antibody identification panel is typical of autoantibodies, although they may show specificity similar to common alloantibodies. The fact that the antibody in the eluate is recovered from a patient who has not been transfused demonstrates that it is auto-reactive, and the fact that the antibody in the serum can be removed by autoadsorption demonstrates this as well. The combination of warm- and cold-reactive autoantibodies is relatively common, present in as many as 30% of cases. We typically presume the warm-reactive component causes the hemolysis, but that would be difficult to prove in this case.

   Hemolytic anemia was suggested by the combination of a history of progressive fatigue and dyspnea on exertion as well as pallor, jaundice, and tachycardia on examination. This was confirmed by the elevations of unconjugated ("indirect acting") bilirubin and LDH, and the low haptoglobin level. The reticulocyte count was very high and attests to the severity and slow development of hemolytic anemia in this case. If we can assume that a reticulocyte matures after 2 to 3 days, red cell survival in this patient was no more than 5 or 6 days, an unsustainable situation as shown by the fall in the hemoglobin level over the first 11 hours of his hospitalization. In cases of WAIHA that develop rapidly the reticulocyte count may be normal at presentation.

   The WAIHA in this case was "primary" in that it was not associated with a predisposing illness such as another autoimmune problem or a lymphoid malignancy. Like the majority of patients with WAIHA the patient responded to steroids, but he relapsed when he discontinued them prematurely.

2. What is the utility of determining the patient's extended blood group phenotype? Why was EDTA/Glycine necessary for the Duffy, Kidd, and Ss typing?

   It is useful to determine the extended blood group phenotype in new patients with WAIHA prior to transfusion because this information may be needed subsequently as part of alloantibody identification, and at that time if the patient has recently been transfused, the phenotype may not be valid. In addition, a critical issue in compatibility testing for patients with WAIHA needing transfusion is demonstration that there are no clinically significant alloantibodies underlying the autoantibody. This is a potential problem for patients who have been pregnant or transfused previously. But like a phenotype, autoadsorption is not valid if there are circulating donor RBCs. In this case one may resort to adsorption with allogeneic RBCs lacking antigens against which the patient may form alloantibodies. And knowing the patient's phenotype allows the laboratory to select such cells in order to perform the alloadsorption more efficiently. Finally, knowing the patient's extended phenotype allows the laboratory to select donor RBCs that lack some of the antigens that the patient lacks. This may increase the safety of transfusion when the laboratory is unsure whether underlying alloantibodies have been ruled out. This maneuver will also avoid future allo-immunization.

   However, determination of the phenotype of patient RBCs having a strongly positive DAT may be a problem. If an individual typing serum requires anti-human globulin in order to agglutinate antigen positive RBCs, any cell coated with IgG will appear antigen positive. Therefore, the IgG coating the cells must first be removed. This can be done by treating the RBCs with EDTA/glycine or chloroquine solutions either prepared in the laboratory or obtained commercially. In this case the typing sera for Duffy, Kidd, and Ss antigens required an IAT so EDTA/glycine was used to pre-treat the cells (controls not shown).