Unexplained Hemolytic Anemia with Multiorgan Failure

Girindra Raval,[1] Joel E. Straughen,[2] Gwendolyn McMillin,[3] and Joshua A. Bornhorst[2*]

[1] Departments of Hematology/Oncology and [2] Pathology, University of Arkansas for Medical Sciences, Little Rock, AR; [3] Department of Pathology, University of Utah, Salt Lake City, UT.

*Address correspondence to this author at: University of Arkansas for Medical Sciences, College of Medicine, Department of Pathology, 4301 W. Markham St., Little Rock, AR 72205. Fax 501-526-4621; e-mail jabornhorst@UAMS.edu.

CASE

A 51-year-old white male with history of osteoarthritis, hypertension, and insomnia presented to the hospital with a 1-month history of fatigue, as well as a 1-week history of back pain, nausea, and dark urine. The patient worked as a construction contractor and lived with his wife. His family history was limited to his mother having diabetes. He was taking scheduled hydrochlorothiazide and celecoxib and taking zolpidem as needed. In addition, he was also taking a wide variety of nonprescribed nutritional supplements.

At presentation, the patient had a decreased hemoglobin concentration of 3.5 g/dL [reference interval (RI) 13.5–17.5 g/dL, with a baseline hemoglobin value of 12 g/dL obtained 6 months previously], a reticulocyte count of 1.2% (RI, 0.7%–3.2%), a total bilirubin value of 17.6 mg/dL (RI, 0.2–1.2 mg/dL), a direct bilirubin value of 4.6 mg/dL (RI, 0–0.5 mg/dL), a lactate dehydrogenase activity of 693 U/L (RI, 0–248 U/L), and a positive result in a direct antiglobulin test for IgG. His haptoglobin concentration was <30 mg/dL (RI, 48–224 mg/dL). A peripheral blood smear from the patient had 1 or 2 schistocytes and 1 or 2 spherocytes per high-power field, a typical platelet morphology, and hyperlobated neutrophils. He was transferred to an intensive care unit 2 days after presentation.

Treatment with intravenous immunoglobulin and methylprednisone was initiated for immune hemolytic anemia. A bone marrow biopsy showed erythroid hyperplasia. His values for red blood cell folate, serum vitamin B_{12}, C3, C4, rheumatoid factor, and red blood cell glucose-6-phosphate dehydrogenase activity were within their respective RIs, and the results of serum tests for antinuclear antibodies, cold agglutinin, and *Mycoplasma* antibodies were negative. He sequentially received rituximab, cyclophosphamide, and then plasmapheresis, in addition to methylprednisolone and intravenous immunoglobulin to treat his ongoing anemia. The patient was given transfusions of packed red blood cells as needed. His hemoglobin concentration increased to 8 g/dL. A course of antibiotics was started for presumed sepsis, although initial blood and urine cultures did not yield any evidence of infection.

Despite continued aggressive treatment for presumed autoimmune hemolytic anemia (AIHA), the patient developed progressive hepatic, renal, and respiratory failure with marked acidosis requiring multiple transfusions of platelets and fresh frozen plasma, hemodialysis, and endotracheal intubation. Before dialysis, the patient's serum creatinine concentration rose to 3.6 mg/dL from 1.1 mg/dL (RI, 0.6 –1.3 mg/dL) at transfer 3 days previously. The patient's alanine aminotransferase and aspartate aminotransferase activities, although within the RIs at the time of transfer, increased slightly to 86 U/L (RI, 5–45 U/L) in the case of alanine aminotransferase and substantially to 257 U/L (RI, 15–

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41 U/L) for aspartate aminotransferase. Samples submitted for electrolyte analysis consistently exhibited hemoglobin concentrations >200 mg/dL (RI, 0–10 mg/dL) according to spectrophotometric index analysis (Synchron DxC; Beckman Coulter). The direct bilirubin concentration increased to >50 mg/dL (RI, 0–0.5 mg/dL). His platelet count decreased from 247 × 10^3/μL to 108 × 10^3/μL (RI, 150–500 × 10^3/μL). Additionally, the patient experienced respiratory failure. His refractory multiorgan system dysfunction continued its aggressive course until his death 4 days after transfer.

The postmortem examination revealed organizing thrombi and multifocal hemorrhages with acute inflammatory infiltrates in most organs, including myocardium, brain, bowel, lungs, and spleen. The liver exhibited diffuse centrilobular congestion and necrosis, and the kidneys exhibited bilateral cortical infarcts and acute tubular necrosis. Cultures of blood and lung tissue were negative.

Questions to Consider
• What are the symptoms and laboratory test results associated with AIHA?
• Are the laboratory test results and the clinical course of this case consistent with AIHA?
• What additional laboratory testing should be performed on available antemortem blood samples in this case to explore potential causes of the patient's symptoms?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the November 2011 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol57/issue11 and follow the link to the Clinical Case Study and Commentaries.

Educational Centers

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