Severe Symptomatic Anemia in a 30-Year-Old Man

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A 30-year-old man is admitted for profound, symptomatic anemia.

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A 30-year-old man is admitted for profound, symptomatic anemia. He has become weaker and more tired and fatigued in recent weeks. In the days before admission, dyspnea with minimal effort developed as well. He denies hemoptysis, melena, hematochezia, or other bleeding. He also denies fever and signs of bleeding, such as petechiae, purpura, or ecchymoses.

HISTORY
The patient had been reasonably healthy until several months before this admission. Since then he has lost more than 11 kg (about 25 lb), and he now weighs 54.5 kg (120 lb). Although his appetite has been diminished, he has had no specific GI symptoms, such as abdominal pain or changes in bowel habits. He went to the public health clinic, where a battery of blood tests was ordered, but he has not returned to find out the results. He is currently unemployed and lives in an apartment with his brother. He has a history of intravenous use of both heroin and cocaine.

PHYSICAL EXAMINATION
This thin man looks older than his stated age. Heart rate at rest is 110 beats per minute. Temperature and blood pressure are normal. Mucosae are very pale. Diffuse 1-cm lymph nodes are palpable bilaterally in the anterior cervical areas. Lungs are clear. Abdomen is soft, without masses or hepatosplenomegaly. No rashes are evident, and results of a neurological examination are normal.

LABORATORY EVALUATION
Hemoglobin level is 3.9 g/dL; hematocrit, 15 mL/dL; and mean corpuscular volume, 104 fL. Platelet count is 151,000/µL. White blood cell count is 3500/µL, with 89% segmented neutrophils, 4% monocytes, and 7% lymphocytes. Smear reveals moderate anisocytosis but is otherwise morphologically normal. Results of routine chemistry and biochemical panels are normal.

Which of the following represents optimal management for this patient?
A. Abnormal hemoglobin electrophoresis results demonstrating hemoglobin S.
B. A high titer of IgM neutralizing antibody to parvovirus B19.
C. A need for IV immune globulin therapy acutely—and perhaps chronically—to control his anemia.
D. A CD4+ cell count in excess of 400/µL.

(Answer on next page)

CORRECT ANSWER: C
This patient has HIV infection. His history of “wasting” and intravenous drug abuse and his profound lymphopenia are clues to the diagnosis, which was confirmed by serological testing. He also has an acute, severe anemia now out of proportion to his other blood cell counts. One likely cause of the anemia is acute red cell aplasia resulting from parvovirus B19 infection. Parvovirus B19 infection is common in humans. Most persons experience the infection at some point in their life (the most common manifestation is erythema infectiosum, or fifth disease, a childhood exanthem that usually manifests as fever and the characteristic “slapped cheek” rash1,2). Immunocompetent persons mount an antibody response, initially with IgM and then with IgG, which confers protection against reinfection. By age 15 years, most adolescents demonstrate specific parvovirus B19 antibodies.1

Parvovirus B19 infection in patients with advanced HIV infection. However, in patients who
are immunodeficient (for any of a number of reasons), the antibody response to parvovirus B19 infection does not occur, and reinfection and chronic infection become possibilities. When the infection becomes chronic, the patient remains viremic, and the virus is thus free to infect one of its most favored host cells, the erythroblast. This causes depletion of erythroid precursors in the marrow; profound reticulocytopenia; and severe, unremitting anemia.

Currently, this occurs most commonly in patients with advanced HIV infection, in whom there is not only T-cell depletion but also derangement of B-cell immunity. HIV-infected patients in whom infection with parvovirus B19 has produced severe anemia almost always have severe immunodeficiency, which correlates with very low CD4+ cell counts. Thus, choice D is incorrect.

**Other settings in which parvovirus B19 infection causes severe anemia.** Patients with chronic severe hemolytic anemias, such as sickle cell disease or hereditary spherocytosis, can also experience acute episodes of severe anemia when infected with parvovirus B19. However, the aplastic crises in these patients are usually transient—5 to 7 days—and resolve with the formation of the neutralizing antibody. In addition, patients with sickle cell variants or spherocytosis uniformly have smear findings that were absent in this patient. Thus, hemoglobin electrophoresis would not demonstrate hemoglobin S, making choice A incorrect.

**Confirmation of parvovirus B19 infection.** Bone marrow aspiration in patients such as this man will reveal the paucity of erythroid precursors; however, it is rarely needed. Currently, diagnosis in patients with suspected persistent infection involves polymerase chain reaction testing for parvovirus B19 DNA. IgM assays are useful in the setting of acute childhood fifth disease, but tests for both IgM and IgG antibodies to parvovirus B19 demonstrate too much individual variation in adult patients and have been replaced by parvovirus B19 DNA amplification studies. Thus, choice B is not correct.

**Treatment.** Therapy for pure red cell aplasia caused by underlying persistent parvovirus B19 infection involves both acute and chronic interventions. The acute administration of preformed antibodies in the form of immune globulin—usually IV immune globulin, 0.4 g/kg for 5 days—results in a rapid decrease in viral DNA hybridization followed by reticulocytosis and a rise in the hemoglobin level. Of course, urgent transfusions of packed red blood cells (RBCs) may be needed pending this response. In addition, highly active antiretroviral therapy (HAART) can reverse the immune deficiency in patients with HIV infection, enabling the endogenous immune response to control the disease. If HIV control and an endogenous immune response are not attained, ongoing intravenous immune globulin therapy on a monthly basis is required. Thus, choice C is correct.

**Outcome of this case.** Because this patient had profound, symptomatic anemia, he was immediately given packed RBCs. His hemoglobin level rose to 7.0 g/dL and his symptoms abated. Reticulocytes were 0.1% of erythrocytes, and DNA studies were positive for parvovirus B19 infection, confirming the diagnosis. Records were obtained from his health clinic visit; these confirmed that he was HIV-positive and showed that he had a CD4+ cell count of 92/μL at the time of testing. Intravenous immune globulin was administered in the hospital, and 4 weeks after discharge, his hemoglobin level had risen to 10 g/dL. HAART was also initiated.

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