CLINICAL VIGNETTE

Fever and Hemolytic Anemia in a 51-year-old Man Returning from New England

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Case Report

The patient is a 51–year-old male previously in good health with no chronic medical conditions, who presents with two-week history of daily fevers and night sweats. The patient reports some shortness of breath, decreased appetite, and a 16-pound weight loss over the past two weeks. Three days prior to admission to the hospital, he was seen by his primary care physician, and was febrile with temperature of 38.4 °C with an otherwise unremarkable physical examination. Laboratory tests included a normal complete blood count (CBC), white blood cell (WBC) count 6.61 x 10E3/ul, hemoglobin of 13.2 g/dl and hematocrit of 39.3%. The patient had no history of recent international travel but had recently traveled to Connecticut. On admission the patient was afebrile. His physical examination did not reveal any abnormalities. His hemoglobin dropped over the first few days of his hospitalization without any obvious source of blood loss. The hemoglobin level decreased from 11.6 g/dl on the day of admission to 9.0 g/dl and 7.3 g/dl on the third and fifth hospital day, respectively. Blood, urine and stool cultures were negative. Computed tomography (CT) scan of abdomen, pelvis and chest with and without contrast were normal. An ultrasound of abdomen showed mild hepatomegaly and splenomegaly.

The patient continued to have mild fever up to 38.2 for few days after hospitalization. His anemia evaluation included a haptoglobin of less than 8 mg/dl; ferritin of 4357 ng/ml; and LDH of 1009 U/L: serum iron 55; and iron saturation 27%. His total bilirubin was 1.8 mg/dl and conjugated bilirubin of 0.9 mg/dl. Red blood cell morphology showed spherocytosis and stomatocytosis and no evidence for red blood cell fragmentation. The patient's direct and indirect Coombs tests were negative. The patient underwent bone marrow biopsy that showed only a mildly hypercellular marrow. Laboratory evaluation was negative for paroxysmal nocturnal hemoglobinuria. No organisms were seen on peripheral blood smear. The laboratory tests for cytomegalovirus, Epstein Barr virus, Lyme disease, and parvovirus infection were negative. Given the laboratory findings that were consistent with non-immune hemolytic anemia and the patient's recent travel to Connecticut, a diagnosis of babesiosis was considered. Thin blood smears were sent for intraerythrocytic parasites, which came back negative.

The patient's fever resolved spontaneously early in the hospitalization. His hemoglobin began to rise without transfusion. Because of high suspicion for babesiosis, a polymerase chain reaction (PCR) test for babesiosis was sent and later returned positive for babesiosis.

Discussion

Human Babesiosis is an intraerythrocytic infection caused by protozoa of the genus Babesia that invade and lyse red blood cells. The disease is mainly acquired via tick bite. Human Babesiosis can also be transmitted through blood transfusion. Most of the cases have been reported in the United States and

Europe. Babesiosis is endemic in northeastern states and upper Midwestern states of the United States. The disease is also sporadically seen in other parts of the world.

Babesia microti is the predominant species causing human babesiosis in the northeastern and midwestern regions of the United States. It is transmitted by hard-bodied tick Ixodes scapularis (I. dammini). Babesia divergens , a pathogen of cattle, is regarded as the main species causing the disease in Europe[1]. White –tailed Deer and white-footed mice are the reservoirs for Babesia microti. Deer are the incompetent reservoir and mice are the main reservoir for B. microti[1].

The clinical manifestations of the disease are widely variable and can range from no symptoms to death. The severity of infection depends on the Babesia species and the immune status of the host. Immune suppression, coinfection with HIV and Borrelia burgdorferi (i.e., those with Lyme disease), splenectomy and age over 50 years are considered risk factors for developing severe illness[2].

Asymptomatic infection or self-limiting flu-like illness occurs in 25% of adults and 50% of children. The most common manifestations are fever, fatigue, malaise, shaking chills, sweats, myalgias, and arthralgias. Fever is the salient feature on physical examination. Mild splenomegaly and hepatomegaly may be noted. Jaundice is rare. Severe infection may present with clinical manifestations of adult respiratory distress syndrome, renal failure, severe anemia, disseminated intravascular coagulation, congestive heart failure and acute myocardial infarction[3].

Diagnosis of babesiosis is made by evaluation of blood smears, looking for the parasite, serology, and polymerase chain reaction (PCR). Wright or Giemsa stained thin blood smears are used for definitive diagnosis of the disease. Multiple organisms can infect red blood cell sand can result in a characteristic maltese cross appearance due to the occasional arrangement of parasites in tetrads. PCR-based techniques are more sensitive and reliable than blood smear examination, especially in the setting of low parasitemia[4].

Treatment for babesiosis is based on two major antimicrobial regimens. The preferred regimen of atovaoquon plus azithromycin is better tolerated. Quinine plus clindomycin is an alternative treatment. Both regimens are used for 7 to 10 days.

Patients with identified risk factors should be hospitalized. Patients with severe babesiosis are at risk of multiorgan failure[5]. Resistant cases of Babesia Microti to azithromycin plus atovaquone in immunocompromised patients have been reported[6]. Optimal therapy for immunocompromised patients with babesiosis is not clear and require further research. Reducing the level of immunosuppression when possible is recommended in the immunocompromised patients.

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Submitted on February 3, 2011