Serodiagnosis of Visceral Leishmaniasis in an American Peace Corps Volunteer

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A case of visceral leishmaniasis in a young American Peace Corps volunteer is reported. Both clinical and epidemiologic evidence strongly supported the diagnosis; however, hepatic and splenic aspirates for the causative organism were negative. The diagnosis was eventually confirmed through serology, employing indirect immunofluorescence and complement fixation testing of serum. The patient clinically responded dramatically to sodium stibogluconate, the drug of choice for the treatment of visceral leishmaniasis. This case is significant because it alerts the physician to an unusual cause of fever of unknown origin in residents of the Western nations and demonstrates the potential usefulness of serology in diagnosing visceral leishmaniasis when the infecting organism cannot be isolated.

Visceral leishmaniasis (kala-azar), caused by the protozoan Leishmania donovani, is a predominantly Third World and tropical disease. Thus, travel history is important in making the proper diagnosis in residents of the United States. The definitive diagnosis is traditionally established by isolation of the amastigote form of L. donovani from aspiration of the liver, spleen, or bone marrow (3, 11). However, when these are negative but clinical and epidemiologic history strongly suggests leishmaniasis, serologic evaluation with indirect immunofluorescence (IF) and complement fixation (CF) testing may aid in reaching the correct diagnosis.

Case report. The patient, a 28-year-old female from Nebraska, had been working as a microbiologist for the Peace Corps in Niger, Africa, for approximately 17 months when she was involuntarily in a motorcycle accident. She sustained a mild concussion with residual headaches, nausea, vomiting, and fever over the next month. She later recalled the presence of a swarm of small flies around her at the time of the accident. The Peace Corps transferred her back to Washington, D.C., for hospitalization and evaluation. When liver and bone marrow biopsies revealed small compact noncaseating granulomas, she was given a preliminary diagnosis of pulmonary tuberculosis, although acid-fast staining was negative. A chest X ray also showed possible granulomatous disease. A purified protein derivative skin test and control were reported negative. Routine blood cultures and serologic studies for infection were negative. The patient was placed on multiple drug therapy consisting of rifampin, isoniazid, and ethambutol, as well as chloroquine for presumptive malaria. She returned to Nebraska somewhat improved. When cultures of liver and bone marrow biopsies proved negative for acid-fast bacilli and fungi, her medications were discontinued. A review of her Washington, D.C., hospital records revealed mildly elevated liver enzymes, including alkaline phosphatase, lactic dehydrogenase, serum glutamic oxalacetic transaminase (SGOT), and diffusely elevated gamma globulin (pooled immunoglobulin). Her hemoglobin remained barely above 10 g/dl. Other tests reported as normal included computerized axial tomography scans of the head, liver, and spleen and a liver-spleen scan.

Approximately 3 months after the medications were discontinued, the patient’s fever, maximum (100 to 101°F [37.8 to 38.3°C] oral) at midday, and general malaise returned. Her headaches were less frequent and less severe. She complained of intermittent mild discomfort over the liver and spleen areas. Her medical history revealed urinary tract infections before her stay in Africa and a brief episode of amebiasis in Niger that responded to metronidazole. The family history was negative.

Physical examination now revealed a lethargic, afebrile female with mild tenderness over the liver and spleen areas. A grade II/VI late systolic ejection murmur could be heard along the left sternal border. The liver and spleen were slightly enlarged. There were no other pertinent physical findings. Laboratory studies revealed a persisting slight elevation of liver enzymes (lactic dehydrogenase, 124 [40 to 110 IU/liter], SGOT, 45 [6 to 25 IU/liter], alkaline phosphatase, 266 [23 to 71 IU/liter]) and gamma globulin (1.42 g/dl, 19.7% [0.53 to 1.37 g/dl; 18.2%]). Blood cultures for bacteria and fungi were negative. A leukocyte count was 3,200, with 61% segmented forms, 17% bands, and 6% eosinophils. Hemoglobin was 10.8 g/dl, and the Westergren sedimentation rate was 19 mm/h. Stool specimens revealed occasional Entamoeba cysts and no other pathogens. A purified protein derivative skin test (5 tuberculin U) was negative for tuberculosis with a positive mumps control. A bone scan was negative, and an indium scan revealed mild hepatosplenomegaly. An echocardiogram demonstrated wild pansystolic mitral valve prolapse but no leaflet vegetations. Serology for Epstein-Barr virus (viral capsid antigen-immunoglobulin G), cytomegalovirus, toxoplasmosis, and histoplasmosis, as well as hepatitis panel, anti-nuclear antibody panel, rheumatoid factors, and rectal biopsy for schistosomiasis, all were reported as negative. Smears for filariasis and malaria were negative. Blood samples also were sent to the Centers for Disease Control, Atlanta, Ga. CF, as well as an IF test with promastigotes of L. donovani (Khartoum strain), was used in accordance with the method initially described by Kagan (10). Titers of 1:32 (CF) and 1:256 (IF) were reported by the Centers for Disease Control. Liver and spleen aspirates failed to reveal or grow any organisms.

Following a World Health Organization protocol, antimony sodium gluconate (Pentostam), the drug of choice, was
obtained from the Centers for Disease Control and administered intravenously at 20 mg/kg (body weight) per day (to a maximum of 850 mg/day) on an outpatient basis for 2 weeks (12). The patient experienced no side effects from the drug and made an uneventful recovery. Follow-up serology 4 months after the completion of drug therapy revealed negative CF titers but a persisting elevation in IIF titers (1:256).

Discussion. Visceral leishmaniasis (kala-azar) is a tropical disease with distribution worldwide, but especially in Asia, Africa, and certain Mediterranean areas. It is an infection infrequently seen in Western nations. Mahmoud and Warren suggested that visceral leishmaniasis be suspected when an individual has been to an endemic area and presents with fever, hepatosplenomegaly, anemia, leukopenia, and hypergammaglobulinemia (9). Although the definitive diagnosis traditionally is made by isolation of the organism from liver, spleen, or bone marrow aspirations, several studies indicate IIF testing is both sensitive and specific in diagnosing visceral leishmaniasis despite negative aspirates (4, 5, 8). CF titers, although typically lower, also have good specificity (7). Serology, therefore, may be particularly helpful when a sufficient amount of aspirate is difficult to obtain, when a low level of infection precludes the isolation of adequate numbers of the organism, or when the diagnostic stage is missing. This approach is also more convenient for the patient. Cross reaction between leishmaniasis and other infectious diseases, such as tuberculosis, typhus, malaria, Chagas’ disease, and schistosomiasis, has been described; however, the leishmaniasis antibody levels are typically much higher, as demonstrated with this patient (4). Titers of ≥1:16 (IIF) or ≥1:8 (CF) are considered significant and may remain positive for years (1, 7). The diagnosis may be further supported on clinical grounds. Thus, elevated IIF and CF titers with positive clinical and epidemiologic history probably are indications for treatment with antimony compounds now believed to be relatively safe (2). Rifampin, which this patient received initially with clinical improvement, has been reported effective against cutaneous leishmaniasis; however, its efficacy against the visceral form of the disease has yet to be determined (6).

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LITERATURE CITED