Case Report: Cutaneous Leishmaniasis with Boggy Induration and Simultaneous Mucosal Disease

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Abstract. A woman had cutaneous, mucosal, and possible visceral leishmaniasis simultaneously. Many of her cutaneous lesions consisted of boggy inductions rather than customary papules, nodules, or ulcers. This unusual case was finally cured after four courses of miltefosine, one course of antimony, and two courses of Ambisome.

INTRODUCTION

The leishmaniases are of increasing interest to the population of the United States in this age of widespread travel. Leishmaniasis is spread from an animal host to humans, and sometimes from human to human, by the bite of the sand fly vector. Once in the skin, some species localize to the visceral reticuloendothelial system and some species remain in the skin. Classic visceral leishmaniasis is characterized by hepatosplenomegaly, pancytopenia, and fever. Classic cutaneous leishmaniasis is characterized by 1–5 skin ulcers, or nodules, papules, or erythematous plaques less frequently. Th1 immunity is present in such cases, but treatment is instituted to speed spontaneous cure. Metastasis of organisms from the skin to the mucous membranes of the nose, mouth, and larynx (mucosal leishmaniasis) rarely occurs. Mucosal leishmaniasis, which can lead to destruction of cartilaginous structures and does not self-cure, is difficult to treat.1

In recent years, exceptions to these classic forms of the diseases have been reported. Mild visceral disease (low-grade fever, asthenia, and moderate hepatomegaly) without cutaneous involvement was caused by a cutaneous species in Iraq.2 Disseminated polymorphic cutaneous disease (10–300 cutaneous lesions that are a mixture of aceniform, papular, nodular, and ulcerated types) often with concomitant mucosal involvement was observed in northeastern Brazil.3 Erysiploid cutaneous disease was recently the subject of a case report.4 We report a patient with an unusual case of cutaneous leishmaniasis. Symptoms included cutaneous lesions that were boggy inductions as well as papules, and ulcers; mucosal disease; and systemic involvement in the sense of asthenia and hepatocellular abnormalities.

CASE REPORT

The patient was a 63-year-old woman (weight = 140 lbs) who traveled to Bolivia in September 2006 to take digital images of indigenous plants. She was in Madidi National Park (Chalalan reserve) for one week. At the end of the week, she noticed what she thought was a chigger bite on her right arm. Her work then took her to the Oxapampa and Paulli regions of Peru in October 2006, and to Madagascar (Antsiranana Province, Nosy Be, and Antananarivo Province) in November 2006. In Madagascar, she had a sore throat and a decreased energy level, and noticed a small lesion in her right ear.

By the end of December 2006, cutaneous lesions had appeared on her forehead, right wrist, left arm, chest, abdomen, and back. The lesions on her wrist and arm consisted of large boggy swellings with and without central ulcerations. She had painful crusts in her right ear, and throat pain that limited swallowing. In addition, she had low-grade fevers and chills. At this point, the patient was taking 2,000–2,500 mg of aspirin per day for the throat pain.

In early January 2007, she was referred to a dermatology unit. Biopsy specimens of the original “chigger bite” lesion on her right arm, a back lesion, and the right wrist lesion were sent to the local dermatopathology laboratory, where Leishmania were visualized, and then to the Centers for Disease Control and Prevention (Atlanta, GA). Leishmania organisms were visualized by staining with Giemsa in all biopsy specimens, and Leishmania braziliensis was cultured from one specimen and identified by isoenzyme electrophoresis. Flexible laryngoscopy on January 19, 2007, showed an erythematous crusty nasal cavity with hypopharynx findings of intense erythema with boggy mucosa and scattered petechia. Laboratory tests showed a hemocrit of 40% and a leukocyte count of 5,800 cells/mm³ (neutrophils = 69%). Results of liver function tests were abnormal (aspartate aminotransferase [AST] = 108 U/L, alanine aminotransferase [ALT] = 169 U/L), and results of a test for HIV were negative.

By February 2007, the cutaneous lesions continued to appear and spread. Particularly notable lesions were 1) a crusty exudative lesion covering approximately two-thirds of the interior of the right ear (Figure 1A) accompanied by a prominent cervical lymph node, 2) a swollen nodule (approximately 2 cm in diameter) on the left elbow, 3) four ulcers surrounded by boggy swellings on the left wrist, 4) a large boggy swelling plus several ulcers on the right wrist (Figure 1B), 5) many small ulcers on the back, and 6) many ulcers on the left leg and the right leg (Figure 1C). Throat pain had increased such that even saliva was hard to swallow. Although the patient had no difficulty in breathing, she was coughing up bloody exudates, and her weight had decreased to 130 lbs. Chills had increased and she was almost prostrate with no energy.

The puzzling symptoms and signs created diagnostic and therapeutic issues. Immunologically intact patients with cutaneous and mucosal leishmaniasis do not have liver dysfunction, and it was thought that the hepatocellular abnormalities were caused by a second disease, although hepatitis B and C titers were negative, as was the result of abdominal ultrasonography.
The standard treatment for leishmaniases, pentavalent antimony (used under an investigational new drug application in the United States), frequently causes hepatocellular dysfunction and might exacerbate the unknown hepatic process. The patient was treated with a new drug (miltefosine) because it rarely causes hepatocellular dysfunction, is orally administered (antimony is administered by injection), and was recently shown to be effective for mucosal leishmaniasis in Bolivia. Treatment with miltefosine was initiated on February 8, 2007, at the standard dose of 2.5 mg/kg/day, three times a day, with meals for 28 days. Other than vomiting when oxycodone was coadministered for throat and ear pain, miltefosine was well tolerated with side effects limited to nausea 30–120 minutes after each dose. After a gastroenterology consultation, the patient stopped taking aspirin because the high doses she was using may have caused or contributed to her hepatitis.

Two weeks after beginning treatment with miltefosine and stopping treatment with aspirin, liver function test results had improved (AST = 96 U/L, ALT = 140 U/L). By the end of the 28-day treatment period, liver function test results had essentially normalized (AST = 48 U/L, ALT = 40 U/L). Because the cutaneous lesions had improved somewhat but had not resolved completely, three additional courses of miltefosine (2.5 mg/kg/day for 28 days) were administered until June 2007. By April–June 2007, the ear lesion had only a small amount of ulcer and discharge (Figure 2A). The boggy lesions on the arm had improved considerably (Figure 2B), as had many of the leg lesions (Figure 2C). However, new papules and ulcers had appeared on the legs during therapy with miltefosine. There was mild pain with swallowing but no exudate. The patient’s energy level improved and chills were absent, although her weight had decreased to 112 lbs.
To deal with the continued throat pain and the leg lesions, therapy was switched to pentavalent antimony (Pentostam, 20 mg of Sb/kg/day for 28 days given intravenously) beginning in June 2007, but no improvement in symptoms or signs was evident by the end of therapy in July 2007, by which time her weight had decreased to 108 lbs. Therapy was then switched to Ambisome (5 mg/kg/day for 5 days given intravenously) in the middle of July 2007. The remaining symptoms and signs responded quickly. Throat pain disappeared, and lesions on the arms and legs became flat and erythematous. An ulcer surrounded by several papules appeared on the buttocks, however, and a second course of Ambisome was administered in the last weeks of July 2007. The ulcer resolved, and a biopsy specimen of one of the papules showed that this lesion was herpetic. By November 2007, all lesions had scarred, the patient’s weight had increased to 122 lbs, and her energy level had increased.

DISCUSSION

An apparently immunologically intact patient had cutaneous, mucosal, and possibly visceral leishmaniasis. We are unable to find a reference in the Leishmania literature to the boggy swellings that characterized many of the arm lesions. Her visceral involvement (elevated levels of liver enzymes) was caused by either leishmaniasis because it rapidly responded to treatment with miltefosine or by the high doses of aspirin, which were discontinued as treatment with miltefosine was started.

Despite substantial improvement in her upper extremity lesions, throat symptoms, ear disease, and elevated levels of liver enzymes, by the end of four courses of miltefosine, some throat symptoms and extremity lesions remained and new leg lesions had appeared. Although she received 280 mg of miltefosine/kg of body weight, probably more than any other U.S. citizen to date, the drug was well tolerated with only minor gastrointestinal difficulties. One course of antimony was then given with no discernable improvement in the short period of 28 days during which it was administered. Complete cure was then rapidly accomplished by two 20-mg/kg courses of Ambisome.

The boggy characteristics of some of her lesions, symptoms in multiple organs, and the slow overall response to a drug to which some of her lesions were susceptible suggests that the patient has a specific immunologic defect in her ability to control infection with Leishmania. We did not have the opportunity to investigate this hypothesis by evaluating the interaction of the parasite with her immune cells in vitro.

As travel continues to facilitate contact of a wide variety of human hosts with parasitic microorganisms, both classic and unusual presentations such as this one are likely to be seen more frequently for leishmaniasis.

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