Case Report: Co-Infection of Leishmania (Viannia) braziliensis and HIV: Report of a Case of Mucosal Leishmaniasis in Cochabamba, Bolivia

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Abstract. We describe the first case of Leishmania/HIV co-infection reported in Bolivia. Initially hospitalized with a diagnosis of pneumonia and bronchitis, the patient had numerous cutaneous and mucosal lesions caused by Leishmania (Viannia) braziliensis. The patient was also diagnosed as severely immunocompromised because of HIV infection.

INTRODUCTION

The leishmaniases are a group of protozoan diseases transmitted to mammals including humans by phlebotomine sand flies. They are characterized by a spectrum of clinical manifestations: disseminated visceral infection (visceral leishmaniasis [VL]), including ulcerative visceral infection (visceral leishmaniasis [VL]); localized cutaneous leishmaniasis (LCL); multiple non-ulcerative nodules (i.e., diffuse cutaneous leishmaniasis [DCL]); and destructive mucosal inflammation (i.e., mucosal leishmaniasis [ML]). The latter is also referred to as mucocutaneous leishmaniasis (MCL) as commonly coinciding with LCL or DCL. Globally, ~350 million people are thought to be at risk of infection and disease. It is estimated that an annual 1.5–2 million new leishmaniasis cases occur, and 70,000 deaths are attributable to the disease.

In Bolivia, the leishmaniases are endemic in seven of nine of the country’s departments; the two departments without notified cases are Oruro and Potosí, largely because their high average altitude limits the geographic habitat of sand fly vectors. The country probably has the highest incidence of LCL and ML in Latin America, with 31,095 cases of LCL and 4,619 cases of ML in the last 24 years (1983–2006). Of all countries in Latin America, Bolivia also reports the greatest LCL:ML case ratio, with national case notification data for 2006 showing a ratio of six LCL cases for every ML case. In contrast, during the 1983–2006 time period, only 10 and 4 cases of VL and DCL were reported, respectively. All VL cases were reported from the Yungas region (i.e., La Paz department); DCL cases were reported from Beni and La Paz departments. The increase in LCL and ML cases in Bolivia is mirrored by the increasing number of LCL and ML patients with a travel history to Bolivia attending travel medicine clinics in non-endemic countries (e.g., of 79 LCL and 6 ML patients seen between 1995 and 2003 at the Hospital of Tropical Diseases, London, UK, 7 and 3 were from Bolivia, respectively).

From 1984 to 2006, the total number of HIV/AIDS cases reported in Bolivia rose to 2,190. HIV/AIDS diagnosis is often delayed, with ~50% of cases having AIDS at the time of diagnosis. The HIV/AIDS epidemic in Bolivia is concentrated, with prevalence rates >5% among the at-risk population, primarily men who have sex with men. Under-reporting is estimated to be >70% country-wide, and The Joint United Nations Program on HIV/AIDS (UNAIDS) estimated that, in 2006, 8,100 people were living with HIV/AIDS in Bolivia.

Over the past 20 years, leishmaniases have increasingly been recognized as an opportunistic infection in HIV-infected patients, with Leishmania–HIV co-infection common in areas where both diseases are endemic. In contrast to VL, only scarce data are available on LCL in HIV-infected patients in the Americas, with isolated case reports available from Argentina, Brazil, Colombia, French Guyana, Peru, and Venezuela. Literature on ML in HIV-infected patients is even rarer, with only a dozen or so of cases reported in Argentina, Brazil, French Guyana, and Peru.

We describe an ML patient attending the Hospital of Viedma Hospital in Cochabamba, Bolivia, who on further examination, was found to be infected with HIV; the patient was started on amphotericin B therapy, responded well, but was lost to follow-up.

CASE REPORT

In June 2006, a 32-year-old male road and market worker from Cochabamba, Bolivia, presented himself to the hospital with a 1-week history of respiratory difficulties, characterized by a cough, productive of mainly clear but occasionally bloody sputum, sore throat, dysphagia, and dysphonia. Chest examination showed decreased breath sounds on both sides and sporadic and disseminated crepitations in the left lung. No fever or weight loss (body weight, 43 kg) was reported. The patient was hospitalized with a diagnosis of pneumonia and bronchitis.

Physical examination showed that the patient had numerous maculo-papulo-nodular lesions on the face, eyebrows, and left ear lobe, as well as ulcerative and crusted lesions on the nose (Figure 1A). There were ulcerative lesions on the lower and upper lip as well as the tongue; the uvula had been completely eroded, and a pussy oropharyngeal discharge was noted (Figure 1B). Another lesion was noted on the hand, with well-delineated borders. Further maculo-papulo-nodular lesions were noted on the patient’s left and right legs and feet (Figure 1C, D), filled with yellow exudate, which the patient attributed to carrying heavy work equipment, as well as to a road accident in which a car had driven over both his feet.

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The patient also reported having gone to work for 3 months in Chimoré (a town located in the low-lying Chapare region) a month before hospitalization, where he had entered the forest for coca cultivation.

A chest x-ray showed right parahilar infiltration. Blood tests showed a hemoglobin of 10 g/dL (13.5–17.2 g/dL); a white blood cell count of 4 × 10^9/L (4–11 × 10^9/L) (neutrophils 77% [40–75%]; lymphocytes 15% [20–45%]; monocytes 7% [2–10%]; and eosinophils 1% [1–6%]); and an erythrocyte sedimentation rate (ESR) of 64 mm/h.

Direct examination of stool samples for parasites showed Entamoeba histolytica cysts, Hymenolepis nana (tapeworm), and Trichuris trichura eggs. Sputum cultures for bacteria and acid fast bacilli were negative, as was the serology for hepatitis B, toxoplasmosis, and Chagas disease. The rapid test, ELISA, and Western blot for HIV were positive, with CD4 and CD8 cell counts of 67/μL and 384/μL, respectively.

Histologic examination of scrapings from lesions on the face, palate, and left foot showed inflammatory infiltrates characterized by leukocytes, neutrophils, and lymphocytes, with large numbers of macrophages infected with a variable number of Leishmania spp. amastigotes. Leishmania etiology was confirmed through GIEMSA-stained slides of scrapings from lesions on the hand and left foot showing numerous intracellular and extracellular amastigotes, as well as through positive parasite culture of lesion aspirates in NNN media according to the guidelines of the National Reference Laboratory for Leishmaniasis. Leishmania DNA was extracted from the parasite culture with DNAZol (Invitrogen, Merelbeke, Belgium) according to the manufacturer’s instructions and amplified using a polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) protocol using primers targeting the hsp70 gene and HaeIII endonuclease for cleavage of amplification products. PCR-RFLP identified L. (Viannia) braziliensis in all samples tested.

Although the patient refused anti-retroviral therapy, he was given primary prophylaxis (with cotrimoxazole) against Pneumocystis carinii pneumonia. Metronidazol (750 mg orally, three times daily for 10 days) and albendazole (400 mg orally, single dose) were given for the intestinal parasites; iron supplements were given for the underlying anemia. Intravenous amphotericin B therapy (50 mg every 48 hours) was started. Although the cumulative dose of amphotericin B had reached 2,000 mg within 80 days, the evolution of the ulcerative lesions was stationary, with active lesions persisting in the face, lower and upper limbs, and the palate; only the lesion on the lower lip and tongue showed signs of re-epithelialization. Systematic weekly analysis of liver and kidney function was carried during the treatment and showed no remarkable alteration.

Approximately 3 months after hospitalization, the patient discharged himself, so that further follow-up could not be made.

**DISCUSSION**

The leishmaniases are characterized by a spectrum of clinical pathologies. More than 15 Leishmania spp. are known to cause VL or CL in humans. Diagnosis and treatment of the leishmaniases is difficult because of a number of differential diagnoses (e.g., leprosy, skin cancers, tuberculosis, cutaneous mycoses) and the limited number of available therapeutic approaches, respectively. ML is a progressive disease that can be disfiguring and life threatening. In most endemic areas,
1–10% of LCL infections result in ML, 1–5 years after LCL has healed; however, reports do exist for which ML presented at the same time as LCL or for which 25% of LCL resulted in ML. Risk factors for ML include *L. (V) braziliensis* infection, male sex, genetic predisposition, and immunosuppression. ML never heals spontaneously, is very difficult to treat, with secondary bacterial infections common, and is potentially fatal.2

Co-infection with HIV results in even more atypical clinical pathology (e.g., *Leishmania* spp. that are thought to be dermatropic may cause VL and *vice versa*), with LCL symptoms tending to be more severe and LCL lesions taking longer to resolve (especially in those HIV patients with low CD4+ T-cell counts).4 Although the first-line treatment of the leishmaniasis, including LCL and ML, is pentavalent antimonials at a dose of 20 mg/kg administered daily for 20–28 days,2 no established therapeutic protocol exists for *Leishmania*-HIV co-infections.8 The treatment of co-infected patients is confounded by the dearth of formalized clinical data. Thus, compared with immunocompetent patients, treatment response of *Leishmania*-HIV infections to antimonials tends to be poor (e.g., whereas efficacy of antimonials is > 85% in immunocompetent CL patients, it is 33–82% in HIV-infected individuals),9,10 with high rates of relapse (14–57% of patients)4 and mortality reported. Amphotericin B has been used for the treatment of co-infected patients; although initial cure rates are moderate to good at 58–82%,9 patients often relapse and suffer from renal toxicity (in up to 35% of cases).4 Lipid amphotericin B formulations (e.g., AmBisome, Gilead Sciences, Inc., Foster City, CA) have a better safety profile than amphotericin B and have proven to be effective for the treatment of *Leishmania* (VL)–HIV co-infections, with cure rates reportedly between 33% and 100% depending on the lipid amphotericin B formulation; nonetheless, relapse rates are high (38–100% of patients).8 Recently, miltefosine has been used in treating co-infected patients. Although the initial treatment response is good, with cure rates between 64% and 89% and low mortality, relapse rates are comparable to other treatment approaches (31–88%).8

Here we report the first case of *Leishmania*/HIV co-infection in Bolivia. The patient was anemic, with a raised ESR and signs of a chest infection, as well as intestinal parasites. In addition, he was severely immunocompromized by HIV infection. Of note is the rapid evolution within 3 months from LCL in both to a disseminated pathology, with multiple ulcerative lesions in both the face and upper and lower limbs, a pathology already observed in other co-infection cases reported in Latin America.10–17 Additionally, the patient presented with ML, characterized by several lesions on the lips, palate, pharynx, larynx, and bronchia, which probably caused the severe dysphonia, dysphagia, and hyper-secretion. The patient reported to have gone to work in an area (i.e., Chapare) known to be endemic for LCL and ML.16 Treatment with amphotericin B did not result in clinical cure of lesions, and it is likely that the poor treatment response was compounded by the severe immunosuppression of the patient.

Given that Bolivia has the highest incidence of LCL and ML in the Americas,4 as well as having an increasing number of reported HIV cases,5 further studies should be made to estimate the burden of *Leishmania*/HIV co-infection in the country. Certainly, in-country case management guidelines should be updated to include a section on diagnosis and treatment of *Leishmania*/HIV co-infections.

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