Case Report: Reactivation of Mucosal and Cutaneous Leishmaniasis in a Renal Transplanted Patient

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Abstract. Mucosal leishmaniasis (ML) is a chronic form of tegumentary leishmaniasis, which causes destructive lesions of nasal, pharyngeal, and laryngeal mucosa. We describe a case of leishmaniasis reactivation with simultaneous cutaneous and mucosal forms in a renal transplanted patient with no history of prior leishmaniasis. Reactivation after renal transplantation was not reported in Brazil. A 67-year-old woman receiving prednisone 20 mg/day, tacrolimus 1 mg/day, and mycophenolic acid 360 mg/day presented with nose edema with erythema and cutaneous lesions. Amastigotes were identified on biopsies and the polymerase chain reaction confirmed *Leishmania (Viannia) braziliensis*. The patient was treated with liposomal amphotericin B but died 3 weeks after as a result of bacterial septic shock. In conclusion, tegumentary leishmaniasis can reactivate with simultaneous cutaneous and mucosal forms in a renal transplanted patient during the immunosuppressant therapy.

INTRODUCTION

The World Health Organization (WHO) has stated that leishmaniasis is one of the most neglected diseases. New world leishmaniasis (NWL) is an important endemic cutaneous disease in Latin America and, in Brazil, NWL is characterized by two clinical forms: the cutaneous and mucosal forms, whose principal agents are *Leishmania (Viannia) braziliensis*, *Leishmania (Viannia) guyanensis*, and *Leishmania (Leishmania) amazonensis*.¹

The protozoan can persist alive in the scar of previous lesions for years, sustained by a persistent Th1 pattern of local immune response even after treatment.^{2,3} In patients submitted to immunosuppression, this immune response is disrupted, given a chance to the parasite escape, increasing the possibility to reactivation of the diseases. In NWL, the reactivation can occur in the visceral form of the disease, and occasionally in the cutaneous form⁴; the mucosal reactivation is rare caused by a hyperimmune pattern of this form of the disease. In a recent review of 1,754 renal and liver transplants from Brazil, only five cases of the visceral form were reported.⁵

We report a case of NWL reactivation in the mucosal and cutaneous forms concomitantly in a kidney transplanted patient.

CASE REPORT

A 67-year-old woman from Igassu falls (Southwest of Paraná, Brazil) was referred because of edema and erythema on nose and cutaneous lesions for 3 months. She was submitted to a renal transplant 1 year ago and was receiving prednisone 20 mg/day, tacrolimus 1 mg/day, and mycophenolic acid 360 mg/day. Igassu falls is a city localized in an endemic region for NWL, but she was living in the urban area Curitiba (capital of the state and an area free of NWL) before the transplantation and beginning of symptoms. There was no history of travel outside Curitiba after transplantation. There

was no previous history of leishmaniasis or cutaneous lesions with scar. On admission, the patient had edema in the nose, with erythema associated with scaling lesion inside, nasal obstruction, and persistent rhinorrhea. There are two cutaneous lesions pictured in (Figure 1A and B). The cutaneous lesions appeared 2 weeks before admission. A parasinus computed tomography scan was performed to evaluate lesion extension (Figure 1D), which showed complete destruction of nasal septum, mucosal swelling, and sinusitis.

The mucosal and cutaneous lesions were biopsied, showing amastigotes in the tissue. One sample of the biopsied skin was sent for a molecular test and culture. The culture was positive for *Leishmania* spp. and the polymerase chain reaction confirmed *Leishmania (Viannia) braziliensis*. Abdominal ultrasound was normal.

The patient was treated with liposomal amphotericin B 3 mg/kg/day with improvement of lesions after 14 days of therapy. However, unfortunately, 3 weeks after, the patient died as a result of a bacterial septic shock with pneumonia following peripheral infectious thrombophlebitis with purulent drainage.

DISCUSSION

This patient was considered as reactivation of NWL because she was living for 1 year in an area free of leishmaniasis. She might have suffered from a sub-clinical leishmaniasis infection in the past. The patient was admitted only 3 months after initial symptoms. The patient had been treated as sinusitis several times. Despite this clinical history, we cannot exclude a less symptomatic form considering the bone destruction evaluated with a computed tomography scan. A hypothesis of leishmaniasis secondary to donor organ infection was not reported for cutaneous-associated species. The reactivation of leishmaniasis is associated with a decrease of inflammatory cytokines (IFN- γ and TNF- α) and increase of cytokines associated with Th2 immune response (IL-4 and IL-10).² The pathogenicity of mucosal leishmaniasis is dependent of an increase in the inflammatory cytokines, mainly TNF- α ,⁶ which is not compatible with reactivation, despite six reports in the medical literature.⁴ However, this is the first case of simultaneous mucosal and cutaneous leishmaniasis reactivation caused by

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FIGURE 1. (A) Cutaneous reactivation of American tegumentary leishmaniasis in a renal transplanted patient. (B) The cutaneous lesion of the leg is amplified. (C) External aspect of mucosal reactivation of American tegumentary leishmaniasis in a renal transplanted patient. (D) Computed tomography scan showing mucosal swelling with destruction of nasal septum.

L. braziliensis reported after a systematic search using PubMed since 1966 to 2013 and the following terms: “mucosal, mucosa, leishmaniasis, reactivation, transplant, braziliensis.”

The treatment of mucosal and cutaneous forms of NWL is well established,^{7,8} however patients with renal transplantation must use drugs with lower nephrotoxicity to avoid the renal failure.⁹ Considering the current arsenal of treatment, the drug used for this case was a lipid formulation of amphotericin B.¹⁰

These reports call attention to physicians to manage these cases for the possibility of leishmaniasis reactivation in transplanted patients.

The complex interaction between the parasite and the host immune response can produce different clinical manifestations of the disease. The disease is considered the clinical expression of an immunological response of the host to the agent or its antigens.

Even when the lesion has been healed, *Leishmania* establishes chronic intracellular parasitism and can survive the entire life of the infected person. Screening of leishmaniasis is not indicated, although serum tests could indicate previous diseases. Furthermore, a positive test would not indicate any prophylaxis. The clinical control can be best approached in these patients from endemic areas.

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