Case Report: Progressive Perforation of the Nasal Septum due to *Leishmania major*:
A Case of Mucosal Leishmaniasis in a Traveler

Nicole Harrison,1 Julia Walochnik,2 Reinhard Ramsebner,3 Luzia Veletzky,1 Heimo Lagler,1 and Michael Ramharter1,4*

1Division of Infectious Diseases and Tropical Medicine, Department of Medicine I, Medical University of Vienna, Vienna, Austria; 2Institute for Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Vienna, Austria; 3Department for Otorhinolaryngology-Head and Neck Surgery, Medical University of Vienna, Vienna, Austria; 4Institute of Tropical Medicine, University of Tübingen, Tübingen, Germany

Abstract. This report describes a case of mucosal leishmaniasis caused by *Leishmania major* with destructive perforation of the nasal septum illustrating the diagnostic challenges of a rare clinical presentation of *L. major* infection in a traveler. The atypical presentation may have been associated with the use of cortisone as a potential trigger for the progressive destruction of the nasal septum.

INTRODUCTION

Leishmaniasis typically manifests itself as one of three classical disease entities—visceral, cutaneous, and mucocutaneous leishmaniasis. So far about 20 different *Leishmania* species have been identified as human pathogens and are commonly divided into New World and Old World *Leishmania* spp. Mucocutaneous leishmaniasis is usually caused by *Leishmania* spp. of the New World, mainly by representatives of the *Leishmania braziliensis* complex, and less often by representatives of the *Leishmania guyanensis* complex, which are only endemic in South and Central America.

However, new terms are used to describe the different manifestations of leishmaniasis more accurately—mucosal leishmaniasis (ML) refers to an involvement of mucous membranes in the oral cavity or the upper respiratory tract. Several case studies have shown that species of Old World leishmaniasis may also involve mucosal membranes. There are reports about ML caused by *Leishmania donovani*,2 *Leishmania infantum*,3 *Leishmania tropica*, or *Leishmania major*.4–6 So far only few cases of ML caused by *L. major* have been reported. One report described a case of ML of the lips in a young boy from Iran.7 In a small case series from Tunisia, four cases with mucosal involvement of the lips and one with an endonasal manifestations were depicted.6 However, only in one case *L. major* was identified. It appears that ML caused by Old World species is less destructive and often follows a cutaneous facial lesion.

The case that led to this report is one of the first to describe ML caused by *L. major* with destructive perforation of the nasal septum and without prior cutaneous manifestations.

CASE PRESENTATION

A 41-year-old male suffered for 2 years of recurrent but self-limiting epistaxis and noted a first nodular and subsequently ulcerative lesion at the nasal septum. Six months prior to initial presentation symptoms had worsened and the patient had consulted several specialists for otorhinolaryngology. Local and systemic application of cortisone was recommended. The small ulcer of the nasal septum rapidly progressed to a large perforation (about 1.5 cm in diameter), destroying a substantial part of the septum (Figure 1). Based on the suspicion of Wegener's granulomatosis, a biopsy of the nasal septum was performed. Histology revealed unspecific necrosis and inflammation without signs of vasculitis or malignancy.

For further management, the patient referred himself to the outpatient ward for tropical medicine at the Medical University of Vienna. He reported frequent travels to various countries including prolonged stays in South America and Spain. Based on the history and clinical development, several infectious etiologies including atypical mycobacteria, leprosy, syphilis, and mucocutaneous leishmaniasis were considered. Laboratory analysis showed an unremarkable blood count and normal inflammation markers. The interferon-gamma release assay for tuberculosis (Quantiferon-TB Gold, Qidiag, Hilden, Germany) and serology for syphilis (VDRL antigen; Becton, Dickinson and Company, Sparks, MD; Serodia-TPPA; Fujirebio, Tokyo, Japan) were negative. *Leishmania* serology revealed a negative immunochromatographic test (Kalazad Detect, Rapid Test, InBios, Maarn, the Netherlands), but a positive IgG Western Blot (Leishmania Western Blot IgG, LDBIO Diagnostics, Lyon, France). The previously obtained histological specimen was reexamined by polymerase chain reaction (PCR) using a commercial oligochromatographic test for the detection of all *Leishmania* species (Leishmania OligoC-Test, Coris BioConcept, Gembloux, Belgium) yielding a negative result.

For further diagnostic evaluation, a second biopsy of the nasal septum was obtained. In this specimen, intracellular microorganisms compatible with *Leishmania* amastigotes were detected in the histological examination and the commercial PCR assay was positive confirming *Leishmania* infection. Based on the travel history to South America and the destructive mucosal inflammation, a presumptive diagnosis of mucocutaneous leishmaniasis was established and treatment with intravenous liposomal amphotericin B was initiated (cumulative dose of 30 mg/kg body weight). No further progression of disease was noted in follow-up visits over 3 months.

For species identification, a second PCR was performed, targeting the internal transcribed spacer 1 (ITS-1) region with the LITSR/L.5.8S primers8 and including as a negative control PCR mix plus ultra-pure water (Sigma-Aldrich, Vienna, Austria) instead of DNA. The amplicon was sequenced by direct sequencing using the BigDye sequencing kit and an

*Address correspondence to Michael Ramharter, Division of Infectious Diseases and Tropical Medicine, Department of Medicine I, Medical University of Vienna, Waehringer Guertel 18-20, 1090 Vienna, Austria. E-mail: michael.ramharter@meduniwien.ac.at
automatic 310 ABI PRISM sequencer (AB Applied Biosystems, Darmstadt, Germany). Sequences were obtained from both strands and sequence data were processed with the GeneDoc sequence editor to obtain a consensus sequence. Species designation was achieved by multiple alignments with reference sequences of all Leishmania species from the GenBank using ClustaX. Surprisingly, the identified causative agent was not of the L. braziliensis or L. guyanensis complex but rather L. major, an Old World Leishmania species typically causing ulcerative cutaneous lesions. A second multiple alignment including all L. major sequences available at GenBank revealed a 100% identity of our sequence with three other sequences of L. major originating from the Middle East and Central Asia (accession numbers: KJ194178, FN677357, and AY573187). Sequence data obtained in this study were deposited at GenBank and are available under the accession number KX821679.

DISCUSSION

It is unclear why L. major infection presented primarily at the nasal mucosa in an immunocompetent host. Considering the slow progression of the disease, it is plausible that the intact immune system of the host was able to control and confine the infection to the nasal mucosa. The sudden progression of the disease and subsequent perforation of the nasal septum may have been caused by the use of cortisone, which was first applied locally to the nasal mucosa and subsequently administered systemically, suppressing the mucosal immune defense and allowing faster growth and replication of the parasite leading to tissue destruction. The association of leishmaniasis and systemic immunosuppression—caused by systemic conditions like human immunodeficiency virus infection, organ transplantation or hematological disorders—has been well established. However, there are only few case reports describing that systemic corticosteroid treatment may worsen mucocutaneous leishmaniasis or lead to a recurrence of the disease.

This is the first description of ML caused by L. major in a traveler as opposed to patients residing in endemic areas. The place of exposure in this patient was most likely North Africa, where he had traveled to Tunisia, Morocco, and Egypt 2 years before the occurrence of the disease. The treatment with liposomal amphotericin B was initiated based on the assumption that this was a case of mucocutaneous leishmaniasis caused by the L. braziliensis or L. guyanensis complex. Systemic pentavalent antimonials and miltefosine are other potential therapeutic options for Old World leishmaniasis. However, to date, miltefosine has not been evaluated extensively in Old World leishmaniasis and systemic pentavalent antimonials are associated with important safety concerns.

In conclusion, this case report illustrates the diagnostic challenges of a rare clinical presentation of L. major infection as ML in a traveler. The atypical presentation may have been associated with the use of cortisone as a potential trigger for the progressive destruction of the nasal septum.

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Note: Supplemental video appears at www.ajtmh.org.

Consent for publication: The patient has provided written informed consent for publication of this case report.

Authors’ addresses: Nicole Harrison, Luzia Veletzky, and Heimo Ramharter, Division of Infectious Diseases and Tropical Medicine Department of Medicine I, Medical University of Vienna, Vienna, Austria, E-mails: nicole.harrison@meduniwien.ac.at, n1042220@students.meduniwien.ac.at, and heimo.lagler@meduniwien.ac.at. Julia Walochnik, Institute for Specific Prophylaxis and Tropical Medicine, Medical University of Vienna, Vienna, Austria, E-mail: julia.walochnik@meduniwien.ac.at, Reinhard Ramsebner, Department for Otorhinolaryngology-Head and Neck Surgery, Medical University of Vienna, Vienna, Austria, E-mail: reinfried.ramsebner@meduniwien.ac.at. Michael Ramharter, Division of Infectious Diseases and Tropical Medicine Department of Medicine I, Medical University of Vienna, Vienna, Austria, and Institute of Tropical Medicine, University of Tübingen, Tübingen, Germany, E-mail: michael.ramharter@meduniwien.ac.at.

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