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

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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*.4,5 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, Qiagen, 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 (Kalazar 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/L5.8S primers 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
automatic 310 ABI PRISM sequencer (AB Applied Bio-
systems, 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. Conside-
ing the slow progression of 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 pro-
gression of the disease and subsequent perforation of the
nasal septum may have been caused by the use of corti-
sone, 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 immunosup-
pression—caused by systemic conditions like human immu-
nodeficiency virus infection, organ transplantation or
hematological disorders9—is well established. However,
there are only few case reports describing that systemic
corticosteroid treatment may worsen mucocutaneous leish-
maniasis or lead to a recurrence of the disease.10,11

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 muco-
cutaneous 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.12

In conclusion, this case report illustrates the diagnostic
challenges of a rare clinical presentation of L. major infec-
tion 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.

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**FIGURE 1.** Nasal septum perforation demonstrated in (A) computed tomography and (B) upon endoscopic nasal examination. (A) Arrow
marks site of perforation. (B) + Marks perforated nasal septum (Supplemental Video). * marks inferior nasal conchae.