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Leishmania braziliensis presenting as a granulomatous lesion of the nasal septum mucosa

P. J. F. M. LOHUIS*, M. M. LIPOVSKY†, A. I. M. HOEPELMAN, G. J. HORDIJK* AND E. H. HUIZING*

Abstract
Differential diagnosis of granulomatous lesions of the nasal mucosa is difficult. One of the possible causes is an infection with *Leishmania braziliensis* as reported in this case. Therefore leishmaniasis should be included in the differential diagnosis of granulomatous lesions of the nasal mucosa in patients who have travelled to endemic areas.

Key words: Leishmania braziliensis; Nasal septum; Amphotericin B

Introduction

Of the many different species of protozoa only *Leishmaniae* spp. are of clinical importance to otorhinolaryngology. *Leishmaniae* are flagellates which, depending on their type, may cause various clinical syndromes, which can be divided into visceral, cutaneous and mucocutaneous (Pearson and de Quieroz Sousa, 1995). Leishmaniasis caused by *Leishmania braziliensis* begins as a cutaneous ulcer and in some cases, months to years after the healing of the initial cutaneous lesion, it may lead to ulceration of the mucous membranes by its metastastic ability. In the case of metastasis the nasal septum seems to be a place of predilection resulting in granulomatous lesions (Marsden, 1986). Since the clinical appearance of such a granulomatous lesion as well as the histopathological presentation from its biopsy material strongly resembles that of other nasal granulomatous diseases such as sarcoidosis, Wegener's granulomatosis and tuberculosis, diagnosis can be delayed if leishmaniasis is not suspected as a possible cause.

In this paper we present the case-history of a patient with a mucosal infection with *Leishmania braziliensis*, presenting itself as a single granulomatous lesion of the septal mucosa five years after treatment of the cutaneous lesions.

Case report

In March 1995 a 33-year-old freelance cameraman was seen in our hospital with complaints of epistaxis, nasal obstruction, hyposmia and chronic discharge from the left nasal cavity. Complaints had started in 1994 after septal surgery. Post-operatively the patient developed a granulomatous lesion of the nasal septum mucosa on the left side, the side of the incision. the lesion showed no healing tendency.

Past medical history revealed the development of several slowly healing skin ulcers on the face and on the back of the neck in March 1989 after a trip to French Guyana. The ulcers were clinically diagnosed as cutaneous leishmaniasis. The patient was treated with intramuscular injections with sodium stibogluconate (Pentostam) for 30 days, 10 mg/kg daily, followed by intramuscular injections with Pentamidine 4 mg/kg daily for 14 days because of initial persistence of the lesions. The latter regimen resulted in cure of the ulcers leaving hypopigmented scars on the skin. From 1990 till 1995 the patient had again made several trips to South America, without developing any new cutaneous ulcers. On physical examination we saw a thickened nasal septum covered with a rugged, discharging, granulomatous mucosa on the left side. Posteriorly, at the end of the lesion a small septal perforation had developed. The skin above the left eyebrow and in the back of the neck showed atrophic scars (Figure 1).

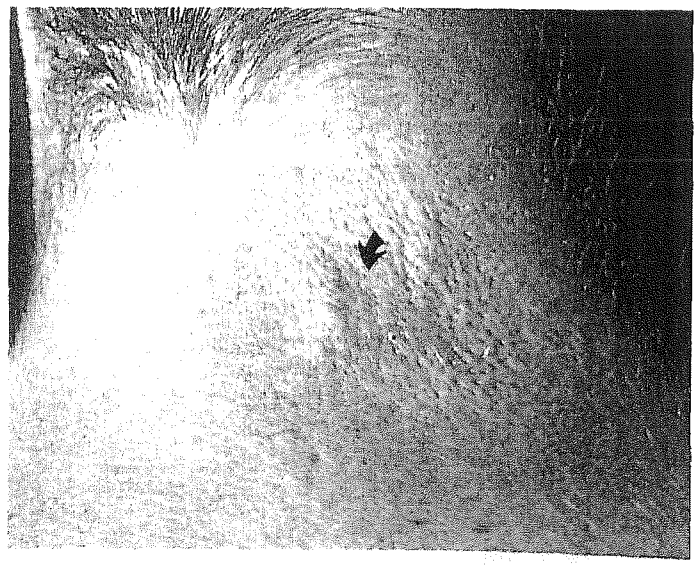

FIG. 1
Typical, hypopigmented and slightly depressed scar of a healed leishmaniasis skin ulcer in the back of the neck of the patient.

From the Departments of Otorhinolaryngology* and Internal Medicine, Division of Infectious Diseases and AIDS†, University Hospital, Utrecht, The Netherlands.
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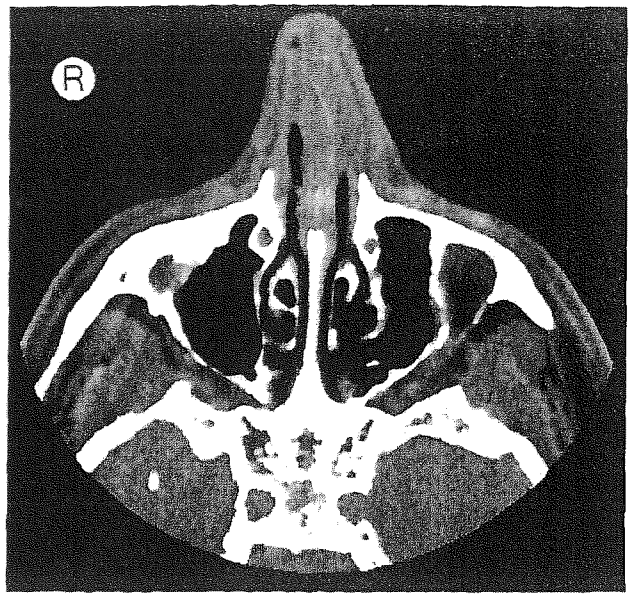


FIG. 2
Axial CT slide through the head showing a thickened nasal septum.

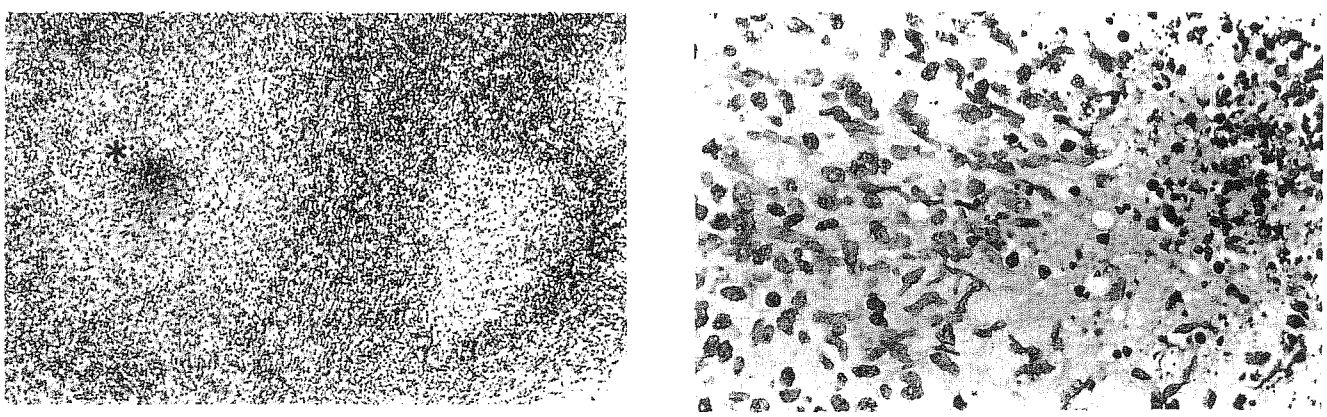
CT-scans proved the nasal septum to be irregularly thickened (Figure 2). Routine blood tests were normal. Both ANCA- and HIV-serology and skin tests for typical and atypical mycobacteria were negative. Histopathological examination of several biopsies from the lesion revealed an ulcerating granulomatous lesion consisting of epitheloid cells surrounded by lymphocytes with a single giant cell (Figure 3). No diagnosis could be made.

One year later, during which time the patient was mainly abroad, he presented himself again to our clinic. This time a relapse of *Leishmania braziliensis* was included in the differential diagnosis and a nasal mucosal biopsy from the margin of the lesion was obtained for histopathology and culture in Novy-McNeal-Nicolle medium. After two days a *Leishmania* parasite could be identified in the culture (Figure 4). PCR determination and rise of antibody titre were consistent with *Leishmania braziliensis*. Since a mucosal recurrence had to be assumed in spite of Pentostam and Pentamidine treatment, intravenous therapy with amphotericin B (1 mg/kg with a total dose of 2 g) was started. After two weeks of treatment the lesion became smaller and less secretory. Nasal breathing and olfaction improved. After eight weeks the lesion and the small perforation had disappeared leaving the septal cartilage covered with atrophic mucosa and a small yellow crust.

Discussion

Leishmaniasis refers to a spectrum of diseases caused by protozoa in the genus *Leishmania*. The disease is often distinguished into a visceral, cutaneous and mucosal syndrome. The subspecies *Leishmania braziliensis* can cause both cutaneous and mucosal syndromes and constitutes a major health problem in South and Central America (Pearson and de Quieroz Sousa, 1995). Two to eight weeks after the bite of an infected sandfly of the genus *Lutzomya* a small erythematous lesion appears that progresses slowly to form a typical leishmanatic ulcer with round, raised borders and a granulating centre covered by exudate. The ulcer heals slowly, even when properly treated, and leaves a slightly depressed, hypopigmented scar (Klotz and Lindenberg, 1923).

In approximately five per cent of the patients, for reasons that are not yet clear, mucosal disease occurs months to sometimes many years after healing of the distant original cutaneous lesion by medical treatment, indicative of a metastatic capacity of *Leishmania braziliensis*. Parasites might have persisted in the phagolysosomes of the macrophages explaining this relapse (Martinez *et al.*, 1992). Although the recurrence can appear anywhere in the aerodigestive tract, the nose seems to be the site of predilection leading to a septal granuloma with ensuing perforation. Possible explanations given for this predominance of nasal involvement include trauma, a lower temperature favouring parasite growth, failure of cell-mediated immune responses to be effective in cartilage and capillary trapping of amastigotes (Marsden, 1994). When nasal mucosal lesions remain untreated, the parasite may infiltrate the underlying tissue and cartilage with massive granuloma formation leading to facial mutilation. The diagnosis of leishmaniasis can be made directly or indirectly. Directly it is made by identification of the intracellular amastigote in stained histological sections of tissue, by culture of the promastigote* from a biopsy under specific media conditions, by



(a) (b)

FIG. 3
(a) Biopsy specimen of the nasal septum mucosa showing a granulomatous lesion consisting of a necrotic central area (*) surrounded by a rim of histiocytes with the appearance of epitheloid cells (H & E; × 90).
(b) Enlargement of the necrotic central area showing the histiocytes (H & E; × 600).

*i.e. the extracellular, flagellete phase of the *Leishmania* parasite as in the insect intermediate host (or in culture).

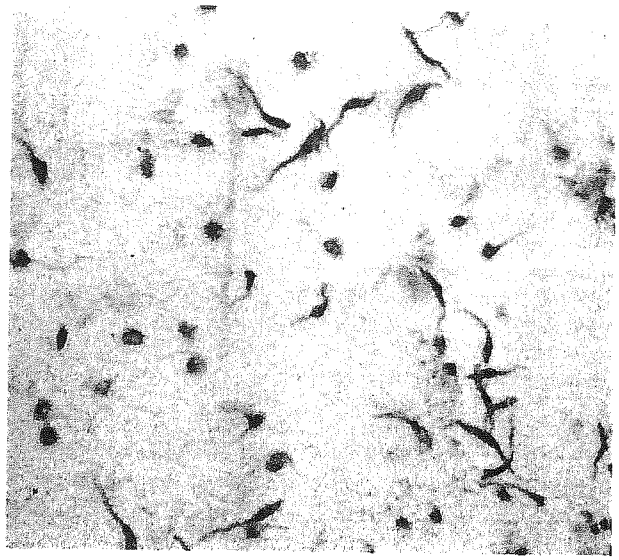


FIG. 4

Leishmania braziliensis promastigotes (footnote in text) cultured from the biopsy specimen (Giemsa staining × 1,650).

PCR or by isolation of the organism after passage through a susceptible animal host (Zajtchuk *et al.*, 1989). *Leishmania braziliensis*, however, is a difficult parasite to isolate and maintain in the laboratory (Lainson, 1982). Marsden (1986) was successful in finding this parasite in only 45 per cent of his patients with mucosal nasal disease. Consequently the indirect diagnostic aids are also of value such as the leishmanin skin test, the indirect fluorescent antibody test and the immunofluorescence of biopsy material (Zajtchuk *et al.*, 1989).

Pentavalent antimony (Sb) in the form of sodium stibogluconate (Pentostam) or meglumine antimoniate (Glucantime) is the treatment of choice for all forms of leishmaniasis in humans. For mucocutaneous leishmaniasis the World Health Organization since 1984 recommends 20 mg Sb per kg body weight per day by intramuscular injection over a period of 30 days (Zajtchuk *et al.*, 1989). However, Sb-unresponsiveness in mucocutaneous leishmaniasis turns out to be a problem, even with this dosage. Grögl *et al.* (1989) clearly demonstrated that *in vitro* a potential risk of inadequate drug therapy is the emergence of parasites resistant to antimonial treatment. Therefore clinical study is still necessary to determine optimal dosages and durations of adequate drug therapy in order to ensure complete cure of the cutaneous lesions and prevent the recurrence of mucosal lesions. However, comparisons with these first line drugs are hard to achieve, because studies are difficult to standardize as their precise chemistry is unknown (Marsden, 1986).

If antimony therapy does not resolve mucosal granuloma the recommended alternative drugs are amphotericin B or Pentamidine. Treatment with Pentamidine is known to give relapses. Although not yet precisely documented, primarily results with amphotericin B are promising (Marsden, 1994).

Our case represents most likely a relapse of *Leishmania braziliensis* of the septal mucosa. The nasal surgery might have triggered the clinical onset. The histopathological specimen showed no amastigotes, so it was only after re-evaluating meticulously the patient's past medical history and travel history that the correct diagnosis was suspected and subsequently confirmed. Although treatment with amphotericin B proved to be successful in this case, follow-up is indicated to detect possible relapse.

Conclusion

Leishmania braziliensis, a subtype of the *Leishmania* parasite, can play an important clinical role in the field of otorhinolaryngology. It may present as a mucocutaneous lesion. Many years after an apparently total cure of a cutaneous form it can emerge as a granulomatous lesion of the nasal septum mucosa, clinically and histopathologically resembling other more common granulomatous diseases. Ideally, when dealing with a granulomatous lesion of the nasal mucosa, the possibility of mucosal relapse of an initial infection with *Leishmania braziliensis* should be considered and the patient should be asked for his/her travel history and past medical history. If applicable the relapse should then be proven by histological identification of intracellular amastigotes or by culturing the parasite in a specific medium. In such a case intravenous amphotericin B is a good treatment of choice.

In retrospect we can conclude that our patient should have been under clinical suspicion from the beginning, since there was an active granulomatous infection of the nasal mucosa, with a history of cutaneous leishmaniasis as proved by the typical scars, which was initiated in a region of the world where *Leishmania braziliensis* is a prevalent disease.

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Address for correspondence:
Peter J. F. M. Lohuis, M.D.,
Department of Otorhinolaryngology,
University Hospital Utrecht,
PO Box 85.500,
NL-3508 GA Utrecht,
The Netherlands.