Oral leishmaniasis: Report of two cases

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Abstract

Leishmaniasis is a chronic inflammatory disease caused by several species of the parasite Leishmania that is transmitted by insects of the genus Phlebotomus spp. or Lutzomyia spp. This disease can affect skin, mucous membranes and viscera being classified as cutaneous, mucocutaneous and visceral leishmaniasis, depending on the spectrum of clinical manifestations. Diagnosis can be achieved through biopsy, microscopical analysis, Montenegro intradermoreaction and/or ELISA. The dentist plays an important role in the diagnosis of this disease due to frequent involvement of oral mucosa. This article reports two clinical cases of leishmaniasis with oral mucosa involvement, their diagnosis workup and treatment.

Keywords: Leishmaniasis, mucocutaneous leishmaniasis, oral medicine

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INTRODUCTION

Leishmaniasis is a chronic inflammatory disease transmitted by an insect vector and caused by the flagellate protozoan of the genus Leishmania. This parasite has a dimorphic life cycle, characterized by the promastigote form in the insect, where it lives and develops extracellularly, and the amastigote form that multiplies intracellularly in the host macrophages.¹⁻⁴ The disease is transmitted by insects belonging to the genus Phlebotomus spp. or Lutzomyia spp. and is considered by the World Health Organization to be one of the most prominent infectious diseases worldwide due to its high detection coefficient and the high level of morbidity that it causes due to its capacity to produce extensive tissue loss.¹⁻⁴⁻⁶

The clinical presentation differs depending on the immune response of the host and the protozoan species involved. The fundamental lesions are similar, consisting of ulcerated and papulonodular lesions that, regarding the extension and involved organs, produce symptoms with systemic or local repercussions.⁵⁻⁸ Leishmaniasis clinical classification is determined by the topographical lesions distribution: cutaneous, mucocutaneous and visceral leishmaniasis.⁶,⁷

Mucosal involvement is relatively rare and results from the hematogenous or lymphatic dissemination of the amastigotes from the skin to the nasal, oropharyngeal, laryngeal or tracheal mucosa.¹⁴ When it affects the oral region, the involvement of the posterior portion of the palate and the tongue is more frequent, but lip involvement has been described either. It is also known to affect middle-aged patients with male predominance.¹¹,⁴⁻⁵,⁹

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The diagnosis of leishmaniasis can be made through a series of tests such as anatomopathological study of biopsy specimens, Montenegro intradermoreaction (IDRM) and/or ELISA and PCR to identify Leishmania species. IDRM is a skin test of high sensitivity, simple to perform and of great diagnostic value. The differential diagnosis of Leishmaniasis-like mucosal lesions is leprosy, lupus vulgaris, squamous cell carcinoma (SCC), Langerhans cell histiocytosis and other granulomatous infections. In addition, skin lesions may bear some resemblance to fungal infections such as blastomycosis, histoplasmosis or coccidioidomycosis.

The objective of this article is to report two cases of atypical leishmaniasis with oral involvement, highlighting the importance of the role of dentist in the diagnosis and treatment of this disease.

**CASE REPORT**

**Patient 1**
An 80-year-old male patient, living in a rural area, ex-smoker and social drinker, HIV negative, was referred to the stomatology clinic complaining of lesions on the upper lip, soft and hard palate that had been presented for 9 months, producing severe pain in the affected regions. The patient underwent two biopsies in other clinical settings with inconclusive results. On physical examination, the right side of the upper lip presented an erythematous swelling associated with a granulomatous ulceration of labial mucosa that extended to the hard palate and seemed to infiltrate to the nasal region. No skin involvement was observed. Cervical lymphadenopathy with inflammatory features as swelling, pain and firm consistency was noticed during palpation.

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The clinical hypothesis of tuberculosis, histoplasmosis and SCC were investigated, and an incisional biopsy was performed under local anesthesia. The patient’s medical history recorded no relevant data.

The microscopical study evidenced areas of intense diffuse inflammatory infiltrate, with organized areas in the form of granulomas. In addition, the presence of multinucleated giant cells was observed, and a descriptive diagnosis of nonspecific chronic inflammatory process was provided. Regarding the clinical and histopathological information, the hypothesis of mucocutaneous leishmaniasis was raised, and IDRM test was requested, which confirmed the suspicion. The patient was referred to an infectious diseases specialist to start treatment with Glucantime® (N-methylglucamine antimoniate). The dosage used was 20 mg Sb5 (pentavalent antimonial) +/kg/day intravenously for 30 days. Complete remission of the lesions was observed post treatment and after a follow-up of 12 months the patient remained with no signs of the disease and just a minor cicatricial sequelae.

**Patient 2**
A 62-year-old male patient, rural worker, smoker, and chronic alcohol user, HIV negative, was referred to the stomatology clinic with upper lip and upper alveolar ridge lesions present for 2 months. During anamnesis, sudden weight loss was reported. Medical history recorded no other important data. Extraoral physical examination showed a cutaneous lesion in the left thigh region along with ulcerated lesions of the nasal mucosa. Cervical lymphadenopathy was undetected on palpation.

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DISCUSSION

Leishmaniasis is an infectious disease of worldwide distribution, with cases reported in Asia, Africa, Europe and the Americas. Brazil is home to most of the cases of leishmaniasis that affect mankind, as all forms of the disease have high incidence in this country, besides the fact that dogs, rodents and other wild animals constitute natural reservoirs of the parasites. \[1\] Leishmania braziliensis is the most common etiological agent in leishmaniasis with mucosal involvement, capable of producing ulcerated and papulonodular lesions, affecting oral mucosa, nasal mucosa and other sites besides the skin. \[1,5,6,9\]

It is estimated that near 2 million people develop leishmaniasis each year with about 50,000 deaths due to complications of the disease and lack of proper treatment. The disease occurs worldwide but mainly in the tropics: Africa, Asia, Southern Europe, Central and South America. Brazil, Ethiopia, Sudan, India and Bangladesh encompass 90% of potentially fatal cases of leishmaniasis. \[12\]

Although leishmaniasis cases occur all over the country in Brazil, the highest incidence occurs in the north, northeast and center-west of the country. \[2\] The patients reported in this study were diagnosed in a large urban center in the southern region, where the level of suspicion for the disease by health teams is much lower than in those places where the occurrence is higher. The same situation shall occur in those countries where the disease incidence is lower or in places that receive imported or nonautochthonous cases.

As was described in the cases reported here diagnosis can be difficult if leishmaniasis is not included in the differential diagnosis. The IDRM test is extremely valuable in the diagnosis of Leishmaniasis, since the histopathology of biopsied lesions can hardly disclose the definitive diagnosis due to the scarcity of parasites in these specimens. \[1,4\] This information corroborates with the first case reported, but the professional should not rule out the biopsy, which allows to eliminate other diagnostic possibilities and increase the level of suspicion regarding leishmaniasis. The IDRM indicates contact with the parasite but not necessarily active disease; however, the symptomatology allied to the positivity of the test enable the diagnosis. The safest way to conclude the diagnosis of leishmaniasis is through the detection of protozoan DNA in immunological tests such as ELISA, immunofluorescence and other techniques. \[2\]

The cases reported here presented mucous lesions very similar to each other, involving nasal mucosa and palate, sites characteristically affected by mucocutaneous leishmaniasis. Distinctive features, which may be considered uncommon in the exposed cases, refer to the involvement of the alveolar ridge mucosa, which both cases have demonstrated, and the coexistence of cutaneous lesions in limbs and mucosal lesions as in case 2, as cutaneous lesion is usually an initial manifestation that heals even with no treatment, followed by late expression of secondary mucosal lesions. Another fact to be highlighted was the absence of previous skin lesion in case 1, or even a reference to it in the anamnesis conducted with the patient.

The process of diagnosis can be challenging according to clinical presentation, health team experience, and
In the case 1. American cutaneous. The effectiveness of the treatment depends on poor people of these countries, with very low investments tropical diseases that affect mainly poor countries and the lack of associated necrotic tissue. In case 2, the possibility of malignancy was also discussed, among other infectious diseases, but leukemia instead of SCC because of the bulging aspect of gingiva and palate mucosa along with multiple fibrinous ulcers.

The treatment is based on the clinical presentation of the disease and on the medical history of each patient. There are two pentavalent antimonial drugs considered as first choice: N-methylglucamine antimoniate and sodium stibogluconate. Without success with these drugs, pentamidines and amphotericin B are alternatives available. The effectiveness of the treatment depends on the form and extent of the disease. Therapy with single drug present recurrence rates around 20%, which justifies and requires prolonged follow-up of the patients, as it has been conducted in the cases presented.

Early detection of Leishmaniasis reduces the risk of mucocutaneous complications such as disfigurement and recurrence of infection. The oral cavity is a frequent site of occurrence in areas of low or unexpected incidence. Such scenario may cause a delayed diagnosis and mistreating, leading to sequelae and poor prognosis. The differential diagnosis encompasses other infectious diseases, and noninfectious diseases such as pemphigus vulgaris, pemphigoid, plasma cell gingivitis, anemia and even malignancies as leukemia and SCC. In the case 1 described before, the clinical aspect of a deep ulcer with elevated borders lead to inclusion of SCC in differential diagnosis, despite the 9 months history of evolution and the lack of associated necrotic tissue. In case 2, the possibility of malignancy was also discussed, among other infectious diseases, but leukemia instead of SCC because of the bulging aspect of gingiva and palate mucosa along with multiple fibrinous ulcers.

Unfortunately, leishmaniasis is included in the group of tropical diseases that affect mainly poor countries and the poor people of these countries, with very low investments towards the development of preventive programs, vectors control or researches on more effective treatment protocols.

CONCLUSION

The manifestations of mucocutaneous leishmaniasis, even in Brazil, which leads the world statistics in number of occurrences, can bring difficulties and delay in diagnosis, due to the variability of clinical presentation, and the need of a combination of test results or more sophisticated and expensive technology, such as protozoan DNA identification. Clinicians should develop a higher level of suspicion regarding the disease in the presence of ulcerogranulomatous lesions located in the oral and nasal mucosa, with or without cutaneous involvement, in order to adopt objective guidelines towards the diagnosis and subsequently to enable early treatment and better prognosis for the patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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Figure 4: (a) Immunohistochemistry for anti-CD68 antibody revealing positive and intense cytoplasmic positivity in macrophages (IHC, ×400). (b) Immunohistochemistry for the anti-Leishmania antibody revealing positive labeling of amastigotes within the cytoplasm of macrophages (IHC, ×400)
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