Case Report

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.[4] 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.[1,4,5,9]

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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.[4,5,9,10] The differential diagnosis of Leishmaniasis-like mucosal lesions is leprosy, lupus vulgaris, squamous cell carcinoma (SCC), Langerhans cell histiocytosis and other granulomatous infections.[4,11] In addition, skin lesions may bear some resemblance to fungal infections such as blastomycosis, histoplasmosis or coccidioidomycosis.[4]

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 [Figure 1a-c]. No skin involvement was observed. Cervical lymphadenopathy with inflammatory features as swelling, pain and firm consistency was noticed during palpation.

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 [Figure 2a and b]. 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 [Figure 3a] and along with ulcerated lesions of the nasal mucosa. Cervical lymphadenopathy was undetected on palpation.

Physical intraoral examination revealed ulcerated and irregular lesions in the mucosa of upper alveolar ridge and palate [Figure 3b and c]. An incisional biopsy was performed under local anesthesia considering a differential diagnosis with paracoccidioidomycosis, tuberculosis and leukemia.

Serologies for histoplasmosis and toxoplasmosis were subsequently requested, both resulting in non-reactive antibodies. Therefore, mucocutaneous leishmaniasis was suspected. Histopathologic data showed a non-specific chronic inflammatory process. Immunohistochemistry procedures revealed cells positive for CD68 and Leishmania antigen [Figure 4a and b]. In addition, the positivity of the IDRM test proved the hypothesis. Treatment, therapeutic

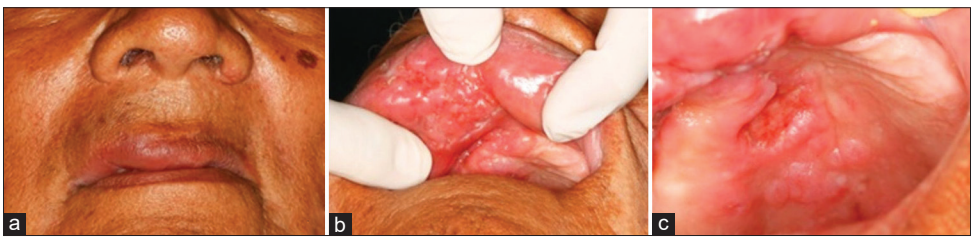

Figure 1: (a) Extraoral aspect showing asymmetry due to an indurated swelling of the upper lip on the right, accompanied by inflammatory features of edema and erythema. (b) Granulomatous lesion with ulceration involving the upper lip mucosa up to the posterior region of hard palate. (c) Granulomatous ulcer on upper lip mucosa extending to vestibule, alveolar ridge and hard palate

response and follow-up of this patient were similar to those cited for the previous patient.

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.[2] 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

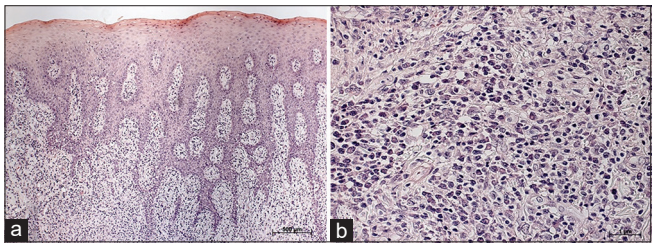

Figure 2: (a) Lining epithelium showing thin and elongated projections, with intense spongiosis and lymphocyte exocytosis. The lamina propria is a dense collagenated connective tissue with intense, diffuse and deep inflammatory infiltrate (H&E, ×100). (b) Higher magnification showing the nature of the inflammatory infiltrate that is lymphoplasmocytic and rich in macrophages (H&E, ×400). (b) It is also possible to observe areas with marked presence of eosinophils with granular cytoplasm (H&E, ×400)

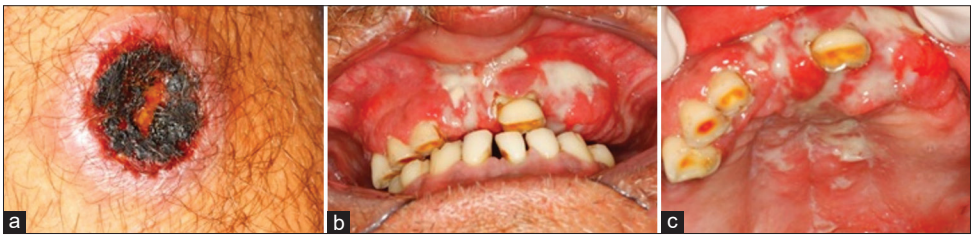

Figure 3: (a) Ulcer covered by a darkened crust, with indurated borders, discrete erythema and regular circular shape on forearm skin. (b and c) Extensive ulcerated irregular lesions, covered by yellowish fibrinous exudate, associated with edema and erythema, involving almost all upper vestibule, anterior alveolar ridge, central region of hard palate and the left side of soft palate

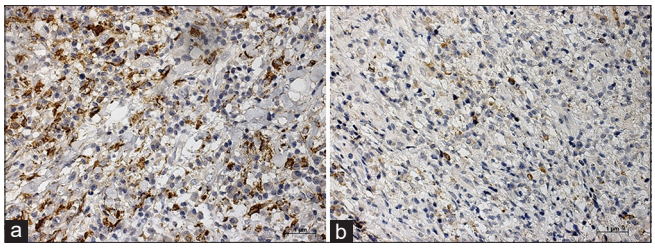

Figure 4: (a) Immunohistochemistry for anti-CD68 antibody revealing positive and intense cytoplasmic positivity in macrophages (IHC, ×400). (b) Immunohistochemistry for the anti-Leishmania antibody revealing positive labeling of amastigotes within the cytoplasm of macrophages (IHC, ×400)

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.[9] 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.

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.[13] 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.[7]

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 manifestation of this severe form of the disease and therefore, the dentist represents a crucial health agent in the detection of initial lesions preventing the progression of the disease to stages of greater tissue loss and favoring more effective therapeutic results.

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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