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Case report

Mucosal leishmaniasis in a patient with leprosy: a case report

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Abstract

Leishmaniasis and leprosy comprise the group of granulomatous diseases. Although both diseases have a known occurrence in Brazil, their concurrent presence is rare, and few cases have been reported in the literature. We report the case of a 46-year-old male patient co-infected with leprosy and mucosal leishmaniasis. Examination revealed an ulcerated lesionon the nose and a lesion with a granulomatous surface on the palate, in

addition to spots on the arms and legs. Histopathological analysis of the oral cavity specimen was suggestive of mucosal leishmaniasis, although no amastigotes were identified. A new biopsy was taken to collect material for PCR and the remaining was subjected to hematoxylin-eosin (H&E) staining. Finally, the diagnosis for *Leishmania braziliensis* was positive. A skin biopsy suggested the diagnosis of leprosy on the right leg and left knee by Fite-Faraco staining (Ziehl-Neelsen). The results obtained indicated simultaneous infection with *M. leprae* and *L. braziliensis*. After diagnosis, the patient was treated for co-infection and has been under follow-up for 2 years without signs of recurrence. The diagnosis of leishmaniasis/leprosy co-infection is challenging because of the broad clinical spectrum. Few cases have been reported in the literature and the dentist may play an important role in its detection.

Keywords: Leishmaniasis; Leprosy; Coinfection; Case report; Oral pathology.

Statement of Clinical Significance

This is a study of a case of leishmaniasis and leprosy co-infection in a rural worker with no systemic alterations. The authors were faced with a case of complex diagnosis, given the possible differential diagnoses involved in the spectrum of granulomatous lesions, including oral squamous cell carcinoma. In view of this specificity, we emphasize the importance of dialogue between health areas in order to assist patients in complex cases. There are few reports in the literature of this co-infection, which makes this case unusual. It is therefore important to discuss its clinical aspects and, above all, the challenges faced in correctly diagnosing it. This could lead dental surgeons to include the possibility of co-infection as a diagnostic hypothesis when patients present with similar clinical characteristics. This would have a positive impact on a more targeted investigation, early diagnosis and better prognosis. In addition, this article reinforces the importance of dentists investigating systemic conditions with oral implications. Lesions such as these are rare in the oral cavity, but when present, they usually represent conditions in the early stages, benefiting the patient with early diagnosis.

INTRODUCTION

Leishmaniasis and leprosy comprise the group of granulomatous diseases that are characterized by the formation of a chronic immune reaction with mucocutaneous tissue involvement. The conditions frequently affect poor populations in tropical regions[1].

Leprosy is caused by *Mycobacterium leprae*, which is mainly transmitted through the upper airways[2]. Skin lesions commonly show loss of sensitivity and are related to a low probability of contagion by contact. The diagnosis of leprosy should be primarily clinical, but some auxiliary tests such as Fite-Faraco staining (Ziehl-Neelsen) in biopsy samples can be carried out in specialized centers[2].

Leishmaniasis is caused by infection with *Leishmania* parasites. The clinical forms in humans are visceral, cutaneous, and mucosal leishmaniasis[3]. Cutaneous and mucosal leishmaniasis frequently manifests as ulcers with a granulomatous base and raised borders. In these cases, the diagnosis is based on the visualization of the parasite through specific parasitological, histological or immunological tests[3].

Although both diseases have a known occurrence in Brazil, their concurrent presence is rare and few cases have been reported in the literature[4-9]. The diagnosis of co-infection therefore represents a challenge since the two diseases share similar features, including the involvement of mucocutaneous tissue, development of a chronic granulomatous response, anda broad clinical spectrum. The present report describes the case of a patient co-infected with leprosy and mucosal leishmaniasis in the mouth and nose, a clinical presentation that represents a new and emerging epidemiological entity in northeastern Brazil.

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CASE REPORT

A 46-year-old male brown patient was seen at the Stomatology Clinic of Dental School – Universidade Federal da Bahia with a 1 year and 2-month history of painful lesions in the mouth and on the nose, complaining of limiting chewing and swallowing. The patient

was a rural worker and reported no systemic alterations, smoking or alcoholism. Extraoral physical examination revealed an ulcerated lesion on the left nasal mucosa with an erythematous base and mild swelling, associated with the presence of a fibrinopurulent membrane.

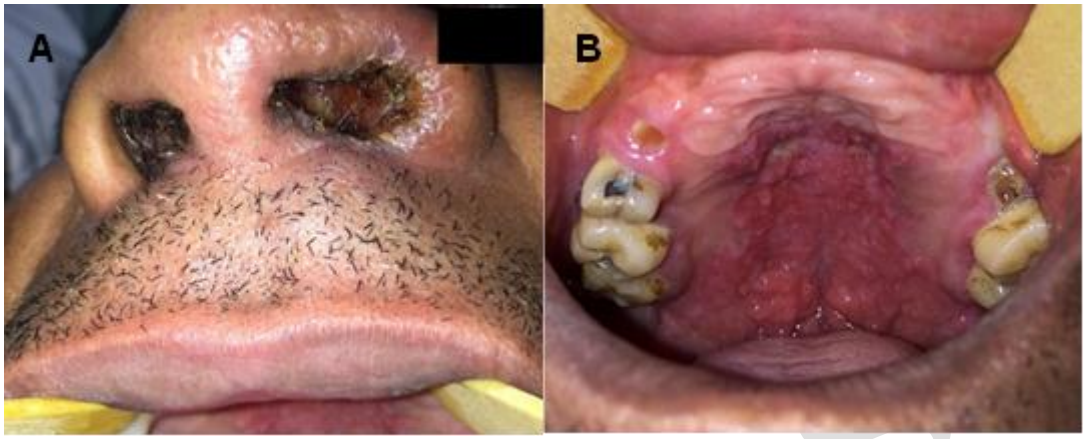

Figure 1. Clinical findings upon extraoral (A) and intraoral (B) examination.

Intraoral examination showed an extensive irregular, reddish ulcer with a granulomatous surface and firm consistency on the hard and soft palate (Figure 1B).

Loss of bone continuity in the region of the hard palate and floor of the nasal fossa was detected upon palpation. Cranial magnetic resonance imaging revealed mucosal thickening of the paranasal sinuses.

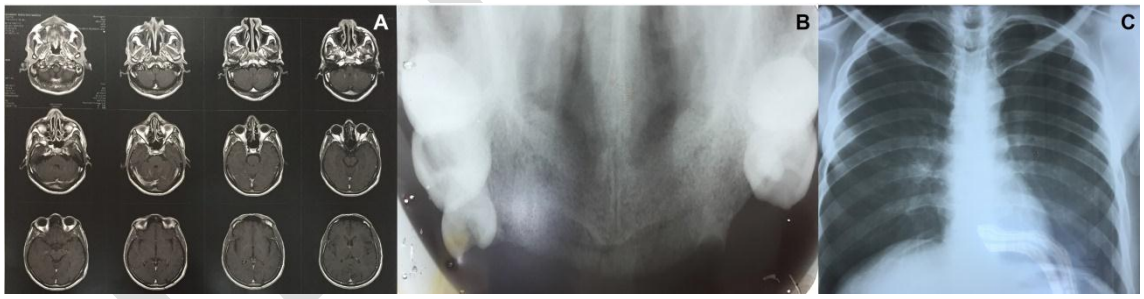

Figure 2. Imaging exams. Cranial magnetic resonance (A). Occlusal radiography (B). ChestX-ray (C).

Occlusal radiography indicated bone rarefaction in the right anterior maxilla (Figure 2B). A chest X-ray and abdominal tomography showed the absence of lung involvement and an abdomen within the normal range (Figure 2C). Preoperative laboratory tests of renal and hepatic function did not reveal systemic involvement.

An incisional biopsy of the palate was performed under local anesthesia. On that occasion, discussing with the patient about the suspicion of infectious lesions, he reported the presence of hyperchromic and reddish spots on the upper limbs and a large area on the lower limbs exhibiting desquamation and measuring more than 30 cm in

diameter.

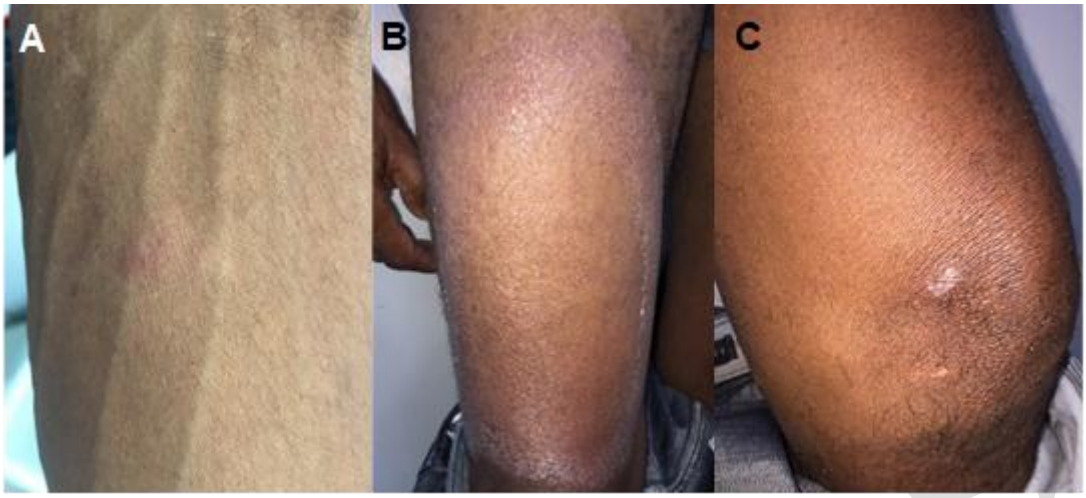

Figure 3. Clinical appearance of the lesions on the upper (A) and lower limbs (B and C).

Thus, concomitantly with the investigation of mucosal lesions, the patient was referred to a dermatologist. Histopathological analysis of the oral cavity specimen was suggestive of mucosal leishmaniasis, although no amastigotes were identified. A Montenegro skin test was therefore requested, which was negative. A new biopsy of the mucosal lesions was then carried out and for a PCR analysis, and the remaining tissue was submitted to a new hematoxylin-eosin (H&E) staining. They were both positive for *Leishmania braziliensis.*

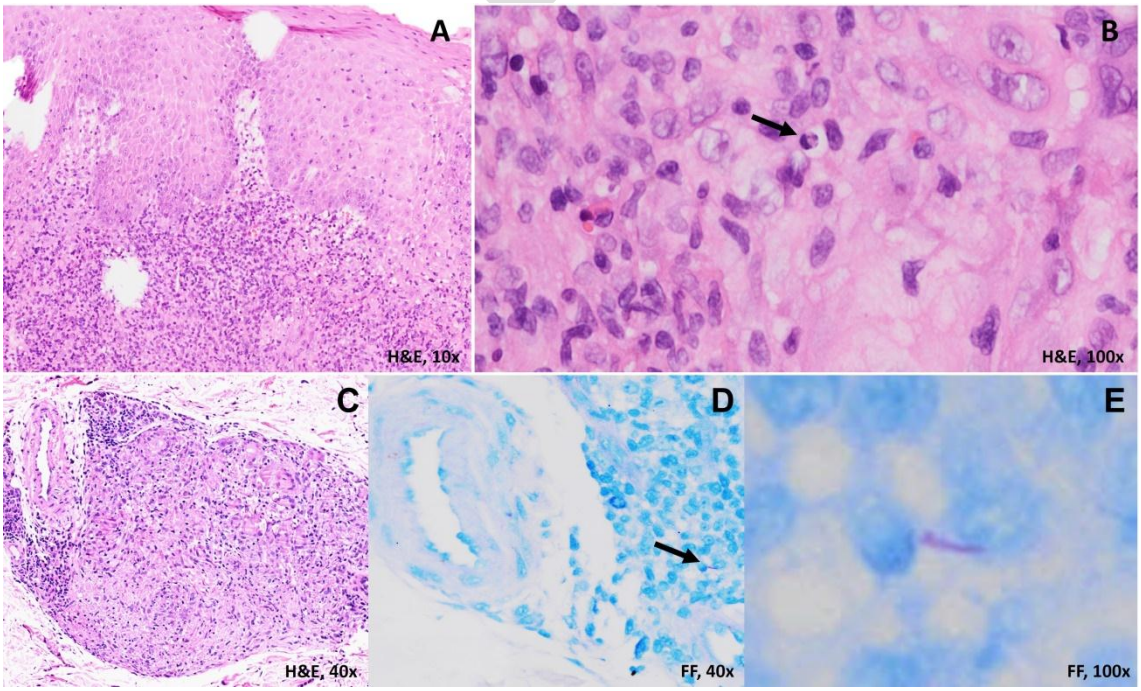

Figure 4. Histopathological aspects of mucosal (A-B) and skin (C-E) biopsies. Hematoxylin-eosin (H&E) stain showing chronic inflammation (A) and amastigote of

Leishmania sp (arrow) (B). H&E stain showing chronic granulomatous inflammation in thedermis (C). Fite Faraco (FF) stain showing bacilli of *Mycobacterium leprae* (arrow) (D-E).

A skin biopsy suggested the diagnosis of leprosy on the right leg and left knee by Fite-Faraco staining (Ziehl-Neelsen) (Figure 4). Using an oral biopsy sample, qPCR targeting the specific 16SRNA of *M. leprae* was thus performed, which was negative. The results obtained indicated simultaneous infection with *M. leprae* and *L. braziliensis*. Thus, the final diagnosis was cutaneous leprosy and mucosal leishmaniasis. The patient was referred to the immunology service where he was treated for the co-infection. He has been under follow-up for 2 years without signs of recurrence.

DISCUSSION

Pathogen-mediated chronic granulomatous diseases share similar clinical features,histopathological findings, and immunological mechanisms. Their diagnosis is therefore a challenge since it is linked to the identification of the infectious agent[1]. In the present case, Fite-Faraco staining of the skin lesions was positive, confirming the presence of *M. leprae*. However, the ulcers on the nasal mucosa and palate were related to leishmaniasis, diagnosed based on the identification of *L. braziliensis* DNA by PCR.

The diagnosis of leprosy is made by evaluating cardinal clinical signs, such as permanent loss of sensitivity in a hypopigmented or reddish skin spot and thickened peripheral nerves associated with weakness in the corresponding muscles[2]. The clinical manifestations observed in the present patient agreed with the classical features of leprosy, except for muscle weakness.

The WHO defines leprosy classification based on treatment, classifying the disease as multibacillary when visible bacilli are present and staining is positive, and as paucibacillary when this condition is not present[2]. The present patient can be classified as multibacillary due to positive Fite-Faraco staining, demonstrating the presence of visible bacilli.

Leishmaniasis is caused by different protozoan species of the genus *Leishmania*, including *L. braziliensis*. The clinical forms are cutaneous, mucosal and visceral

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leishmaniasis, indicating a broad spectrum of clinical presentations. Cutaneous leishmaniasis is the most common form and pathognomonic clinical features, while primary mucosal involvement is rare. The oral and nasal mucosa are the most affected sites and are associated with difficult-to-treat cases[3]. In the present patient, the lesion on the palate exhibited characteristics that correspond to a wide spectrum of pathologies, either malignant such as squamous cell carcinoma, or infectious with a granulomatous pattern such as paracoccidioidomycosis, tuberculosis, and histoplasmosis.

The clinical manifestations observed in the present patient represent two endemic infectious diseases in Brazil, i.e., leprosy and leishmaniasis. The northeastern region, particularly the state of Bahia, is characterized by high endemicity, active transmission and late diagnosis, factors that are responsible for the persistence of these diseases as a critical public health problem. The situation is aggravated in rural areas and in communities with a lower socioeconomic index[10], as observed in the present case.

Despite the high rates of infection with leprosy and leishmaniasis, co-infection is rare[11]. The majority of patients are young adult males who show different clinical presentationsof leprosy and leishmaniasis, especially cutaneous and mucocutaneous forms[4-9,11,12]. In Brazil, the reported cases follow the general trend but a predilection for older men has been reported[4-9]. In only one of these cases was the oral cavity affected by one of the co-infections[9]; hence, the present case is the second described in the literature. However, incontrast to the present case, the oral lesion was caused by *M. leprae*, while the lesions associated with leishmaniasis involved the skin and nasal septum, without communication with the oral cavity.

The immunological mechanism underlying co-infection, especially in immunocompetent patients, has not yet been fully elucidated. Although the simultaneous presence of the two diseases in an endemic region may have favored contact and consequent co-infection, this fact alone does not seem to be sufficient to explain such involvement. Within this context, Vernal et al.[4] observed a possible correlation between the number of microorganism strains and immunological and genetic conditions. Both *M. leprae* and *L. braziliensis* are intracellular pathogens that, once in contact with tissues, are phagocyted by macrophages and antigen-presenting cells. These cells trigger a cellular immune response mediated by CD4+ Th cells, which culminates in the activation of Th1 and Th2 responses and subsequent release of cytokines such as IFN-γ, IL-2, and TNF-α[4,5].

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The literature diverges regarding the existence of a correlation between the cellular immune response elicited by each pathogen in the presence of co-infection. Vernal et al.[4] found no correlation between the immune response elicited by each microorganism. There were also no changes in the clinical manifestations of leishmaniasis or leprosy in simultaneous infection. This fact suggests that each pathogen elicits a specific immune response and that the mechanisms are different and independent[4]. However, in a molecular biology study, Azeredo-Coutinho et al.[9] provided evidence that the response mediated by infection with *M. leprae* induces the regulatory activity associated with IL-10, which seems to control and limit the exacerbation of infection caused by *L. braziliensis*. Taken together, thesedata suggest that leprosy directly influences the clinical course of leishmaniasis, as demonstrated by an increase in the manifestations of mucosal leishmaniasis after removal of the suppressive effect of the antigen related to *M. leprae*[9].

In view of this, there is not enough evidence to confirm whether the co-infection of leishmaniasis and leprosy is associated with a worse prognosis. Although some studies have reported molecular associations that could support this theory, this has not yet been confirmed clinically. In this case, the patient was treated for co-infection and has been under follow-up for 2 years without signs of recurrence. The patient's conditions were treated in an external department. Even after attempts to contact the center, it was not possible to access the entire protocol. This is a limitation of this case report.

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CONCLUSION

The present case portrays the diagnostic difficulty of chronic granulomatous diseases, which share a spectrum of clinical and immunological characteristics, especially in cases of co-infection. Although involvement of the oral cavity is rare, it may be the only or the firstsite of clinical manifestation of these diseases. Thus, the dentist is essential for the early diagnosis of these pathologies in order to improve the prognosis of the patient. Future studies that investigate the mechanisms underlying co-infection may identify valuable tools for the treatment of this condition.

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AUTHORS' CONTRIBUTIONS

LVS: data curation, investigation, visualization, writing – original draft, writing – review & editing. LAC: visualization, writing – original draft, writing – review & editing. JNS: investigation, writing – review & editing. SMA: investigation, writing – review & editing. MC: conceptualization, investigation, writing – original draft, writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Competing interests: The authors have no relevant financial or non-financial interests to disclose.

Ethical approval: This case was submitted for approval to the Research Ethics Committee, under number 60650122.9.0000.5024.

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