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Parasitological association between human leishmaniosis mucosa and paracoccidioidomycosis. Case report

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ABSTRACT

INTRODUCTION: Leishmaniasis Mucosa (LM) is a tropical disease that affects the upper respiratory tract and/or oral mucosa. Its etiological agent is Leishmania spp. Paracoccidioidomycosis disease caused by the fungus Paracoccidioides brazilienses. The aim is to report a case of Leishmaniasis Mucosa in association with Paracoccidioidomycosis.
PRESENTATION OF CASE: A male patient, 24 years old; Intraorally, presence of a non-bleeding erythro-leucoplastic lesion that affected the soft palate and oropharynx; 3 years of evolution. On the face Computerized Tomography (CT) examination, it was possible to observe muco-periosteal thickening in the soft palate region; immunohistochemical markings for Paracoccidiodes brasiliensis. He was diagnosed with Leishmaniasis by Montenegro intradermoreaction (MIDR).
DISCUSSION: The predisposition to Paracocodioidomycosis after Leishmaniasis infection is justified by factors already elucidated – hygiene, nutrition habits and immunodeficiency, but the reason for the non-progression of the fungus after years of evolution could be related to its inhibition due to the presence of the protozoan in the same wound.
CONCLUSION: This phenomenon may be explained by future studies that need to be performed to answer such questions.

1. Introduction

Leishmaniasis is a tropical disease clinically classified according to the involvement of anatomical regions, such as: visceral (VL), cutaneous (CL) and Mucocutaneous (MCL); It may affect oral mucosa areas alone. Leishmaniasis Mucosa (LM) is a chronic infection that affects the upper respiratory tract and/or oral mucosa. The etiological agents *Leishmania brazilienses*, followed by *L. panamensis* and *L. amazonenses* are the main causers of LM [1–3].

It is a geographically dispersed disease. There are transmission relates on five continents and endemic rates in 98 countries. The incidence of leishmaniasis is very high in India, Bangladesh, Nepal, Brazil and Sudan. According to the World Health Organization (WHO), the disease has spread worldwide and two million new cases are estimated per year (1, 5 million cases of CL and 500 000 V L cases, with approximately 12 million infected individuals). In the Americas, there are case records in all countries except Chile and Uruguay [4–6].

The MCL form is the most severe and it appears a few years after the integumentary manifestation. It affects the upper part of the aerodigestive tract, with mainly lesions in the oral and nasal mucosa and occasionally in the larynx and pharynx. The exclusive involvement of oral mucosa is quite rare [6].

Clinical presentation is largely determined by the host's immune response. In general, it presents as erythema and ulceration or as exophytic plaque, papules and/or nodules, usually affecting hard palate, soft palate and tongue. However, they can affect any site such as the lip, uvula, gingiva, amygdala and retromolar region, associated with pain, edema, foul smell, bleeding and sialorrhea [3].

Other infectious/non-infectious diseases may show similar lesions, among them: paracoccidioidomycosis; histoplasmosis; tuberculosis; leprosy; lethal midline granuloma; pemphigus vulgaris; pemphigoid; plasmacytic gingivitis; anemias; leukemia and verrucous carcinoma [7].

The diagnosis of leishmaniasis is a real challenge for all professional team. At first, the clinical manifestations of the disease

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present a wide differential diagnosis and the findings may be associated with other diseases, such as Paracoccidioidomycosis, which is an infectious disease caused by the fungus *Paracoccidioides brazilienses*. It causes tegumentary lesions as one of its main clinical manifestations. The patients often present ulcerations in bucal, nasal and pharyngeal mucosa; besides pulmonary findings [8,9].

The aim of this work is to report a case of Leishmaniasis Mucosa in association with Paracoccidioidomycosis and to discuss the existence of an infectious relationship between parasites for exclusive findings on oral mucosa in humans. This work has been reported in accordance to the Surgical Case Report (SCARE) guidelines [10].

2. Case report

A male patient, meloderma, a construction worker, 24 years old. He presented himself at the Oral and Maxillofacial Surgery Service complaining about mouth injury, causing dysphagia due to burning and pain. In the anamnesis, there was a clinical course with an evolution of approximately 3 years, with hospitalizations occurring under suspicion of severe tonsillitis with no positive response for treatment.

Physical examination revealed an individual with a symmetrical, normocorate and a febrile face; Absence of regional infracted and painfully lymph nodes. Intraorally, total denture with satisfactory hygiene; presence of a non-bleeding erythro-leucoplastic lesion with irregular surface and diffuse contours that affected the soft palate and oropharynx (Fig. 1).

On the Computerized Tomography (CT) of the face examination, it was possible to observe muco-periosteal thickening of apparently inflammatory origin in the soft palate region with absence of bone involvement in the involved region, with free airways (Fig. 2).

Negative results for HIV, Syphilis (VDRL / FTABS) and Tuberculosis (Escarro T.); without radiographic signs of paracoccidioidomycosis (*Paracoccidiodesbrasiliensis*) in the thorax. Material was collected for incisional biopsy demonstrating non-specific chronic inflammatory tissue sections with immunohistochemical markings for *Paracoccidiodesbrasiliensis* (Fig. 3).

The patient was asked to go to the Center for Tropical Diseases of the Evandro Chagas Institute/PA where he was diagnosed with Leishmaniasis by Montenegro intradermoreaction (MIDR). The treatment was started with Fluconazole 400 mg twice a day for one month in combination with Nystatin-based mouth wash three times a day. In 10 days', return there was a slight improvement in the condition.

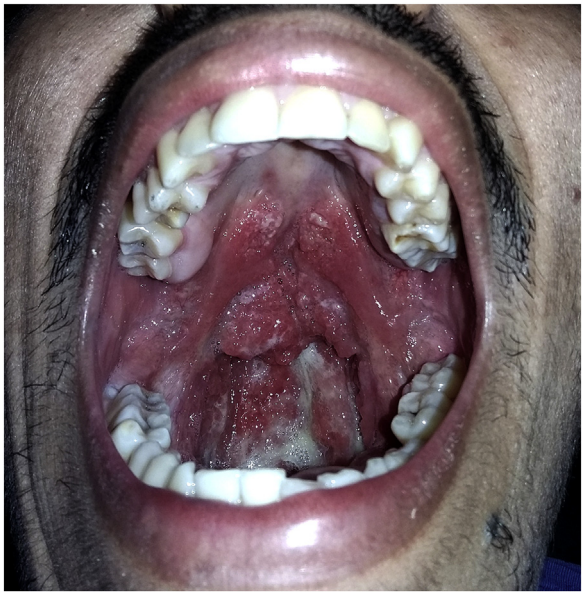

Fig. 1. Initial clinical aspect. Erythematous lesion with whitish areas, irregular and granulomatous surfaces involving the soft palate, pharyngeal arches and pharynx.

3. Discussion

Leishmaniasis is an infectious disease obligatory caused by protozoan parasites of the genus Leishmania. American tegumentary leishmaniasis can reach individuals of any age, being more frequent from 20 to 40 years old. The incidence of leishmaniasis as an opportunistic disease has increased in recent years due to the increasing number of patients with immunological depression secondary to chronic diseases, neoplasms, organ transplants, immunosuppressive treatments and human immunodeficiency virus (HIV) becoming a public health problem [6,7,11].

In Brazil, the highest incidence of Leishmaniasis is in the Northern Region, which comprises the States of Acre, Amapá, Amazonas,

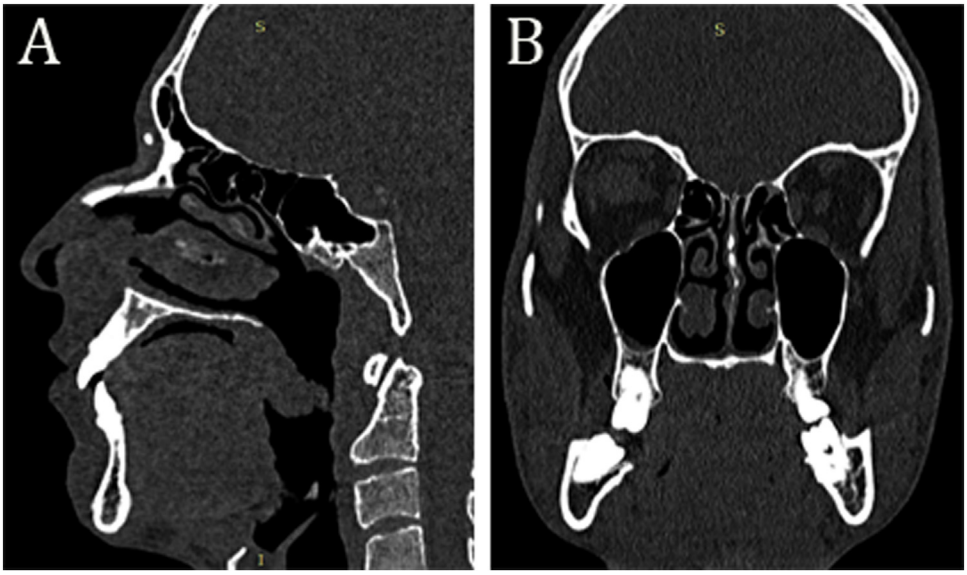

Fig. 2. CT Scan. (A and B) Images suggest muco-periosteal reaction in palatal region not compatible with neoplasia. Free airways.

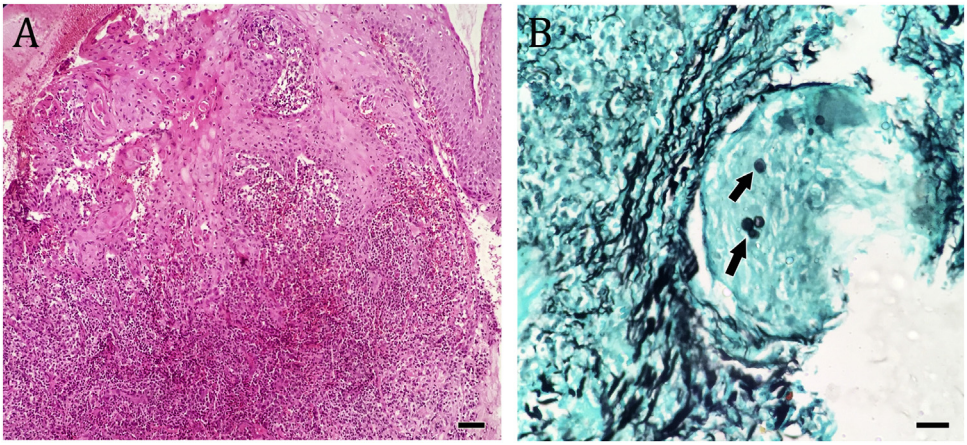

Fig. 3. Histopathological Findings. (A) Mucosa coated by hyperparqueredized squamous epithelium exhibiting exocytosis and pseudoepitheliomatous hyperplasia. The lamina propria consists of dense connective tissue with intense chronic inflammatory infiltrate and the presence of multinucleated giant cells of the Langerhans type. (B) PAS staining and Grocott demonstrated yeasts with birefringent circular structural fields compatible with *Paracoccidioides brasiliensis* (arrows).

Pará, Rondônia, Roraima and Tocantins. Actually, it is one of the macro regions considered endemic by the disease [12].

The presented article refers to a case of Leishmaniasis with exclusive involvement of oral mucosa and oropharynx, without affecting nasal mucosa area and previous skin lesions as in most cases of muco-cutaneous Leishmaniasis, which made it difficult to diagnose the disease. The time of evolution is the factor that determines the dissemination of the parasite and is one of the main responsible for the severity of the mucosal lesions and their consequences. Therefore, it is essential to diagnose the disease early [7].

The diagnosis is made by clinical findings, epidemiology and laboratory tests. The test is positive in 75 % of the lesions whose evolution varies from two to six months and in 20 % after this time. Hamster culture and inoculation have sensitivity of 30 and 50 %, respectively. Montenegro intra derma reaction (MIDR) is positive in 82.4–100% at the time of diagnosis. It may be negative in the disease with up to four months of evolution, in diffuse cutaneous Leishmaniasis (DCL) and in immunocompromised patients [11,12].

Generally, cuts for the evaluation of Leishmania amastigotes are difficult to visualize and differentiate from amastigotes from other microorganisms. Considering the rarity of Leishmaniasis in the upper aerodigestive tract region, the diagnosis of (LM) can be challenging, because even with clinically active lesions, amastigotes are generally scarce and other auxiliary methods for confirming the diagnosis are used, as in the case in question that the final diagnosis was closed by (IDRM) which is effective and low cost [13].

The characteristics of the case reported in association with the longtime of progression suggested some diagnostic hypotheses such as squamous cell carcinoma, tuberculosis and paracoccidioidal mycosis. The presence of *Paracoccidioides brasiliensis* in the histological sections initially showed the parasite as a possibly causing agent of the clinical condition which could be related to the professional activity of the individual, nutritional deficiencies and inadequate hygiene. However, the lack of other clinical signs justifying Paracoccidioidomycosis, such as lung lesions and the negative response to initial therapy encouraged the search for new hypotheses and confirmation of the diagnosis of Leishmaniasis after a positive MIDR test [14].

It is believed that the cellular immunity of the host is very important in the therapeutic response of Leishmaniasis in view of being an intracellular parasite. Mucosal Leishmaniasis is a debilitating disease that can cause malnutrition and immunodepression, leading to secondary infections that may become more serious than the underlying disease itself, which may explain paracoccidioidomycosis as a secondary parasitic form of the disease [11,12].

Paracoccidioidomycosis is an endemic systemic mycosis in Latin American countries. The etiological agent *Paracoccidioides brasiliensis* is a thermore glyphic fungus that grows as a yeast in the host at 37 °C and as a mycelium at 25 °C. Primary infection usually occurs in the lungs by inhalation, and can spread to the body through the lymphatic or hematogenic system. Mucosal and skin lesions, as well as involvement of lymph nodes and adrenal glands can be clinically identified [8,14–16].

Secondary manifestations of this pathology can affect the oral cavity, which leads the patient to seek the dental surgeon. Exceptionally, traumatic inoculation of the fungus by the tegument system is possible. Infection can also be established in the skin and mucosa by inoculation through other pre-existing lesions, which may explain the presence of yeasts in the histological sections and the non-involvement of the lungs in the reported case [14,15].

Authors study the possible association of Leishmaniasis and Paracoccidioidomycosis in serum studies of 836 dogs, of which 449 were positive serum for Leishmaniasis, while 387 were negative serum. The main antigen of *Paracoccidioides brasiliensis* (gp43) had a higher reactivity in dogs with Leishmaniasis (79.9 %) than in negative serum dogs (54 %) [15].

The reported case showed coexistence of both parasites in the same infected individual. The predisposition to Paracocodioidomycosis after Leishmaniasis infection is justified by factors already elucidated, but the reason for the non-progression of the fungus after years of evolution could be related to its inhibition due to the presence of the protozoan in the same wound. This phenomenon may be explained by future studies that need to be performed to answer such questions [15].

The management of leishmaniasis still represents a great challenge, its treatment is equally variable and still controversial, with no universal consensus on the most effective type of medication, period of use, latency periods and control of its sequelae. Local treatment of small lesions may not be necessary, as larger lesions may be treated with surgical excision, curettage or cryotherapy. A limited number of drugs are available for the treatment of leishmaniasis, and some systematic reviews tried to reach a consensus on an ideal drug treatment for patients using different interventions. In general, no single therapy is 100 % effective for leishmaniasis [4,7,17].

The use of some medications has been proposed, such as pentavalent antimony, lipid compounds associated with amphotericin, oral imidazole compounds, and several other local or topical treatments. There is interest in oral anti-manic agents and azole therapy, which comprises fluconazole, ketoconazole and itraconazole which

can be an alternative that fulfills this requirement. Fluconazole has advantages over other azoles, including a longer half-life, increased skin tissue concentrations, and low toxicity [7,18].

We opted for drug treatment since the patient had no bone or airway involvement, no fistula or infectious process that would justify the surgical approach, conservative therapy is always the first choice and has been shown to be effective, as observed in a systematic review with azole therapy [18].

4. Final considerations

The strictly mucosal involvement in Leishmaniasis is the most serious complication of *L. brasilienses* infections and may lead to a disfiguring and potentially fatal condition in a variable proportion of patients. In addition, associations with other infectious diseases, such as Paracoccidioidomycosis may exist with potential parasitological synergism that needs to be better studied.

Declaration of Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Ethical approval

Does not refer to our study, exempt ethical statement for this type of paper.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

All authors contributed to each stage of the paper's development. The Ophir Loyola Hospital (Belém, Pará, Brazil) for their valuable contribution in reference monitoring for patients and support to professionals; also, to able to give conditions for this study could be performed. Centro Universitário do Pará – CESUPA (Belém, Pará, Brazil) and Evandro Chagas Institute (Belém, Pará, Brazil) for all collaboration in the diagnosis, treatment and preparation of this manuscript.

Registration of research studies

1 Name of the registry:
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