Case Report
A Case of Oral Histoplasmosis Concomitant with Pulmonary Tuberculosis

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Received 21 August 2019; Accepted 8 October 2019; Published 3 November 2019

The superficial intraoral lesions of histoplasmosis occurring concomitant to tuberculosis, in a 46-year-old man, are reported. The human immunodeficiency virus (HIV) infection test was negative. The immunosuppression caused by tuberculosis in our patient probably had an important role in the development of intraoral lesions of histoplasmosis. Here, we discussed the role of the dentist in the diagnosis of these infectious diseases, highlighting the importance of anamnesis and the histopathology/immunohistochemistry exams.

1. Introduction

H. capsulatum infects the human host and grows in yeast form [1–7]. The disease may be self-limiting or asymptomatic in healthy individuals, or still to occur in the disseminated form, including the oral cavity [1–7].

In the mouth, the histoplasmosis manifestations may affect any region but are commonly in the tongue, palate, and oropharyngeal mucosa [7, 8]. Furthermore, the oral lesions present from granulomatous nodules to painful shallow or deep ulcers with symptoms of odynophagia and dysphagia [7].

The single oral manifestation of histoplasmosis in immunosuppressed individuals is rare and the diagnosis is challenging [3, 9]. In addition, at the time of diagnosis of oral histoplasmosis, the health professional should investigate the presence of concomitant diseases, such as malignant neoplasms or other infections as tuberculosis [10].

The occurrence of oral histoplasmosis in patients with pulmonary tuberculosis has been reported in some studies mainly due to immunosuppression and physical weakness caused by bacterial disease [8, 10, 11]. The tuberculosis has been concomitantly diagnosed in approximately 10% of Brazilians with histoplasmosis [12]. Antonello et al. [8] showed that 36% of patients with oral histoplasmosis had concomitant active pulmonary tuberculosis, 18% had malignant neoplasia, 9% had chronic obstructive pulmonary disease, and 9% had no other disease at the time of diagnosis of fungal infection.

Here, we report a case of oral histoplasmosis in a patient with a diagnosis of pulmonary tuberculosis. The role of the dentist in the diagnosis of this infectious disease including the importance of detailed anamnesis and the histopathology/immunohistochemistry exams is discussed.

2. Case Report

A 46-year-old man was attended in the dental clinic complaining of symptomatic oral lesions with two months in duration. The intraoral physical examination revealed diffuse, friable, vegetative areas on the right upper alveolar ridge, hard palate, and left inferior alveolar ridge (Figures 1(a) and 1(b)). His medical history revealed a diagnosis of tuberculosis about a month ago in which the
expectorated sputum smears were positive for bacteria and acid-fast bacilli. In addition, at the time of diagnosis of tuberculosis, the patient had a significant weight loss and asthenia. The patient was under antibacterial therapy (oral isoniazid (INH) 225 mg/day, rifampicin (RFP) 450 mg/day, pyrazinamide 1,200 mg/day, and ethambutol (EB) 825 mg/day). Testing for human immunodeficiency virus (HIV) infection was negative. Furthermore, the patient confirmed smoking and chronic alcoholism. He worked as a night flow controller on the side of a highway and lived very close to the countryside. After knowing the patient’s medical history, the main hypothesis for oral lesions was tuberculosis.

An incisional biopsy of the right upper alveolar ridge showed connective tissue with intense inflammatory infiltrate with a granulomatous pattern, consisting of giant multinucleated inflammatory cells and vacuolated macrophages, with innumerable fungi suggestive of *H. capsulatum* (Figures 2(a) and 2(b)). Staining slides with periodic acid-Schiff (PAS) (Figures 2(c) and 2(d)) and Grocott-Gomori methenamine silver were positive for the morphological

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**Figure 1**: Clinical aspect of intraoral lesions in the palate and alveolar ridge regions (a, b).

**Figure 2**: Connective tissue with intense inflammatory infiltrate with a granulomatous pattern, consisting of giant multinucleated inflammatory cells and vacuolated macrophages, with several fungi suggestive of *H. capsulatum*—(hematoxylin-eosin stain; (a) ×200, (b) ×400). In (c) and (d), the periodic acid-Schiff (PAS) staining showed vacuolated macrophage with positivity for *H. capsulatum* ((c d) ×400). Note the numerous small rosy dots (arrow).
characteristics of *H. capsulatum*. In addition, the immuno-
histochemical reactivity to Histoplasma using polyclonal
antibody was positive; for polyclonal *P. brasiliensis, Leish-
mania spp.* and Calmette-Guérin bacillus were negative.
The diagnosis of oral histoplasmosis was established. We
did not search for fungi in other biological samples.

Initially, the drug was maintained for tuberculosis and
prescribed fluconazol (400 mg/day) for seven months for
treatment of oral histoplasmosis. During the follow-up, when
a gradual increase in body weight was noted, fluconazole was
substituted for itraconazole 200 mg/day for eight months
with the resolution of oral histoplasmosis lesions. The clinical
control one year after initiation of itraconazole treatment can
be seen in Figures 3(a) and 3(b). One year after the initial
treatment of tuberculosis, the patient was cured.

3. Discussion

Tuberculosis remains a public health problem in many coun-
tries including Brazil; and with the immunosuppression
resulting from the disease, some opportunistic infections
may develop, especially in cases associated positive HIV
[10, 13]. In the present case reported, a 46-year-old man
who presented to her dentist with superficial lesions located
in several intraoral sites was in treatment for tuberculosis.
The detailed clinical investigation showed that our patient
was HIV negative and the oral histoplasmosis diagnosis was
established after laboratory exams excluding other infections.
The immunosuppression caused by tuberculosis in our
patient probably had an important role in the development
of intraoral lesions of histoplasmosis.

Sometimes, the diagnosis of intraoral histoplasmosis is
challenging because the lesions can be mimicking malignan-
cies, other fungal diseases, or traumatic ulcers, and the biopsy
has been a useful resource to establish the final diagnosis
[1, 2, 14]. In routine staining (hematoxylin and eosin),
PAS and Grocott-Gomori silver methylamine staining can
detect fungi within prominent macrophages and giant
Langhans-type giant cells. In summary, initially, the histopa-
thyology directed our diagnostic hypotheses and, finally, the
use of immunohistochemistry was essential to eliminate
other oral infectious diseases and establish the final diagnosis.
Although we used polyclonal antibodies in our pathological
investigation, the analysis made it possible to eliminate the
possibility of other infections, including oral tuberculosis
and paracoccidioidomycosis. Besides, serology and culture
tests may assist in establishing the diagnosis of this fungal
disease [1].

Tuberculosis mainly affects the lungs and can present
several complications in its clinical course causing weakness,
cough, weight loss, shortness of breath, among other signs
and symptoms, and the possibility of concomitant infections
[1, 10]. As shown in our case, weight loss and asthenia are
common clinical signs in patients with concomitant active
pulmonary tuberculosis and histoplasmosis [8]. In addition,
dysphagia and fever can also be found among these patients
[8]. Interestingly, at the time of diagnosis, our patient had
several complications but the laboratory tests were negative
for HIV. In case a similar to ours, the main suspect has been
of oral tuberculosis [2]. All these clinical characteristics and
information collected during the anamnesis become the diag-
nostic process challenging.

Initially, our patient could not be treated with itracona-
zole. The physician instituted this medicament after e
fective response to tuberculosis treatment. This decision was also
made due to the drug interaction between rifampicin and
itraconazole, where itraconazole levels significantly decrease
in the presence of the other, so these two drugs should not
be administered concomitantly [15, 16]. Additionally,
amphotericin B deoxycholate is another medicament that
can be used to treat acute and chronic cavitary pulmonary
histoplasmosis [17].

*H. capsulatum* has been considered a fungus endemic in
the Mississippi and Ohio River Valleys, also in Central and
South America, Asia, and Australia [3, 6, 7, 14]. In all
Brazilian regions, this infectious disease has been very
common in men between the fourth and fifth decades of
life with a high mortality rate; this data may be underesti-
mated due to the lack of mandatory reporting [12]. More-
over, in Brazil, oral lesions of histoplasmosis may lead the
dentist to suspect of other infections such as the paracoc-
cidioidomycosis [3, 7].

Although the number of fungal oral lesions diagnosed in
Brazilian Referral Centers is relatively low [7, 18], the cases of
disseminated histoplasmosis with oral manifestation have
increased in recent years, especially in South American men.
[1] and consequently has caused concern. Then, the biopsy for histopathology and culture of oral suspected lesions by dentists, particularly in immunosuppressed patients, is mandatory for establishing the diagnosis of this fungal infection.

4. Conclusion

In summary, it is prudent for the dentist to investigate the patient’s health status considering the opportunistic oral mucosal infections, especially in immunosuppressed patients. The clinical diagnosis of oral histoplasmosis can be challenging, and a detailed anamnesis associated with complementary laboratory tests are required. Correct therapeutic indication and prolonged follow-up are essential for patient healing to avoid recurrence of this fungal infection.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

The authors declare that the paper-processing charges were supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; No. 155359/2016-9).

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