Oral Diag. 2020;05:e20200025.

ORIGINAL ARTICLE

Tuberculosis: Primary Diagnosis From an Oral Ulcer

Bruno Teixeira Gonçalves Rodrigues[1]*
Alexandre de Freitas Caetano Guimarães[1]
Fábio Ramôa Pires[1]
Mônica Simões Israel[1]

Abstract:

Tuberculosis (TB) is a contagious chronic disease caused by Mycobacterium tuberculosis. Tuberculosis can manifest within the oral cavity as a painless chronic ulcer - which resembles several other oral diseases - at this moment, diagnosis can be achieved through an incisional biopsy. We report a case of TB diagnosed from an oral ulcer in a 54-year-old male referred for evaluation of a 1-month lasting non-healing ulcer in the tongue. Intraoral clinical examination revealed a single painless chronic ulcer with irregular borders located in the apex of the tongue. Squamous cell carcinoma was the main clinical diagnosis; however, after performing an incisional biopsy and histopathological examination, TB was suggested, and confirmed through the purified protein derivative (PPD) skin test. Patient was then referred to a medical service and confirmed lung involvement by the disease, starting the treatment protocol for TB. A 1-month follow-up showed complete regression of the oral lesion. The patient completed the TB treatment and is under clinical follow-up for 2 years.

Keywords: Tuberculosis. Oral Ulcer; Tongue; Mycobacterium tuberculosis.

[1] Rio de Janeiro State University, Department of Diagnosis and Therapeutics - Rio de Janeiro - Rio de Janeiro – Brasil.

Correspondence to:
Bruno Teixeira Gonçalves Rodrigues
E-mail: brodriguesodonto@gmail.com

Article received on November 19, 2020.
Article accepted on December 23, 2020.

DOI: 10.5935/2525-5711.20200025

INTRODUCTION

Tuberculosis (TB) is a contagious chronic infectious disease caused by *Mycobacterium tuberculosis* - also called Koch's bacillus – usually transmitted by air, from individual to individual through infected droplets that are expelled when coughing[1,2]. Rarely, TB can manifest primarily within the oral cavity as a painless chronic ulcer, mimicking other ulcerative oral conditions, such as squamous cell carcinoma (SCC)[3]. In these cases, dentists can play an important role in the diagnosis, leading to a better prognosis for the patient[1-3].

Therefore, we report a case of a 54-year old male presenting a 1-month lasting non-healing ulcer in the tongue diagnosed as primary oral TB.

CASE REPORT

A 54-year-old male was referred to the Stomatology clinic, Rio de Janeiro State University, for evaluation of a 1-month lasting non-healing ulcer in the tongue that resulted in dysphagia and dysphonia. Medical history was non-contributory, and the patient denied any tobacco or alcohol consumption. Extraoral clinical examination showed no alterations. Intraoral clinical examination revealed the presence of a single painless ulcer, measuring 4 cm in its largest diameter with irregular indurated borders in the apex of the tongue (Figure 1). Although uncommon in this anatomical location, due to the clinical aspect of the lesion, SCC was the clinical diagnosis and an incisional biopsy was performed under local anesthesia.

The specimen was immersed in 10% formaldehyde and sent for histological analysis. Hematoxylin and eosin stained 5 µm histological sections showed multiple granulomas with central necrotic areas, surrounded by an intense mixed inflammatory infiltrate, and exocytosis. Also, Langhans-type multinucleated giant cells could be observed in higher magnification (Figure 2). Due to the clinical and histological features, TB was suggested. The tuberculin skin test (purified protein derivative - PPD) was requested and its positivity confirmed the diagnosis of TB. The patient was referred for medical evaluation in the Infectious Diseases department and pulmonary evaluation showed lung involvement, thus the oral ulcer was a sign of the disseminated TB. He was prescribed the drug protocol treatment for TB, including isoniazid, rifampicin, pyrazinamide and ethambutol. In a 1-month follow-up at the Stomatology clinic, oral examination showed no signs of the disease (Figure 3). The patient completed the TB treatment and is under clinical follow-up for 2 years.

Figure 1. Initial clinical features of oral Tuberculosis. A single painless ulcer, measuring 4 cm in its largest diameter with irregular indurated borders in the apex of the tongue.

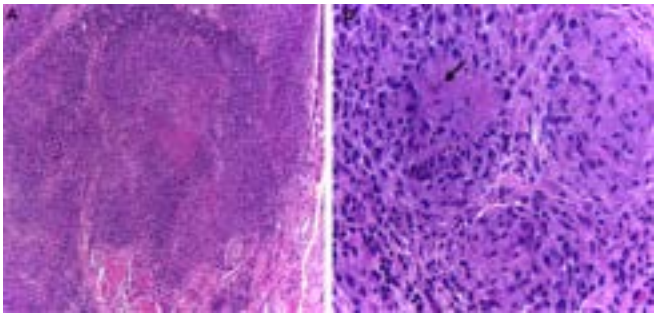

Figure 2. A - Histological characteristics of oral Tuberculosis showing the presence of granulomas with multinucleated giant cells and macrophages in the central portion (HE, 100x). B - Histological characteristics of oral Tuberculosis showing the presence of focal areas of necrosis (HE, 400x).

DISCUSSION

Tuberculosis is one of the 10 main causes of death originating from a single infection throughout the planet - every year around 10 million people become sick due to TB worldwide. It is estimated that 1.7 billion people worldwide are infected with *M. tuberculosis* and are at risk of developing TB[2]. The disease is more prevalent in developing countries, which do not offer adequate sanitary conditions for the whole population, thus favoring its dissemination[3].

Tuberculosis can affect individuals at any age - showing higher prevalence in adults – and shows a predilection for males (2:1)[2], as shown by the current report. The lung is the predominant anatomical site of TB; however the extra pulmonary form of the disease

Figure 3. Final clinical aspect after isoniazid, rifampicin, pyrazinamide and ethambutol drug protocol on a 1-month follow-up.

can affect other sites such as the lymph nodes and the oral cavity[4]. Lesions located within the oral cavity are rare, with a reported incidence of 0.5 to 5% of all patients with TB[5]. These can be primary - when it occurs from direct inoculation of the oral tissues - or secondary, due to the spread from other infection sites, especially the lungs[5]. Systemic factors are believed to have a major influence on the onset of oral ulcers in TB, especially associated with immunosuppression[6]. Local factors such as poor oral hygiene, local trauma, chronic inflammation, cysts, and dental abscesses can also contribute to the development of lesions[6].

Oral TB usually affects the tongue, but the gingiva, vestibule, palate and lips can also be affected[4]. In most cases it presents as a chronic painless ulcer or, less commonly, as a nodular mass[7]. In the current report, oral primary TB manifested as a chronic painless ulcer with irregular borders in the apex of the tongue, causing dysphagia and dysphonia.

Diagnosis of oral tuberculosis can be challenging due to its nonspecific clinical characteristics. The most important clinical differential diagnosis is SCC, due to its clinical presentation as a painless ulcer in early stages[7]. As SCC is much more common than TB in the oral cavity, it is likely that SCC should be considered as a clinical diagnosis when dealing with an oral chronic non-healing ulcer, especially in patients presenting no pulmonary/respiratory symptoms that could suggest tuberculosis. Differential diagnosis of oral TB should also include syphilis, actinomycosis, traumatic ulcers, paracoccidioidomycosis and Wegener's granulomatosis[7,8]. Therefore, an incisional biopsy and histopathological examination of the specimen are essential for early correct diagnosis enabling prompt treatment[4], as shown by the current report.

Histological features of oral TB include the presence of granulomas surrounded by histiocytes, intense mixed inflammatory infiltrate, multinucleated giant cells and central areas of necrosis[7]. Special stains with acid-resistant substances such as carbolfuchsin or the Ziehl Neelsen technique can be used to stain *M. tuberculosis*[9]. However, in some cases few mycobacteria will stain using this method, so a negative result does not rule out the suspicion of TB[5]. In the current report, histopathological examination was suggestive of TB, that was later confirmed by the PPD skin test.

When TB is diagnosed from an oral lesion, additional exams are required to identify the source of infection before assuming that the mouth is the primary site, due to the rarity of this presentation[9]. TB diagnosis is based on a positive PPD test (also called Mantoux test), but this test has some limitations in differentiating infection from active disease and has a low sensitivity in immunocompromised patients[10]. Chest radiographs are widely used for evaluation of pulmonary involvement in TB[4]. Polymerase chain reaction for *M. tuberculosis* DNA is also used for diagnosis and is considered the best alternative for its detection[11]. In the present study, the patient was referred for medical follow-up and tests to investigate other infection sites and as the PPD skin test was positive and chest radiograph showed lung involvement the diagnosis of TB was confirmed.

TB treatment is based on a combination of drugs and the most widely used drug protocol includes isoniazid, rifampicin, pyrazinamide and ethambutol[12-14]. These drugs are administered daily for the first two months, followed by another four month period with only isoniazid and rifampicin intake[14]. The current report showed a rapid involution of the oral lesion after 1 month of isoniazid, rifampicin, pyrazinamide and ethambutol drug protocol. Even with the regression of the oral lesion, the patient must be motivated to undergo the complete treatment to treat the primary pulmonary site in order to prevent bacterial antibiotic resistance.

CONCLUSION

Tuberculosis must be included in the differential diagnosis of oral chronic painless ulcers. Despite being unusual in the oral cavity, early detection of oral TB is extremely important as it allows immediate starting of

appropriate treatment leading to better prognosis for the affected patients.

ETHICS

We state that we have followed the Helsinki declaration and that written permission was obtained from the patient included in the present report.

REFERENCES

1. Pinto ASB, Furuse C, Soares HA, Thomaz LA, Teixeira LN. Simultaneous oral, bone, and lung manifestations of tuberculosis. J Oral Diag. 2017;2(1):e20170033.
2. World Health Organization (WHO). Global tuberculosis report 2019 [Internet]. Geneva: WHO; 2019; [access in 2020 Jul 07]. Available from: https://apps.who.int/iris/bitstream/handle/10665/329368/9789241565714-eng.pdf?ua=1/
3. Arora KS, Garg S, Kaur P, Mohapatra S. Primary oral tuberculosis on the tongue mimicking squamous cell carcinoma. Indian J Tuberc. 2018 Jan;65(1):84-6.
4. Ju W, Fu Y, Liu Y, Tan Y, Dong M, Wang L, et al. Clinical and pathologic analyses of tuberculosis in the oral cavity: report of 11 cases. Oral Surg Oral Med Oral Pathol Oral Radiol. 2018 Jan;125(1):44-51.
5. Jain P, Jain I. Oral manifestations of tuberculosis: step towards early diagnosis. J Clin Diagn Res. 2014 Dec;8(12):ZE18-ZE21.
6. Nagaraj V, Sashykumar S, Viswanathan S, Kumar S. Multiple oral ulcers leading to diagnosis of pulmonary tuberculosis. Eur J Dent. 2013 Apr/Jun;7(2):243-5.
7. Hale RG, Tucker DI. Head and neck manifestations of tuberculosis. Oral Maxillofac Surg Clin North Am. 2008;20:635-42.
8. Ryan GJ, Shapiro HM, Lenaerts AJ. Improving acid-fast fluorescent staining for the detection of mycobacteria using a new nucleic acid staining approach. Tuberculosis (Edinb). 2014 Sep;94(5):511-8.
9. Souza BC, Lemos VMA, Munerato MC. Oral manifestation of tuberculosis: a case-report. Braz J Infect Dis. 2016;20(2):210-3.
10. González-Martín J, García-García JM, Anibarro L, Vidal R, Esteban J, Blanquer R, et al. Consensus document on the diagnosis, treatment and prevention of tuberculosis. Arch Bronconeumol. 2010 May;46(5):255-74.
11. Salian NV, Rish JA, Eisenach KD, Cave MD, Bates JH. Polymerase chain reaction to detect Mycobacterium tuberculosis in histologic specimens. Am J Respir Crit Care Med. 1998 Oct;158(4):1150-5.
12. Sacchettini JC, Rubin EJ, Freundlich JS. Drugs versus bugs: in pursuit of the persistent predator Mycobacterium tuberculosis. Nat Rev Microbiol. 2008 Jan;6(1):41-52.
13. Alsultan A, Peloquin CA. Therapeutic drug monitoring in the treatment of tuberculosis: an update. Drugs. 2014 Jun;74(8):839-54.
14. Sierra C, Fortun J, Barros C, Melcon E, Condes E, Cobo J, et al. Extra-laryngeal head and neck tuberculosis. Clin Microbiol Infect. 2000 Dec;6(12):644-8.