

Secondary Oral Tuberculosis in HIV-Negative Patient

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Abstract: Oral manifestations of tuberculosis (TB) are exceedingly uncommon and are usually secondary to pulmonary TB. The development of extrapulmonary TB is mainly facilitated by immunosuppression. The oral manifestations of TB can be highly variable and non-specific therefore they can cause difficulties in diagnosis and delay in instituting the appropriate treatment. This article describes an infrequent case of secondary oral TB in an adult HIV-negative patient. The aim of this case report was to emphasize the importance of considering TB in the differential clinical diagnosis of ulcers affecting the oral mucosa.

Keywords: Oral tuberculosis, oral ulcers, HIV infection

1. Introduction

According to WHO (2018), tuberculosis (TB) represents a serious public health problem nowadays, with approximately 10.0 million (range, 9.0-11.1 million) new cases worldwide. Among all TB cases, 8.6% were persons living with HIV. Globally, TB is the leading cause of death due to a single infectious agent and the leading cause of death among individuals living with human immunodeficiency virus (HIV) (1,2). In 2018, the United States of America, recorded a total TB incidence of 9800 cases (3 cases per 100,000 population) with a TB-HIV incidence rate of 0.15 (CI 0.13-0.18). During the same year, 12,000 cases of TB were reported in Argentina, resulting in an incidence rate of 27 cases per 100,000 population (CI 23-31) In addition the rate of incidence of TB-HIV co-infection was 1.9 (CI 1.1-2.9) per 100,000 inhabitants (1).

TB is a chronic infectious disease usually caused by *Mycobacterium tuberculosis*. Although pulmonary TB is the most frequent, all parts of the body, including the oral mucosa, may be affected (3, 4, 5, 6).

Extrapulmonary TB represents 5% to 50% of all TB cases (7,8). The frequency of extrapulmonary presentation is genetically determined (9), although there are other factors that facilitate its development. These non-genetic factors are mainly related to the existence of immunosuppression (HIV-infected patients, transplanted patients or under prolonged treatment with steroids) and they could explain the increase of extrapulmonary forms over the last few years (10, 11). Furthermore, several risk factors associated with TB such as smoking, alcohol consumption, use of other drugs and diabetes have been described (12).

Oral manifestations of TB are exceedingly rare (0.5-1.5% of patients with the disease) and are generally secondary to pulmonary TB (3, 6, 13, 14, 15). The oral manifestations of TB can be highly variable and non-specific therefore they can cause difficulties in diagnosis and delay in instituting the appropriate treatment. This article describes an infrequent case of secondary oral TB in an adult HIV-negative patient.

2. Case report

A 47-year-old male patient presented for consultation at the Oral Medicine Department of the School of Dentistry, University of Buenos Aires, with a history of smoking cigarettes, weight loss, fever, chronic cough and respiratory problems caused by polyurethane fume exposure. The patient reported the presence of a painful lesion of 35 days evolution. Despite treatment with three different antibiotics (amoxicillin, cephalosporin and penicillin benzathine) lesion did not heal.

Examination of the oral cavity revealed the presence of a painful single ulcer covered with a yellowish exudate, with irregular contours and indurated to touch in the dorsal surface of the tongue (Fig. 1). No other oral mucosa lesions were observed. Physical examination showed multiple small submandibular lymphadenopathy on both sides of upper neck.



Figure 1: Tongue ulcer with a slightly undermined border covered with a yellowish exudate

Based on the oral lesion of the dorsal surface of the tongue and associated lymphadenopathy presumptive diagnosis of TB and HIV coinfection was established and Blastomycosis or Histoplasmosis as differential diagnosis. In order to obtain diagnosis of certainty the following diagnostic tests were indicated: sputum bacilloscopy, chest radiography, antibodies to HIV 1-2 and VDRL.

Relevant routine investigations were normal. Results of diagnostic tests were consistent with TB: sputum was positive for acid-fast bacillus (AFB), X ray chest revealed cavitory lesion, treponemal test and HIV 1-2 antibodies were negative.

The patient was referred to infectiology and after about 2 months of drug therapy (triple association: isoniazid-rifampicin-streptomycin) clinical follow-up showed complete remission of tongue ulcer.

3. Discussion

Oral TB lesions may be either primary or secondary in occurrence. Secondary oral TB is the most common (3, 6, 8). Oral tuberculous ulcer may be the result of spread by hematogenous or lymphatic route but can also be caused by self-infection through infected sputum, as probably happened in the case reported (16, 17). While the constant flow of saliva and its antibacterial properties protect from tubercle bacilli invasion to the oral mucosa, local trauma, poor hygiene and inflammation may promote infection (14, 15).

The case report presents several features coincide with literature: Tuberculous ulcer, which affects most often middle-aged individuals and the elderly, is the most frequent manifestation of secondary TB. This ulcer causes a deep pain that hinders speech and food intake. In the case presented this situation caused weight loss in the patient (3, 13, 17). Moreover, extrapulmonary TB is common in HIV-positive individuals (16, 18, 19) but as discussed previously the patient was HIV negative. In addition, the patient was a heavy smoker and tobacco is one of the risk factors associated with the development of TB (12).

Extrapulmonary oral TB is very uncommon and their clinical appearance is variable. This situation, particularly in immunocompetent patients, coupled with the absence of rapid diagnostic test can hinder and delay the start of treatment. This explains delayed diagnosis in the case reported; the patient consulted three professional and was medicated with three different antibiotics without improvement. In this context and given that TB remains a serious public health problem today, it is important that health professionals are aware that detection of oral lesions caused by *Mycobacterium tuberculosis* is an effective strategy in the early diagnosis of TB allowing the appropriate therapy administration and promptly disease control.

4. Conclusion

The present study reported the presence of a single tuberculous ulcer in the tongue of HIV-negative patient. This uncommon manifestation, particularly in an immunocompetent patient, should alert health professionals about the importance of considering TB in the differential diagnosis of ulcers affecting the oral mucosa to establish without delay diagnosis certainty and timely treatment of disease.

5. Conflict of interest

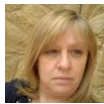
The authors declare no conflicts of interest.

References

- [1] Global tuberculosis report 2019. Geneva: World Health Organization; 2019. License ICCBY-NC-SA3.0160.
- [2] Gupta RK, Lucas SB, Fielding KL, Lawn SD. Prevalence of tuberculosis in post-mortem studies of HIV-infected adults and children in resource-limited settings: a systematic review and meta-analysis. *AIDS* 2015;29:1987–2002.
- [3] Ebenezer J, Samuel R, Mathew GC, et al. Primary oral tuberculosis: report of two cases. *Indian J Dent Res* 2006; 17: 41-4.
- [4] Pavlinac PB, Lokken EM, Watson JL, Richardson BA, Crup JA, Jhon-Stewart GC. *Mycobacterium tuberculosis* bacteremia in adults and children: a systematic review and meta-analysis. *Int J Tuberc Lung*.2016;20(7):895-902
- [5] Araj GF, Saade A, Itani LY, Avedissian AZ. Tuberculosis burden in Lebanon: evolution and current status. *J MedLib* 2016;64(1):1-7
- [6] Kim SY, Byun JS, Choi JK, Jung JK. A case report of a tongue ulcer presented as the first sign of occult tuberculosis. *BMC Oral Health*. 2019;19(1):67. Published 2019 Apr 29. doi:10.1186/s12903-019-0764-y
- [7] Ramírez-Lapausa, M., Menéndez-Saldaña, A., & Noguerado-Asensio, A. (2015). Extrapulmonary tuberculosis. *Revista Española de Sanidad Penitenciaria*, 17(1), 3-11. doi.org/10.4321/S1575-06202015000100002
- [8] Kakisi OK, Kechagia AS, Kakisis IK, Rafailidis PI, Falagas ME. Tuberculosis of the oral cavity: a systematic review. *Eur J Oral Sci*.2010;118:103-109
- [9] Britton WJ, Fernando SL, Saunders BM, Sluyter R, Wiley JS. The genetic control of susceptibility to *Mycobacterium tuberculosis*. *Novartis Found Symp*, 281 (2007), pp. 79-89
- [10] Khateeb D, Kang M, Capitle E, Feurdean M. Oral Tuberculosis: A Rare Manifestation of Disseminated Disease in a Patient with Dermatomyositis on Chronic Corticosteroids. *Case Rep Med*. 2016;2016:8193178. doi:10.1155/2016/8193178
- [11] Kapoor S, Gandhi S, Gandhi N, Singh I. Oral manifestations of tuberculosis. *Chrimed J Health Res*. 2014;1:11-4.
- [12] Silva DR, Muñoz-Torrico M, Duarte R, et al. Risk factors for tuberculosis: diabetes, smoking, alcohol use, and the use of other drugs. *J BrasPneumol*. 2018;44(2):145–152. doi:10.1590/s1806-37562017000000443.
- [13] Taute RB, Wylie J, Carter L. Oral and Maxillofacial Surgery: An unusual extranodal presentation of *Mycobacterium Tuberculosis* in the upper lip. *DentUpdate*2015;42:473-5
- [14] Awasthi S, Singh V, Nizamuddin M. Tuberculosis of oral mucosa. *Internet J Infect Dis* 2010; 8(2).

- [15] Krawiecka E, Szponar E. Tuberculosis of the oral cavity: an uncommon but still a live issue. *Postep Derm Alergol*.2015;4:302-306
- [16] Jain P, Jain I. Oral Manifestations of Tuberculosis: Step towards Early Diagnosis. *J Clin Diagn Res*. 2014;8(12):ZE18–ZE21. doi:10.7860/JCDR/2014/10080.5281
- [17] Michalak A, Wojtas G, Kidawa I, et al. Tuberculosis of tongue in patient with disseminated pulmonary tuberculosis. *Pneumonol Alergol Pol* 2004; 72: 28-31.
- [18] Bruchfeld J, Correia-Neves M, Källenius G. Tuberculosis and HIV Coinfection. *Cold Spring Harb Perspect Med*. 2015;5(7):a017871. Published 2015 Feb 26. doi:10.1101/cshperspect.a017871
- [19] Shivakoti R, Sharma D, Mamoon G, Pham K. Association of HIV infection with extrapulmonary tuberculosis: a systematic review. *Infection*. 2017;45(1):11–21. doi:10.1007/s15010-016-0960-5

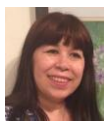
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