Tuberculosis of the oral cavity

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Abstract
Tuberculosis (TB) of the tongue is not a common finding diagnosis, even if consider endemic areas. Tuberculosis of the tongue sometimes can mimic lingual neoplasm. Oral tuberculosis is rarely primary as mechanism, and frequently secondary to pulmonary tuberculosis. There are many suspect lesions that can be classified as tuberculosis, such as tumor mass, ulcerative lesion or fissure. It is very important for diagnosis to perform histopathological examination of the biopsy. We present here the case of a 74-year-old man who developed lingual tuberculosis with a tumor aspect concomitant with pulmonary tuberculosis. Histopathological and immunohistochemical examinations established the diagnosis of lingual tuberculosis.

Keywords: oral ulcers, tongue tuberculosis, tumor mass, histopathological examination.

Introduction
Primary tuberculosis (TB) of the oral cavity, including tongue, is very rare because of continuous cleaning of oral mucosa by saliva and absence of lymphoid follicles in tongue [1–3]. Secondary tuberculosis of oral cavity is 0.2 to 1.5% of extrapulmonary tuberculosis cases [4, 5]. The most common locations are: pleural TB, lymphadenitis TB, osteoarticular TB, vertebral TB, urogenital TB, pericarditis, peritoneal TB, TB laryngitis TB, meningitis TB (with or without miliary TB) [6].

There are many factors that can contribute in oral tuberculosis lesions, such as long-term smoking, less oral hygiene or different oral traumas. Local clinical exam, a good anamnesis, histopathological exam are very important for the diagnosis. Golden standard for diagnosis is performing histopathological exam of the biopsy from the suspect lesion.

Aim
We present here the case of a 74-year-old man who presented with an ulcerative tumor of the tongue, in whom the histopathology and immunohistochemistry exams were positive for lingual tuberculosis.

Case report
A 74-year-old men, worked in a foundry, toxic environment for 25 years (SiO₂), was presented in September 2012 in the outpatient department and was diagnosed with community pneumonia left upper lobe (LUL), after a routine chest X-ray, being without clinical symptoms. Patient comes from low socioeconomic status; he is a chronic smoker 60 pack-years and occasional alcoholic. On examination, patient was well built with good general condition.

Despite the administration of antibiotics, the radiological lesions remain unmodified, showing ulcerous homogeneous opacities, which tend to conflate found on the LUL and Fowler segment.

Between September 2012 and March 2013, no data was found concerning the patient.

In March 2013, due to an ENT (ear, nose, and throat) service check-up, he was diagnosed with ulcerated tumor of the tongue. Examination of oral cavity revealed an ulcerated lesion, about 1.5 cm involving right lateral border of tongue, whitish, opaque with smooth surface and well-defined margins. Other examination of oral cavity and larynx was normal. There was no cervical lymphadenopathy.

A month later, while being hospitalized, surgery with excision of the tumors lump tongue was performed. Biopsy of the ulcer was taken, which showed granulomatous inflammation, suggestive of tuberculosis: a multitude of granulomatous nodes deep muscle layer, made of epithelioids nodes and multinucleated Langhans giant cells, same with central necrosis, partially looking effusion, ultra-infected with a tendency to confluence (Figures 1–3).

Trichrome staining revealed the presence of intense collagen fibrosis within the epithelial erosion zones (Figure 4) and within the tuberculosis node (Figure 5).

In order to emphasize specific inflammatory cells, in the paraffin-embedded material, we have performed serial
sections in the rotary Microm HM350 microtome equipped with a transfer system of the sections in a water bath (STS, Microm); these were collected on slides coated with poly-
L-Lysine, and dried in a thermostat at 37°C for 24 hours. Then, we followed the protocol for performing classic sections, highlighting some specific immunohistochemical markers for immune system cells. Thus, for macrophage cell types we used the CD68 antibody (clone KP1, 1/200, Dako); to highlight T-lymphocytes, we used the CD3 anti-
body (clone F7.2.38, 1/100, Dako) and CD20 antibody (clone L26, 1/100, Dako) to highlight B-lymphocytes.

As one can see from our images (Figures 6 and 7), the dominant cellularity within the nodule was the macrophage system. The CD68 antibody showed heavy scoring for multinucleated giant cells (Langhans cells), epithelioid cells and macrophages of the lymph tuberculosis inter-

nodular diffuse inflammatory infiltrate.

T-lymphocytes were identified as a spread diffuse infiltrate within the tuberculosis node (Figure 8), the inflammatory infiltrate, while B-lymphocytes were found only in the outskirts of tuberculosis nodules (Figure 9).

The patient was referred to our Pulmonology Hospital for further management of tuberculosis stating May 2013. Respiratory system examination revealed scattered upper left coarse crepitations corresponding persistent radiolo-
gical changes (bilateral upper lobe consolidation). Repeated direct examination of sputum and culture for AFB (acid-
fast bacilli) was negative. Serological studies for HIV (human immunodeficiency virus) and VDRL (venereal disease research laboratory) were non-reactive. Blood tests were within normal limits except for a raised erythrocyte sedimentation rate (48 mm/h).

The standard radiological examination revealed the presence of numerous nodular and micronodular lesions predominantly disseminated in the upper two-thirds of both lungs, with different intensities, sometimes with a tendency to confluence and areas of included hypertrans-
parency generated by partial evacuation of necrotic tissue (Figure 10). Some were sharply demarcated opacities and others had diffuse contours.

At bronchoscopy, there were no visible endobronchial specific changes, except a bilateral bronchitis aspect. A diagnosis of pulmonary tuberculosis was confirmed by the culture of Mycobacterium tuberculosis from bronchial aspirate.

Figure 1 – Microscopic image on the tongue with the presence of lingual mucosa erosion affecting both super-
ficial epithelium and chorion. In the lesion, we noted the abundant presence of inflammatory infiltrate, consisting predominantly of lymphocytes. HE staining, ×100.

Figure 2 – Profound ulcerative areas, which reach the muscular plane of the tongue. HE staining, ×100.

Figure 3 – Tuberculous nodule within the lingual chorion, with multiple giant cells with numerous nuclei (Langhans cells) with acidophilic cytoplasm and peripheral nuclei in a “horseshoe image”. HE staining, ×100.

Figure 4 – Intense collagen fibrosis within the lingual chorion, within the epithelioid necrosis area. Trichromic Goldner–Szekely staining, ×100.
Figure 5 – Tuberculous nodule with collagen fibrosis intra- and perinodular. Trichromic Goldner–Szekely staining, ×100.

Figure 6 – Overview image of two confluent tuberculous nodules within the tongue, intensely reactive to CD68 antibodies. Immunostaining with CD68 antibody, ×100.

Figure 7 – Detail from previous figure, in which we can observe the intense positivity of the Langhans cells to the CD68 antibody. Immunostaining with CD68 antibody, ×200.

Figure 8 – T-lymphocytes, diffusely disseminated within the tuberculosis nodule structure. Immunostaining with CD3 antibody, ×100.

Figure 9 – B-lymphocytes arranged at the periphery of the tuberculosis nodule. Immunostaining with CD20 antibody, ×200.

Figure 10 – Postero-anterior thoracopulmonary radiography, in which we can observe the distribution of the nodular lesions within the upper two-thirds of both lung areas.
CT (computerized tomography) scan showed areas of consolidation with a pseudonodular aspect looking retractile center in the left upper lobe and micronodular lesions isolated and confluence in the bilateral upper lobes (Figure 11).

Figure 11 – Computed tomography showing lesions in both lungs.

It was the first new episode of tuberculosis for which the patient was placed on antituberculous therapy, DOTS (directly observed therapy short-course) regimen, since July 2013. After six months, the patient was completely cured and is on regular follow-up with no residual or recurrent lesion.

**Discussion**

It is very rare to find the case with tuberculosis of oral cavity. Morgagni described the first case of lingual tuberculosis in 1761 [7].

The diagnosis of extra-respiratory tuberculosis is the responsibility of the organ specialist. This diagnosis is mainly supported by histopathological exam [7].

Extra-respiratory TB diagnosis is difficult and is established excluding other pathological conditions by the physicians in specialties involved.

The therapeutic approach in extra-respiratory tuberculosis is multidisciplinary. The origin of extra-metastatic tuberculosis is usually in the hematogenous metastatic outbreaks developed after primary infection period.

The evolution of this type of tuberculosis may be early, before primary infection has healed or far distance from the primary infection by reactivation of healed lesions.

Extra-respiratory tuberculosis usually has several general characteristics. Symptoms are less familiar to physicians, therefore when encountered concomitant with primary lesions, the outbreaks are neglected. Extra-respiratory locations are often inaccessible for investigations; this, combined with the presence of a small number of bacilli in such locations makes more difficult the bacteriological confirmation.

A HIV infection should always be suspected in patients with extra-respiratory tuberculosis.

Extra-respiratory tuberculosis has low risk or no risk of infectivity.

Before the emergence of HIV, extra-respiratory tuberculosis represented approximately 15–20% of all cases of tuberculosis [8–11].

In 2011, the *World Health Organization* (WHO) reported a total number of 6.2 million cases of tuberculosis. Among them were 5.8 million new cases of tuberculosis and 0.8 million (15%) were extra-respiratory tuberculosis.

In the Europe–WHO region, in the same year, were notified 253 769 new cases of tuberculosis, 42 489 (17%) cases of extra-respiratory tuberculosis [12].

A total of 16 116 cases of extra-respiratory tuberculosis were reported in the European Union during 2011. This number represents 22% of all tuberculosis cases in the European Union Declaration [11]. The proportion of cases of extra-respiratory tuberculosis remained relatively stable over the last four years [13].

Lateral border of tongue is the most common place where we can find tongue tuberculosis [14]. Painful oral ulcer is the main symptom of tongue tuberculosis, but our patient had no symptoms [15, 16].

Oral ulcers may be indurated and is often painful (pain on deglutition, burning sensation and otalgia). The gingival involvement is the second form of oral tuberculosis after tongue TB [17, 18].

We can find different morphological aspects in lingual tuberculosis [19, 20], such as tubercular ulcerative lesion: appear as form or softens ulcerative lesion, undetermined margins, usually shallow. A tuberculoma can appear anywhere in the tongue, presenting as a smooth lesion. The tuberculous fissure especially arises on the side of the tongue. Tubercle papillomas are abnormal growths of the margins of tubercular fissures. Finally, a tuberculous cold abscess is collection due to TB infection.

The diagnosis of oral cavity tuberculosis is based on sputum culture by evidence of acid-fast bacilli (AFB), chest X-ray and biopsy. A biopsy of an oral lesion is mandatory for diagnosis, but sometimes only a biopsy may not be enough. It is possible not to find the granulomatous aspect in early lesions [21].

For the differential diagnosis of a tuberculous ulcer of the oral cavity, we can despite of Wegener granuloma, actinomycosis, mycotic infections, traumatic tongue ulcers, syphilitic ulcers, other granulomatous conditions such as sarcoidosis, Crohn’s disease, tongue mycoses, cat scratch disease, foreign body reactions and malignancy or salivary gland tumor and metastatic lesions [22].

For ulcers of the tongue, deeper biopsies are mandatory. Biopsies as superficial may not find the histopathological lesion due to epithelial hyperplasia [23].

Polymerase chain reaction (PCR) assays as development of DNA probes may use as more sensitive and rapid diagnosis tests, but are more expensive. The risk for TB is greater in patients with HIV infection than in non-HIV [24]. Our patient was HIV negative.

During the treatment of tuberculosis pulmonary lesions, remission of tuberculous ulceration of the tongue can appear together with remission of lung tuberculosis lesions [24, 25].

Lingual tuberculosis does not need surgical resection and prognosis is favorable after anti-tuberculous treatment.

**Conclusions**

We would like to conclude that primary tuberculosis of a tongue is even rarely, yet tuberculosis needs to be kept
in the differential diagnosis of a tongue mass especially in endemic area. Biopsy is mandatory in finding the diagnosis in this situation. A clinical and pathological evaluation of atypical but curable lesion of tongue is necessary. Oral ulcer is a rare presenting complaint of tuberculosis in a patient with simultaneous pulmonary TB but without clinical symptoms. Tuberculosis lesions of the tongue can be primary or secondary. In this patient, we believe the possible mechanism could be the infected secretion from the lungs inoculated in the tongue. Tuberculosis in the oral cavity, especially tuberculosis of the tongue even it is a rare entity, should not be treated as a “forgotten disease”.

Conflict of interests
The authors declare that they have no conflict of interests.

Author contribution
All authors had an equal contribution to preparing this manuscript and thus share first authorship.

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