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ORIGINAL ARTICLE

Simultaneous oral, bone, and lung manifestations of tuberculosis

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Abstract:

Tuberculosis (TB) is a chronic granulomatous disease caused by Mycobacterium tuberculosis, which is transmitted by saliva droplets from patients with active pulmonary disease to persons in close contact with those infected. TB remains a leading cause of morbidity and mortality in developing countries, including Brazil. This disease primarily occurs in the lungs; however, other organs can be affected. Cervical tuberculous lymphadenitis or scrofula is the commonest form of extrapulmonary TB, particularly in immunocompromised patients. In the stomatognathic system, the tongue is the site most often affected by TB, whereas bone is rarely affected. The diagnosis of the active form of TB is made based mainly on clinical and radiographic findings, histopathologic features and sputum culture for M. tuberculosis, while the latent form of TB can be detected by tuberculin skin test or an interferon-γ release assay. The present article aimed to report a case of TB occurring concurrently in the oral cavity, bone and lungs.

Keywords: Tuberculosis; Communicable Diseases; Oral Medicine.

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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* responsible for millions of deaths worldwide yearly[1]. Despite advances in diagnosis and treatment, the incidence of this disease remains high, particularly in developing countries[1]. Such increase may be partly attributed to an increased incidence of HIV co-infection, which reduces cell-mediated immunity[2], as well as the development of multidrug-resistant strains of *M. tuberculosis*[3].

TB affects mainly the lungs, although other extrapulmonary sites may be involved. Cervical tuberculous lymphadenitis or scrofula is the most common form of extrapulmonary TB and is the presenting form of the disease in 5% of the cases in the community, whereas in immunocompromised patients, scrofula may be the presenting form of TB in up to a third of cases[4]. In the head and neck region, TB may affect several structures such as the buccal mucosa, gingiva, lips, jaw bones and tongue[5,6]. Bone TB may account for approximately 10-20% of extrapulmonary TB cases, with the spine being the most affected anatomical structure[7]. In spite of being a rare condition, multifocal skeletal TB has been described elsewhere[7]. The present paper aimed to report an unusual case of TB arising simultaneously in the oral cavity, bones and lungs.

CASE REPORT

A 44-year-old woman was referred to the primary care center of Campo Limpo, São Paulo State – Brazil, complaining of a wound on the dorsum of her tongue for 45 days, which was accompanied by a report of backache. On extraoral examination, palpable, painful and mobile lymph nodes were noticed in the submandibular region on both sides. Intraoral examination revealed an ulcer with irregular erythematous borders on the dorsum of tongue (Figure 1A).

Her medical history was positive for anemia, kidney stones and cervical arthrosis. Her social history included a high alcohol intake and smoking 15 cigarettes daily for 30 years. As a first approach, an incisional biopsy was performed and the specimen was fixed in 10% buffered formalin. Additionally, a chest radiograph was taken to assess the lungs, which showed multiple nodules in a miliary pattern, particularly in the upper lobes (Figure 1B). Based on these clinical and radiographic findings, the differential diagnosis included TB and paracoccidioidomycosis.

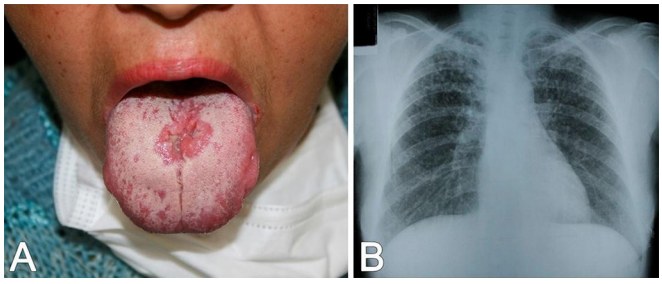

Figure 1. A) clinical aspects of the lesion in the tongue; B) radiographic features of the lungs.

The histopathological analysis revealed a fragment of oral mucosa lined by parakeratinized stratified squamous epithelium exhibiting acanthosis, exocytosis, and ulceration. In the lamina propria, an intense chronic inflammatory infiltrate composed by lymphocytes and epithelioid macrophages was noticed (Figure 2A). Areas of caseous necrosis surrounded by multinucleated giant cells, epithelioid macrophages and lymphocytes were also promptly detected (Figure 2B). The samples were subsequently Ziehl-Neelsen stained, where the bacilli were detected in some areas of the lesion (Figure 2C). The sputum culture confirmed the diagnosis of TB.

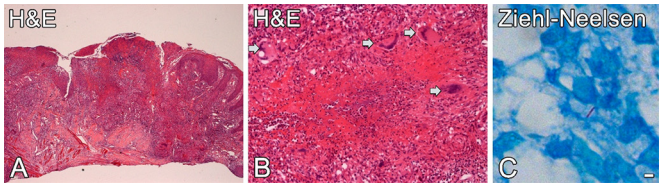

Figure 2. A) H&E revealing a fragment of oral mucosa covered with a parakeratinized stratified squamous epithelium exhibiting an intense chronic granulomatous inflammatory process in the lamina propria, B) Areas of caseous necrosis surrounding by multinucleated giant cells (arrows) was also detected C) Rare bacilli were detected in the sample. Scale Bar: A= 100 µm; B= 50 µm; C= 20 µm.

The patient was put on anti-tubercular therapy, though after 3 months of treatment, the patient still reported pain in her back and hips. A computed tomography (CT) scan of the spine as well as an antero-posterior radiograph of the pelvis were then performed. The CT showed hypodense areas in the vertebral bodies (Figure 3A), while a diffuse bone rarefaction was detected in the wing of the ilium (Figure 3B).

These findings combined with a previous diagnosis of TB led to a diagnosis compatible with osteoarticular tuberculosis and spondylitis tuberculosis. After 6 months of treatment, there was complete remission of the ulcer in her tongue (Figure 4A). Furthermore, a significant improvement was noticed in the radiographic appearance

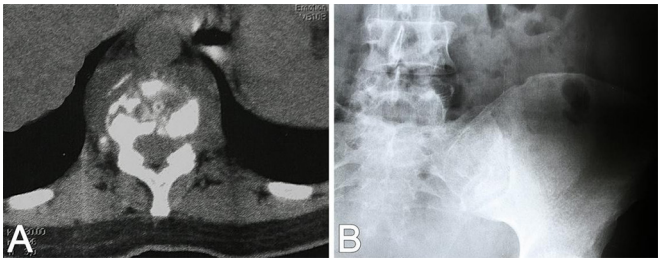

Figure 3. A) Radiolucent areas localized in the vertebral body and B) in the wing of ilium.

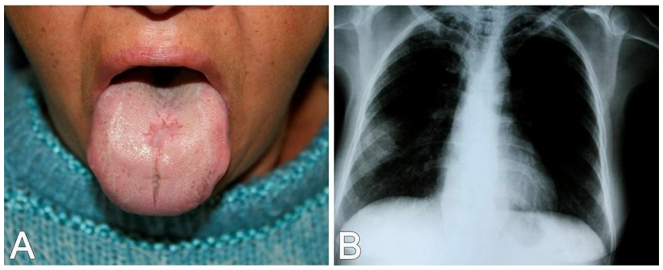

Figure 4. A) Clinical aspects of the tongue and B) Lungs after the treatment.

of her lungs (Figure 4B). The bone lesions were treated conservatively at first using orthopedic approaches such as bed rest and spine protection using a back support belt. After 12 months of treatment, the patient underwent surgery to remove the necrotic bone tissue that was not eliminated following tuberculostatic therapy and conservative approaches and the patient is currently under clinical and radiographic follow-up.

DISCUSSION

TB represents one the major causes of death and morbidity worldwide, particularly in developing countries. In 2015, the World Health Organization estimated 10.4 million new TB cases around the world with 1.4 million of deaths[1]. Fifty-six percent of the cases occurred in men, while women and children represented 34% and 10% of the cases, respectively. People infected with HIV accounted for 11% of all new cases of TB[1].

This chronic granulomatous disease is transmitted between humans primarily via the respiratory tract. Following *M. tuberculosis* infection, some individuals may either progress to the active form of TB or live with the latent form of the disease. It is believed that one-third of the world's population is latently infected with *M. tuberculosis* and such individuals may serve as a great reservoir of potential cases of TB and, consequently, one of the main challenges in the process of control and eradication of TB[8-10].

M. tuberculosis is an aerobic bacillus that grows effectively in tissues with high levels of oxygen. Indeed, the lungs are usually the first organs affected by this disease[10]. However, other anatomical sites may be involved, such as the oral cavity and bones[6,8-10]. The lesions in these sites occur either by direct inoculation of the bacilli or dissemination of *M. tuberculosis* via the lymphatics or bloodstream.

Oral TB is an uncommon manifestation of extrapulmonary TB occurring in nearly 0.1-5% of all cases[11]. Oral TB can be classified as primary or secondary lesions. The occurrence of primary oral TB is rare, probably due to the continuous wash-out effect of saliva on the oral mucosa, which protects the oral tissues against *M. tuberculosis* invasion[12]. The secondary oral TB lesions are related to pulmonary disease and represent approximately 58% of all cases of oral TB[11]. This form of oral TB affects primarily middle-aged individuals and elderly people[13,14]. The infection may affect any structure of the stomatognathic system, including lips, palate, floor of the mouth, mandible, maxillary sinuses, and temporomandibular joint. However, the tongue has been described as the most commonly affected site[15].

Clinically, oral TB lesions in the tongue typically present as a single ulcer with irregular margins and a necrotic base[11]. These non-specific clinical features may lead to misdiagnoses as other unrelated diseases, particularly when they arise before the systemic symptoms of TB become evident. Indeed, due to the history of heavy smoking (15 cigarettes daily) for 30 years associated with alcohol intake reported by the patient described herein, it was initially thought that the lesion could be a squamous cell carcinoma.

The dorsum of the tongue, however, is not a common site for development of such neoplasm, which usually arises in the posterior border of the tongue[16]. Thus, other diseases were also considered as differential diagnoses, including TB, paracoccidioidomycosis, and eosinophilic ulcer. The combination of backache with the imaging features observed on the chest radiograph strongly suggested a case of TB. This hypothesis was reinforced by positive Ziehl-Neelsen staining and further confirmed by sputum culture.

Bone TB comprises 10-20% of all the extrapulmonary TB and affects particularly the spine, long bones and joints. The affinity of the *M.*

tuberculosis for these sites can be attributed to the intense vascularization of the vertebra and growth plates of the long bones[7]. The involvement of multiple sites in the skeleton is rare and represents less than 5% of all cases if bone TB, even in countries where the disease is endemic[8,17,18]. The development of bone TB lesions is insidious and may lead to a delay in the diagnosis.

The first symptoms are usually pain, fever and diaphoresis, which may be associated or not with radiographic alterations in the lungs[19,20]. In these situations, bone TB lesions can mimic malignant neoplasms or other diseases, such as Brodie's abscess, sarcoidosis, and eosinophilic granuloma[21]. In our case, the bony defects were detected after the final diagnosis of TB, which promptly lead us to suspect bone involvement by *M. tuberculosis*.

The diagnosis of the active form of TB is made based on clinical and radiographic findings, histopathologic features and sputum culture for the identification *M. tuberculosis*. The diagnosis of the latent form of TB can be established by a positive result on either a tuberculin skin test or an interferon-γ release assay, in the absence of active TB[21]. Some molecular methods have been designed to identify the presence of *M. tuberculosis* and to detect resistance to isoniazid and/or rifampin, such as nucleic acid amplification-based techniques[22].

The treatment of TB is based on a combination of different drugs comprised by isoniazid (I), rifampicin (R), ethambutol (E), and pyrazinamide (P). Traditionally, the patients are treated with IREP for 2 months followed by 4 for months with IR[10]. However, in our case, this regime was extended for 12 months, due to the bone involvement. The drug therapy approach selected resulted in a significant reduction of bone lesions, though it did not eliminate them completely. For the remaining bone lesions, surgery was performed to prevent damage to the spinal cord.

In conclusion, simultaneous involvement of the lungs, oral cavity and bones by TB is a very rare occurrence. Considering the complications caused by bone TB when vertebrae are affected, especially of neurological basis, early diagnosis and treatment is essential to prevent such sequelae, which could bring catastrophic consequences to quality of life.

CONFLICT OF INTERESTS

The authors declare no conflict of interests regarding the publication of this paper.

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