

TONSILLAR TUBERCULOSIS MIMICKING CANCER: A FORGOTTEN DISEASE

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Abstract: An 83-year-old immunocompetent man with no systemic disease presented to the emergency department of our hospital with severe progressive odynophagia over the last 5 months, which prevented him from eating and led to weight loss. He did not report fever, cough, or dyspnea. A year and a half earlier, after total knee replacement surgery, he developed septic arthritis with a torpid course, ultimately resulting in a supracondylar amputation of the lower limb. The patient was not diabetic and was not on any chronic treatment. He had quit smoking more than 40 years ago. The initial suspected diagnosis was tonsillar carcinoma, so a tonsillar biopsy was performed, and an unremarkable cervicothoracic CT was ordered. The tonsillar biopsy ruled out malignancy and identified ulcerated necrotizing granulomas. Acid-fast bacilli were identified, with 2-28 bacilli per 50 fields. Finally, the patient was diagnosed with disseminated tuberculosis with an active tuberculous focus in the tonsil. The aim of this paper is to update our knowledge on frequently neglected aspects of extrapulmonary tuberculosis in the head and neck, based on the case of tonsillar tuberculosis presented.

Keywords: Generalized Tuberculosis. Tonsillar Tuberculosis. Tonsil Cancer. Necrotizing Granuloma.

INTRODUCTION

Tuberculosis (TB) is the most lethal infectious disease in the world. After almost asymptomatic generalized tuberculosis, many patients may retain foci in various organs, which may subsequently manifest as extrapulmonary tuberculosis. Extrapulmonary TB of the head and neck area is currently a reemerging infectious disease that is generally confined to the cervical nodes, but, exceptionally, TB can be found anywhere in the upper airway (1,2), regardless of whether or not there are pulmonary symptoms. It can also coexist with squamous cell carcinoma in the same location (2).

We present a case of severe progressive odynophagia with physical deterioration due to a torpid ulcer in the tonsil, which initially simulated a carcinoma. Finally it was the initial symptom of latent generalized TB.

The aim of this study is to review the diagnosis of extranodal extrapulmonary TB in the head and neck region, an uncommon diagnosis in the upper airway and frequently forgotten, but relevant for specialists.

CLINICAL CASE

An 83-year-old man, with no diseases of interest, came to the emergency department of our hospital, referred by his family physician for severe progressive odynophagia in the last 5 months that prevented him from eating, with thinning. He had been treated with oral antibiotics and tramadol. She did not report fever, cough or dyspnea. A year and a half before, after a total knee prosthesis operation, he presented a septic arthritis of torpid evolution that ended in supracondylar amputation of the lower limb. The patient was not diabetic, was immunocompetent, and was not taking any chronic treatment. He had stopped smoking more than 40 years ago.

In the urgent evaluation she presented generalized physical deterioration, with good cognitive status and family support. On ENT examination, the only finding was an ulcerative lesion in the right tonsil, suggestive of carcinoma. No suspicious cervical nodes were palpable. Given the suspicion of oncologic disease, an urgent biopsy was taken and cervicothoracic CT was requested for an extension study (*Fig.1*).

The biopsy taken at the emergency department ruled out malignancy and identified necrotizing granulomas with severe ulceration, although the Ziehl-Neelsen (ZN) stain failed to identify acid-fast bacilli (AFB). Cervical computed axial tomography (CT) identified a lesion compatible with

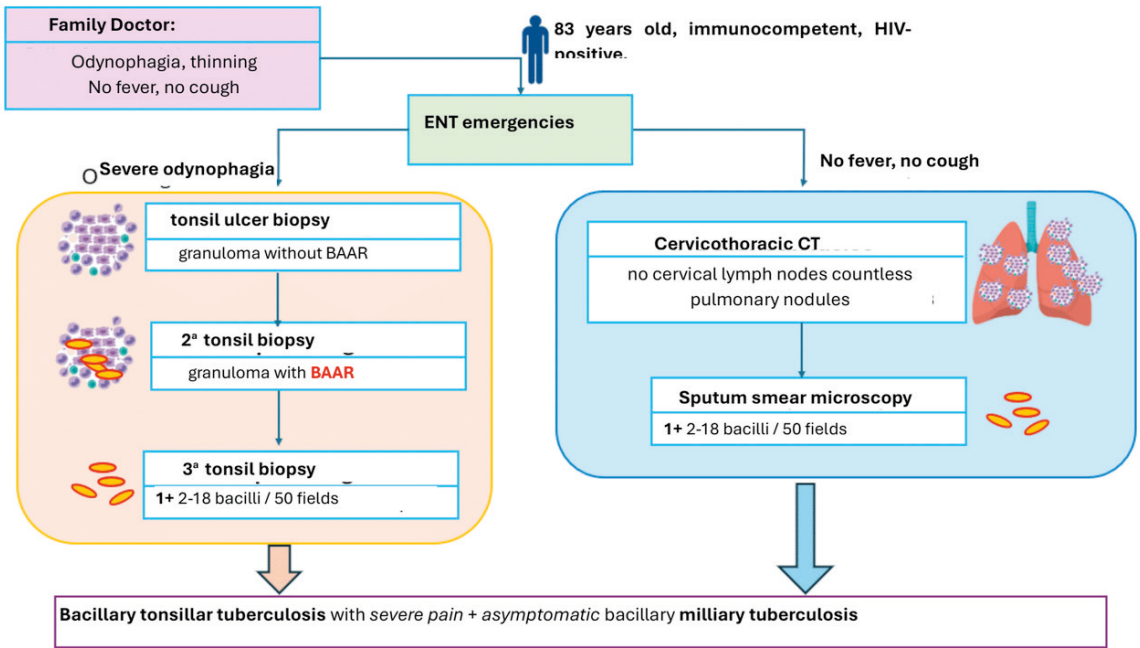


Figure 1. Diagnostic process of our patient from referral by a family physician to confirmation of tonsillar and pulmonary TB.

ulcerated neoplasia of the right tonsil, without pathological lymph nodes (**Fig. 2**).

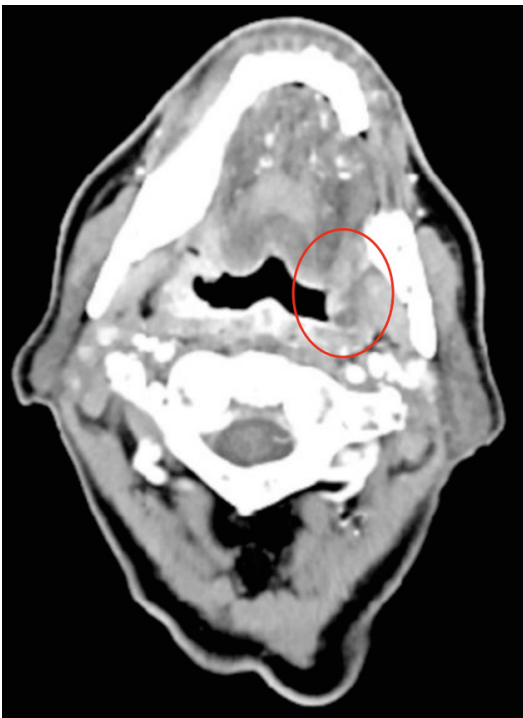


Fig 2. Cervical CT image with intense contrast uptake in the right tonsil, compatible with ulcerated tonsillar neoplasia of the right tonsil.

Chest CT (**Fig. 3**) showed innumerable centrolobulillary nodules in both lung fields, predominantly in the left lung.

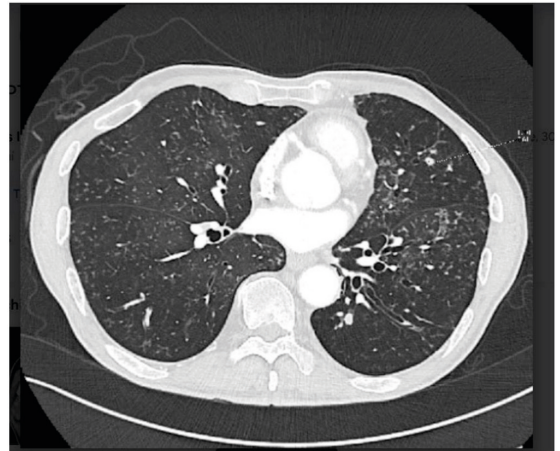


Figure 3. Chest CT image with innumerable generalized "budding" centrolobular nodules.

Given the high suspicion of disseminated TB with tonsillar focus, a repeat tonsillar biopsy was performed, in which BAAR was identified in the necrotizing granulomas, with positive bacilloscopy (1+) with 2-18 bacilli/50 fields. Sputum was positive for BAAR with smear microscopy 1+ (2-18 bacilli/50

fields). Urine study was negative. Serology for hepatitis B and C viruses and HIV were negative. Quantiferon-TB was positive and PCR identified rifampicin-sensitive strains.

The Infectious Diseases Unit was consulted and started the standard antituberculosis treatment, achieving acceptable swallowing by mouth in the first week. The patient was followed up in the Infectious Diseases Unit of our hospital.

DISCUSSION

Extranodal extrapulmonary tuberculosis in the head and neck region, especially in the upper airway and salivary glands, is usually a neglected diagnosis by Western head and neck specialists (3), except in immunocompromised patients or in migrants from endemic regions. Review of the literature indicates that tonsillar tuberculosis is frequently identified in immunocompetent patients (1), as was the case in our patient. To evaluate the difference in incidence between Western countries and endemic regions, we have compared the experience of one hospital in India (4) with that of another in Great Britain (5), both with large case series, over a 10-year period. The incidence of head and neck tuberculosis did not show major differences between the two hospitals: 165 cases in the Indian hospital and 128 in the British hospital during the same period. In both centers, tuberculous lymphadenitis was the most frequent site (73.3% of cases in India and 78% in Great Britain). As for the oral cavity, the Indian hospital reported 5 cases, while the British hospital reported 2. These data show that, despite the distance of more than 6,000 km, cultural differences and levels of development between the two countries, there appear to be no differences in the incidence of TB presentation in the head and neck between endemic and non-endemic countries.

The evolution between *Mycobacterium tuberculosis* infection and active tuberculosis is multifactorial. The immune response generated by the infection is highly protective against active tuberculosis, and severe immunosuppression can only explain 10% of the cases of active tuberculosis, while the rest is favored by comorbidities, inflammatory clinical contexts and an unknown genetic propensity (6). In our patient, immunosuppression and HIV+ infection were ruled out, although perhaps it was favored by the chronic septic arthritis that the patient developed after implanting a total knee prosthesis, with several surgical interventions and which finally required supracondylar amputation. In **Figure 4** we present a pathogenic hypothesis that could chronologically explain the development of the disease.

Our patient presented tonsillar tuberculosis simulating carcinoma. As observed in the literature (1,4,5,7-9) and in our case, not all tonsillar ulcers are cancer. There are very few published cases similar to this one (1,4,5,7-9). After identifying live bacilli on smear microscopy of "fresh" tonsillar tissue, we were concerned about the possibility of coexistence of carcinoma and tuberculosis in the same tonsil, given the severe pain presented by the patient. In the Indian series of 158 cases (4), only 5 patients (3%) had coexistent malignant neoplasms. In the literature review, we have found only one case (7) cancer and TB in the same tonsil, in addition to the five cases discussed from the Indian hospital (4). Immunohistochemical studies performed in our two biopsies ruled out malignancy, and the patient has improved his odynophagia since the start of anti-TB treatment, with an improvement in the tonsillar ulcer observed on examination. The patient is under periodic follow-up in our offices.

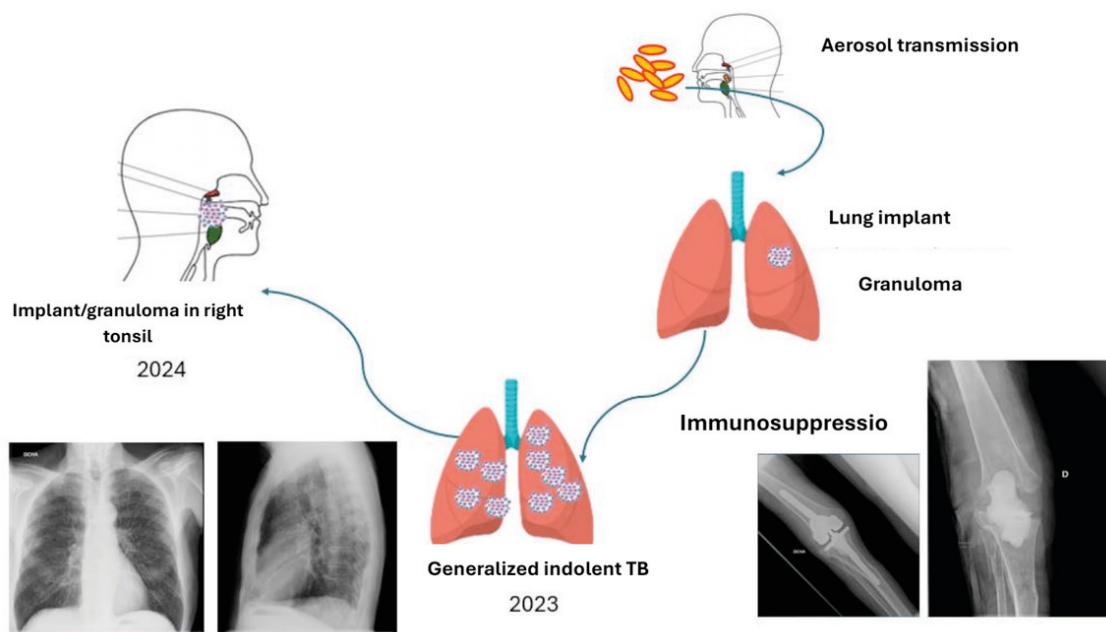


Figure 4. Proposed pathogenic hypothesis. On a previous asymptomatic pulmonary tuberculous focus, the complicated and long-lasting septic arthritis suffered a year before by the patient could have triggered the development of an asymptomatic generalized TB, with a clinically active tonsillar focus.

The diagnosis of tuberculosis was suggested by the pathologist after the biopsy results. Odynophagia, tonsillar ulcer and CT were compatible with tonsillar carcinoma. A meta-analysis (1) has shown that cervicofacial tuberculosis is usually paucibacillary, and sputum is not an effective diagnostic method in these cases. The investigators conclude that fine needle cytology or excisional biopsy is necessary for diagnosis and initiation of treatment. The key to suspicion in this case has been histopathologic study, as conventional diagnostic techniques such as Ziehl-Neelsen staining for acid-fast bacilli (AFB) and smear microscopy are simple and routine. Just as not all ulcers are cancer, not all tonsillar granulomas are tuberculosis. Other clinical entities should be considered in the differential diagnosis. A retrospective study of 22 tonsillar biopsies with granulomas, performed between 1940 and 1999 at the Armed Forces Institute of Pathology (10), showed that in 8 cases sarcoidosis was diagnosed, in 3 cases tuberculosis, in 2 cases Hodgkin's lymphoma,

and in 1 case tuberculosis together with coexistent squamous cell carcinoma.

Regarding the coexistence of tonsillar and pulmonary TB, we saw in our patient that the absence of pulmonary symptoms did not rule out pulmonary disease, with CT revealing numerous pulmonary nodules. In the series of 158 patients with pulmonary TB in the Indian hospital (4), 75% had no pulmonary involvement and only in 40 cases did tonsillar TB coexist with pulmonary TB. In the most recent meta-analysis (1), half of the patients had no pulmonary disease.

The aim of this work was to update our knowledge about frequently forgotten aspects of extrapulmonary tuberculosis in the head and neck, based on the case of tonsillar tuberculosis presented. This case is remarkable because a non-specific symptom such as severe odynophagia, without respiratory symptoms or fever, was the first indication of subclinical generalized pulmonary tuberculosis without previous diagnosis or treatment.

In conclusion, we have seen that the key is to maintain a high degree of clinical suspicion in atypical presentations of the disease, either in lymph nodes or in the upper respiratory tract. If we suspect CT, the definitive diagnosis is made by conventional techniques such as biopsy, Ziehl-Neelsen staining and smear microscopy in affected organ tissue. A global approach to tuberculosis as a systemic infectious disease, which can manifest in any organ with non-specific symptoms, will allow an adequate diagnosis and the initiation of an effective treatment in curable stages of the disease.

ETHICAL RESPONSIBILITIES

Protection of humans and animals. The authors declare that no experiments on humans or animals have been performed for this research.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The patient gave consent to the authors to publish the clinical case with data anonymization.

Conflict of interest: the researchers declare that they have no conflicts of interest.

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