

Scrofula Caused by Multidrug-Resistant Tuberculosis

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ABSTRACT

Tuberculosis (TB) is one of the top 10 causes of death worldwide. Multidrug-resistant tuberculosis (MDR-TB) occurs when at the minimum there is resistance to isoniazid and rifampin. Prevention of new infections of *Mycobacterium tuberculosis* and progression to TB disease is critical to reduce the burden and mortality of this disease. We present the case of a 73-year-old human immunodeficiency virus (HIV)-negative female who presented with cervical lymphadenopathy and who was diagnosed with MDR-TB.

LEARNING POINTS

- Tuberculosis is one of the most important causes of morbidity and mortality worldwide and approximately a quarter of the world's population is estimated to be latently infected by *Mycobacterium tuberculosis*.
- Multidrug-resistant tuberculosis lymphadenitis is a rare manifestation of the disease in Portugal.
- With the advent of multidrug-resistant tuberculosis, disease surveillance by the government should be intensified, with the aim of national and global TB control, focusing on prevention.

KEYWORDS

Mycobacterium tuberculosis, lymphadenitis, scrofula, multidrug-resistant tuberculosis

CASE DESCRIPTION

A 73-year-old woman who had recently arrived from Cape Verde presented a slow-growth cervical mass with 4 weeks of evolution. In the 2 previous weeks, she reported complaints of local heat, oedema and flushing, associated with pruritus. She had a dry cough and sweating but no fever and anorexia. She had lost weight quantified at approximately 15% of her body mass over the previous 8 months. The patient denied other respiratory, gastrointestinal and genitourinary symptoms.

At admission, the patient showed flushed suprasternal and supraclavicular masses, painful to palpation, with signs of fluctuation (Fig. 1). Numerous lymph nodes were also palpable in the neck. Viral serologies were negative, including for HIV. Blood cultures and sputum cultures were negative. A chest x-ray did not show evidence of cavitation. Ultrasound of soft parts of the neck described a non-pure, poorly circumscribed collection of anfractuous borders that reached the deep planes, in the anterior and inferior cervical region, with other images of an identical nature in the supraclavicular topography. Neck and chest computed tomography (CT) scanning showed the images seen in the ultrasound, attributing these with a cystic component; the tracheobronchial tree was permeable, with no evidence of alterations in the pulmonary parenchyma. The fine needle aspiration (FNA) procedure was performed with sample collection for microbiological study and a sample was sent for pathologic anatomy assessment. A probable diagnosis of peripheral tuberculous lymphadenitis or scrofuloderma was assumed and a skin biopsy was performed; the Mantoux test was reactive, 30 mm (Fig. 2).



Figure 1. Cervical mass affecting bilateral supraclavicular topography at admission



Figure 2. Positive Mantoux test (30 mm)

Given the diagnostic presumption, the patient began empiric anti-tuberculostatic quadruple therapy (isoniazid, rifampin, pyrazinamide and ethambutol). Meanwhile, echo-guided percutaneous drainage was performed, with an output of thick viscid pus, of which polymerase chain reaction (PCR) analysis for *Mycobacterium tuberculosis* was positive. PCR analysis for non-tuberculous mycobacterium, RNA 16S and panfungal PCR were negative. PCR testing for *Mycobacterium tuberculosis* in medullary blood was also positive.

The patient evolved favourably, continuing out-patient treatment for disseminated tuberculosis, while the cervical masses progressed with suppuration and later cicatrization (Fig. 3).



Figure 3. Two months after admission, the cervical mass progressed with suppuration and cicatrization

Cultural examination of the pus yielded *Mycobacterium tuberculosis* and the drug susceptibility test (DST) showed multidrug-resistant tuberculosis (MDR-TB). The treatment was switched to pyrazinamide, ethionamide, clofazimine, moxifloxacin and amikacin. The patient was subsequently referred for close follow-up to the local department of health and was scheduled to undergo therapy for at least 18 months.

DISCUSSION

Tuberculosis (TB) is 1 of the most important causes of morbidity and mortality worldwide, caused by various strains of mycobacteria, usually *Mycobacterium tuberculosis*. Approximately 23% of the world's population is estimated to be latently infected by *Mycobacterium tuberculosis* (LTBI). Diagnostic and therapeutic challenges constitute management problems as TB mimics other pathological processes and yields inconsistent clinical and laboratory findings^[1,2]. In 2017, there were approximately 10 million new cases of TB around the world with 3.5% due to MDR-TB, with 18% of MDR-TB occurring in previously treated cases^[1]. In Portugal, during the last 10 years, the incidence of TB has decreased by approximately 40%, with a low prevalence (<20 cases/100,000 population) since 2015. In 2017, 1,741 cases were notified, of which 1,697 were new cases and 12 were multidrug resistant (0.7%)^[2].

Tuberculous lymphadenitis (TBL) is among the most frequent presentations of extrapulmonary TB in countries with a low prevalence of TB, while in high prevalence areas, the TBL incidence is second to that of tuberculous pleuritis^[1]. TBL has a female-to-male ratio of 1.4:1, while pulmonary TB is more common among men^[1,3]. The peak age for TBL ranges from 30 to 40 years. TBL located in the cervical region is known as peripheral tuberculous lymphadenitis or scrofula and it is usually due to reactivation of disease by haematogenous spread from a site during primary TB infection, perhaps years earlier; however, miliary dissemination with prominent lymph node involvement in the setting of primary infection can also occur. A definitive diagnosis is made by culture or nucleic acid amplification of *Mycobacterium tuberculosis* in an affected lymph node, but demonstration of acid-fast bacilli and granulomatous inflammation may also be helpful. FNA is less invasive and may be useful for diagnosis, but excisional biopsy has the highest sensitivity (80%) and may produce a more rapid and favourable symptomatic response^[3]. The most common presentation of TBL is an isolated, chronic non-tender lymphadenopathy in the anterior or posterior cervical triangles, that can be present for up to 12 months before diagnosis and can be complicated by ulceration, fistula or abscess formation. Systemic symptoms are not common. Physical examination reveals a firm, discrete mass or matted nodes fixed to surrounding structures and the skin may be indurated. The differential diagnosis is extensive and includes malignancy, Kikuchi disease, sarcoidosis and other infections such as non-tuberculous mycobacteria, cat scratch disease, fungal infection and bacterial adenitis^[3,4].

Before the era of antibiotics, in the Middle Ages, it was believed that a touch from royalty could heal skin; scrofula was known as 'king's evil'. Patients rarely died from it and were unlikely to progress to pulmonary TB. However, there is a lack of information in the literature regarding multidrug resistance in scrofula. However, it seems that nothing has changed with respect to the natural history of the disease and its association with pulmonary TB. In addition, although scrofula is known to have a good prognosis, our patient had a disseminated MDR-TB lymphadenitis, which in her home country could progress into pulmonary TB, with high risk of transmission and death.

Thus, MDR-TB lymphadenitis is a rare manifestation of significant public health concern and it is an atypical presentation of the disease in Portugal, being more common in TB-endemic regions. In the present day, with the advent of increased globalization and immigration, cases of TB and drug-resistant TB may continue to rise and represent a threat to global TB control. The main causes of the increasing spread of resistant TB strains are limited resources with weak medical systems, poverty, amplification of resistance through incorrect treatment and ongoing transmission in most vulnerable communities. Ultimately, for long-range success, policies that intensify disease surveillance efforts, particularly in high-risk populations, should be created and implemented^[1,5]. Drug-resistant TB has widespread health, social and economic implications, as its emergence threatens gains already made with respect to national and global TB control. Public health systems may need to be reinforced to ensure closely monitored treatment (directly observed therapy, DOT), to prevent the development of resistant forms of the disease. Thus, urgent action is required to improve the coverage and quality of diagnosis, treatment and care for people with MDR-TB^[5].

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