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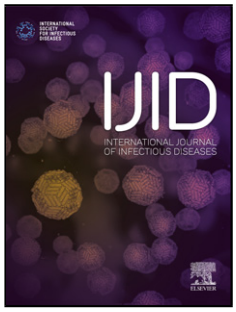

Chest pain and a left parasternal soft tissue swelling in an immunocompetent refugee with disseminated tuberculosis

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Title: Chest pain and a left parasternal soft tissue swelling in an immunocompetent refugee with disseminated tuberculosis

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Highlights

- Tuberculosis in foreign-born immunocompetent individuals
- Cardiac tuberculosis is a rare condition
- High incidence of extra-pulmonary tuberculosis in migrant patients

Abstract

An immunocompetent migrant with chest pain was admitted to an Italian hospital. CT scan showed a left pectoral abscess and osteomyelitis of the sternum. The infection spread into the anterior

mediastinum near to the pericardium and the heart, where an atrial mass was confirmed by echocardiography. Disseminated tuberculosis was diagnosed.

Keywords: disseminated tuberculosis, heart mass, TB, bronchoscopy, migration

Text

Case presentation

A 28-year-old Malian male refugee (height: 185 centimeters; weight: 73.4 kilograms; body mass index: 21.5) was assessed in an Italian Emergency Department complaining of mild chest pain associated with a left parasternal soft swelling. This had increased in size over the last four months. The patient did not report weight loss, malaise, and cough.

He had left Libya one year earlier and had been staying in a refugee hostel in Italy, where he was screened to rule out active tuberculosis (TB). At that point he was asymptomatic, his tuberculin skin test (23 millimeters) and Quantiferon test (QF-TB Gold plus®) were positive; a chest X-ray was normal. Treatment for latent TB infection (LTBI) was not prescribed as he reported having had 6 months of anti-tuberculosis therapy (ATT) before he left his country of origin.

The patient looked well and was afebrile. Abdominal, pulmonary and cardiac examination was unremarkable. A subcutaneous soft swelling was noted in the left parasternal region.

Positive initial laboratory blood tests were: mild monocytosis (0.85 x 10^3/μl; normal reference range: 0.2-0.8 x 10^3/μl), increased lactate dehydrogenase (657 U/L; normal reference range: 313-618 U/L) and serum C-reactive protein (21.1 mg/L; normal reference range: <5 mg/L); lymphocyte counts (2.07 x 10^3/μl; normal reference range: 1-3.4 x 10^3/μl) and hemoglobin level (12.2 g/dL; normal reference range: 12-16 g/dL) were unremarkable. His electrocardiogram showed right bundle branch block.

A contrast-enhanced chest computed tomography (CT) showed several partially cavitated lung nodules in both upper lobes plus mediastinal lymphadenopathy. A thin walled fluid-containing cavity sized 7x3 cm was detected in the left pectoral muscle, together with focal osteolysis surrounded by an area of osteosclerosis in the sternal body. In the right atrium a large contrast enhancing mass was detected.

(Figure 1A-E). No pulmonary artery or vena caval thromboses were present and abdominal imaging was normal.

A transthoracic echocardiography showed a large mass extending caudally across the tricuspid valve with a smooth surface and attached to the roof and to the antero-lateral wall of the right atrium (Figure 1F), characterized by a heterogeneous echogenicity with areas of echolucency. Furthermore, mild tricuspid regurgitation, without any other flow obstruction, was detected by color Doppler echocardiography,

The patient was admitted and other co-infections were excluded (*i.e.*, Treponema pallidum, human immunodeficiency virus (HIV), hepatitis C virus, hepatitis B virus). Sputum specimens could not be collected.

A bronchoscopy with a bronchoalveolar lavage (BAL) in the left upper lobe and a transthoracic CT-guided biopsy of the parasternal lesion were performed. Xpert MTB/RIF® on both specimens was positive for rifampicin-susceptible *Mycobacterium tuberculosis* complex (MTB), subsequently confirmed by liquid culture results. Drug susceptibility testing was performed on both BAL and pectoral abscess samples and did not reveal any drug resistances to the first-line anti-TB drugs.

The standardized regimen recommended by the World Health Organization (*i.e.*, Isoniazid 300 milligrams (mg)/day, Rifampicin 600 mg/day, Ethambutol 1,600 mg/day, and Pyrazinamide 1,500 mg/day) for a 2-month intensive therapy, followed by a 4-month continuation phase with Isoniazid and Rifampicin) was administered together with low molecular weight heparin for the high thrombotic risk (Nahid et al, 2016). Self-administered therapy regimen was adopted. Clinical recovery was prompt. However, after 14 days of treatment he refused to stay in hospital to have further procedures including cardiac magnetic resonance imaging and transoesophageal echocardiography. Following the first outpatient visit (one month after the administration of the anti-TB drugs), he did not seek further care, and was lost to follow-up.

Discussion

Disseminated TB is a rare form of disease (1–5% of all TB cases) caused by MTB identified in blood or bone marrow samples, from liver biopsies, or from specimens collected in ≥2 non-contiguous organs (Crump et al., 2003; Suarez et al., 2019). Extra-pulmonary dissemination, whose pathogenesis is largely unknown, depends on the haematogenous or lymphatic spread of MTB from the primary site of infection (Suarez et al., 2019; Qian et al., 2018). Myocardial TB may occur following hematogenous/lymphatic MTB spread or direct transmission from the lung to the pericardium.

Notably few cases of cardiac TB have been described, with the majority affecting the right atrium ((Suarez et al., 2019; Rao et al., 2012; Goyal et al., 2005).

Here, we hypothesize that the patient might have been exposed to inadequate therapy to cure his previous pulmonary disease, and that MTB reactivation occurred after his arrival in Italy as a result of a potential temporary immunodeficiency related to poor environmental conditions, which favoured a mycobacterial haematogenous/lymphatic dissemination from the lung to the pectoral muscle (migrant groups are at high risk of reactivation following displacement and arrival in their new country). The muscular infection caused osteomyelitis of the sternal body and, then, spread into the anterior mediastinum near to the pericardium and the heart.

Despite a cardiac thrombus or neoplasm may not be ruled out, based on clinical findings, CT and echocardiography signs, the atrial mass was deemed highly suspicious for myocardial TB. The atrial mass might represent the clinical outcome of a MTB infection which started from the mediastinal abscess.

Disseminated TB occurs more frequently in immunocompromised patients (up to 85% of the cases), mostly in people living with HIV (Crump et al., 2003; Suarez et al., 2019; Qian et al., 2018). However, cases of disseminated disease in healthy refugees have been recently described, suggesting the role of potentially virulent *Mycobacterium tuberculosis* strains and/or a specific genetic pattern of the host, or the stress associated with movement (Suarez et al., 2019).

During the last decade, intensified migration flows from Africa to Europe have increased the total number of TB cases in low TB incidence countries, such as Italy (Dara et al., 2016; Mondoni et al.,

2018). Furthermore, unusual clinical presentations are frequently described in migrants, with extra-pulmonary TB forms being most frequently diagnosed in Africans (Mondoni et al., 2018; Sotgiu et al., 2017; Suarez et al., 2019).

Stressful events, malnutrition, and poverty can affect the immune system, increasing the probability of TB disease from LTBI acquired in the country of origin, and/or severe and rare clinical events (Sotgiu et al., 2017; Suarez et al., 2019).

Furthermore, limited access to healthcare facilities, atypical or rare clinical pictures, and poor TB knowledge of healthcare workers in high income countries may result in a delayed diagnosis and therapy (Sotgiu et al., 2017; Suarez et al., 2019).

In cases of suspected disseminated TB the diagnostic algorithm should be comprehensive and rapid: the spread of MTB to multiple and/or vital organs (e.g., the heart) may result in life-threatening events Suarez et al., 2019; Khan et al., 2019).

Sensitive and specific imaging tests (e.g., CT, magnetic resonance imaging, positron emission tomography) are crucial to assess the extent of the disease. In case of sputum smear negative patients and of those with multiple body-site infections, invasive tests (e.g., bronchoscopy, imaging-guided biopsy, etc.) should be performed promptly to collect adequate specimens for microbiology and histopathology to rule out TB disease and its life-threatening complications prior to blind treatment (Mondoni et al., 2017; Suarez et al., 2019; Khan et al., 2019). Notably, the differential diagnosis may include the following medical conditions: lymphoma, connective tissue malignancies, fungal and bacterial infections (Khan et al., 2019).

No specific guidelines exist on the ideal duration of therapy for disseminated (both drug susceptible and resistant) TB. It should depend on the affected organs (Suarez et al., 2019).

The cascade of care for migrants should be implemented and scaled-up at national and local level. More efforts are needed in high income countries to improve the TB management of vulnerable populations at highest risk of TB disease (e.g., migrants and refugees) (Dara et al., 2016).

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This observational study did not require an ethical approval according to the Italian law on observational studies.

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Figure legends

Figure 1: Contrast-enhanced CT scan showing cavitated lung nodules in the left upper lobe (A), left pectoral abscess (B), osteomyelitis of the sternal body and involvement of the anterior mediastinum (C) and the pericardium and the heart (D). (E): Right atrium mass. (F): Echocardiography: apical 4-chamber view showing a large mass (sized 4.8x2.5 cm) attached to the roof and to the anterolateral wall of the right atrium.