



Case Report

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



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ABSTRACT

An immunocompetent migrant with chest pain was admitted to an Italian hospital. Computed tomography showed a left pectoral abscess and osteomyelitis of the sternum. The infection had spread into the anterior mediastinum near to the pericardium and the heart, where an atrial mass was confirmed by echocardiography. Disseminated tuberculosis was diagnosed.

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Case presentation

A 28-year-old male Malian refugee (height 185 cm, weight 73.4 kg, body mass index 21.5 kg/m²) was assessed in an Italian emergency department with complaints of mild chest pain associated with a left parasternal soft tissue swelling. This had increased in size over the last 4 months. The patient did not report weight loss, malaise, or cough.

He had left Libya 1 year earlier and had been staying in a refugee hostel in Italy, where he had been screened to rule out active tuberculosis (TB). At that point, he was asymptomatic; his tuberculin skin test (23 mm) and QuantiFERON-TB Gold Plus test (QFT-Plus) were positive, and 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 examinations were unremarkable. A subcutaneous soft tissue swelling was noted in the left parasternal region.

Positive initial laboratory blood tests were as follows: mild monocytosis (0.85 × 10⁹/l; normal reference range: 0.2–0.8 × 10⁹/l), increased lactate dehydrogenase (657 U/l; normal reference range: 313–618 U/l), and increased serum C-reactive protein (21.1 mg/l; normal reference range: <5 mg/l). His lymphocyte count (2.07 × 10⁹/l; normal reference range: 1–3.4 × 10⁹/l) and haemoglobin level (12.2 g/dl; normal reference range: 12–16 g/dl) were unremarkable. An electrocardiogram showed right bundle branch block.

A contrast-enhanced chest computed tomography (CT) scan showed several partially cavitated lung nodules in both upper lobes plus mediastinal lymphadenopathy. A thin-walled fluid-containing cavity 7 × 3 cm in size 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 cava thromboses were present and abdominal imaging was normal.

Transthoracic echocardiography showed a large mass extending caudally across the tricuspid valve, with a smooth surface and attached to the roof and to the anterolateral wall of the

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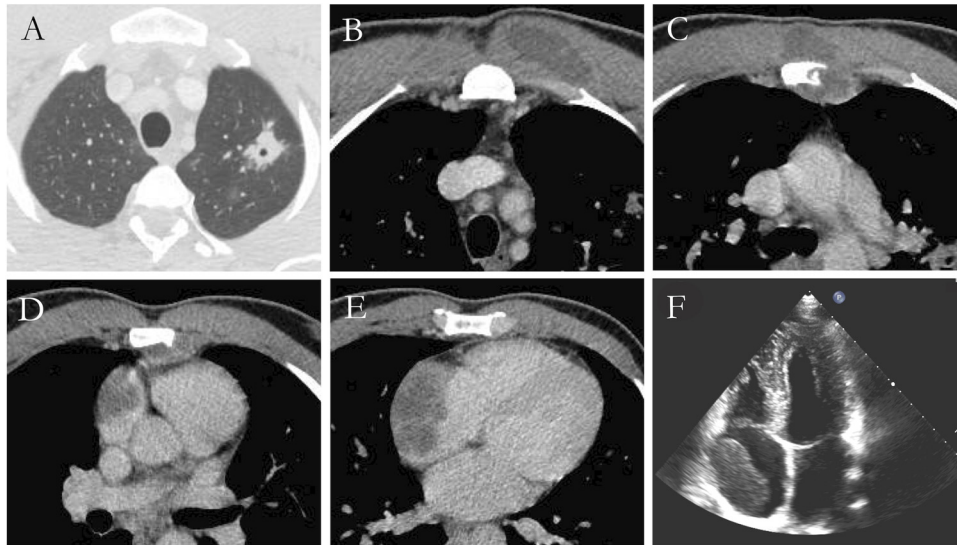


Figure 1. Contrast-enhanced CT scan showing cavitated lung nodules in the left upper lobe (A), a left pectoral abscess (B), osteomyelitis of the sternal body and involvement of the anterior mediastinum (C) and the pericardium and the heart (D). (E) Right atrium mass. (F) Echocardiography: apical four-chamber view showing a large mass (4.8 × 2.5 cm in size) attached to the roof and to the anterolateral wall of the right atrium.

right atrium (Figure 1F); this was characterized by a heterogeneous echogenicity with areas of echolucency. Furthermore, mild tricuspid regurgitation, without any other flow obstruction, was detected by colour 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.

Bronchoscopy with bronchoalveolar lavage (BAL) in the left upper lobe and a transthoracic CT-guided biopsy of the parasternal lesion were performed. Xpert MTB/RIF testing of 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 resistance to the first-line anti-TB drugs.

The standardized regimen recommended by the World Health Organization (i.e., isoniazid 300 mg/day, rifampicin 600 mg/day, ethambutol 1600 mg/day, and pyrazinamide 1500 mg/day) was administered for a 2-month intensive therapy, which was followed by a 4-month continuation phase with isoniazid and rifampicin. This regimen was administered together with low molecular weight heparin for the high thrombotic risk (Nahid et al., 2016). A self-administered therapy regimen was adopted. His clinical recovery was prompt. However, after 14 days of treatment, the patient refused to stay in hospital to have further procedures including cardiac magnetic resonance imaging (MRI) and transoesophageal echocardiography. Following the first outpatient visit (1 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 the disease (1–5% of all TB cases) caused by MTB identified in blood or bone marrow samples, from liver biopsies, or from specimens collected from two or more non-contiguous organs (Crump and Reller, 2003; Suárez et al., 2019). Extrapulmonary dissemination, for which the pathogenesis is largely unknown, depends on the haematogenous or lymphatic spread of MTB from the primary site of infection (Suárez et al.,

2019; Qian et al., 2018). Myocardial TB may occur following haematogenous/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 (Suárez et al., 2019; Rao et al., 2012; Goyal et al., 2005).

In the case presented here, it is hypothesized 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 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.

Although a cardiac thrombus or neoplasm could 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 may represent the clinical outcome of an MTB infection that 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 and Reller, 2003; Suárez et al., 2019; Qian et al., 2018). However, cases of disseminated disease in healthy refugees have been described recently, suggesting the role of potentially virulent *M. tuberculosis* strains and/or a specific genetic pattern of the host, or the stress associated with movement (Suárez 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 extrapulmonary TB forms being most frequently diagnosed in Africans (Mondoni et al., 2018; Sotgiu et al., 2017; Suárez 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; Suárez 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; Suárez 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 (Suárez et al., 2019; Khan, 2019).

Sensitive and specific imaging tests (e.g., CT, MRI, positron emission tomography) are crucial to assess the extent of the disease. In the 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 in order to rule out TB disease and its life-threatening complications prior to blind treatment (Mondoni et al., 2017; Suárez et al., 2019; Khan, 2019). Notably, the differential diagnosis may include the following medical conditions: lymphoma, connective tissue malignancies, fungal and bacterial infections (Khan, 2019).

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

The cascade of care for migrants should be implemented and scaled up at the 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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Ethical approval

This observational study did not require ethical approval according to Italian law for observational studies.

Conflict of interest

The authors do not have any conflict of interest.

References

- Crump JA, Reller LB. Two decades of disseminated tuberculosis at a university medical center: the expanding role of mycobacterial blood culture. *Clin Infect Dis* 2003;37(8):1037–43.
- Dara M, Solovic I, Sotgiu G, D'Ambrosio L, Centis R, Tran R, et al. Tuberculosis care among refugees arriving in Europe: a ERS/WHO Europe Region survey of current practices. *Eur Respir J* 2016;48(3):808–17.
- Goyal NK, Saxena A, Chopra P. Complete resolution of a large intracardiac mass with medical treatment: an echocardiographic follow up. *Heart* 2005;91(8):1046.
- Khan FY. Review of literature on disseminated tuberculosis with emphasis on the focused diagnostic workup. *J Family Community Med* 2019;26(2):83–91.
- Mondoni M, Reossi A, Carlucci P, Centanni S, Sotgiu G. Bronchoscopic techniques in the management of patients with tuberculosis. *Int J Infect Dis* 2017;64:27–37.
- Mondoni M, Viganò O, Ferrarese M, Bimbatti M, Cavallini M, Codecasa L, et al. Haemoptysis and fever in a young refugee from Somalia. *Int J Infect Dis* 2018;77:57–60.
- Nahid P, Dorman SE, Alipanah N, Barry PM, Brozek JL, Cattamanchi A, et al. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. *Clin Infect Dis* 2016;63:e147–95.
- Qian X, Nguyen DT, Lyu J, Albers AE, Bi X, Graviss EA, et al. Risk factors for extrapulmonary dissemination of tuberculosis and associated mortality during treatment for extrapulmonary tuberculosis. *Emerg Microbes Infect* 2018;7(1):102.
- Rao VR, Jagannath K, Sunil PK, Madhusudana N. A rare disappearing right atrial mass. *Interact Cardiovasc Thorac Surg* 2012;15(2):290–1.
- Suárez I, Maria Fünfer S, Jung N, Lehmann C, Reimer RP, Mehrkens D, et al. Severe disseminated tuberculosis in HIV-negative refugees. *Lancet Infect Dis* 2019;19:e352–9 pii: S1473-3099(19)30162-8.
- Sotgiu G, Falzon D, Hollo V, Ködmön C, Lefebvre N, Dadu A, et al. Determinants of site of tuberculosis disease: an analysis of European surveillance data from 2003 to 2014. *PLoS One* 2017;12(11):e0186499.