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Pericarditis caused by *Mycobacterium africanum*: case report

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Abstract

Background: *Mycobacterium africanum* is a member of the *Mycobacterium tuberculosis complex* (MTBC) and is endemic in West Africa, where it causes up to half of all cases of pulmonary tuberculosis. Here, we report the first isolation of *Mycobacterium africanum* from the pericardial effusion culture of a patient with tuberculous pericarditis.

Case presentation: A 31-year-old man, native from Senegal, came to the emergency room with massive pericardial effusion and cardiac tamponade requiring pericardiocentesis. *M. africanum* subtype II was identified in the pericardial fluid. The patient completed 10 months of standard treatment, with a favorable outcome.

Conclusions: We report the first case of tuberculous pericarditis caused by *Mycobacterium africanum*, which provide evidence that this microorganism can cause pericardial disease and must be considered in patients from endemic areas presenting with pericardial effusion.

Keywords: *Mycobacterium africanum*, *Mycobacterium tuberculosis complex*, Tuberculous pericarditis, Interferon-gamma release assays, Case report

Background

Mycobacterium africanum (M. africanum) is a member of the *Mycobacterium tuberculosis complex* (MTBC) and a primary cause of human tuberculosis disease globally [1]. The MTBC consists of seven phylogenetically distinct lineages (L1–L7) and the phylogenetic study of *M. africanum* classifies it into two groups of different biochemical characteristics and geographical origin: *M. africanum subtype I* (L5) and *M. africanum subtype II* (L6) [2, 3].

M. africanum is endemic in West Africa, where it causes up to half of all cases of pulmonary tuberculosis [4]. In developed countries, cases are mostly restricted to migrants from endemic areas [5]. Although the pulmonary form has predominantly been described, some cases of extrapulmonary presentations (pleural,cutaneous, bone, cerebral, prostatitis or epididymitis) have been published [6–11]. To the best of our knowledge, no cases of pericardial involvement have ever been reported.

We describe the first case of tuberculous pericarditis caused by *M. africanum.* The patient presented with massive pericardial effusion and cardiac tamponade requiring pericardiocentesis and *M. africanum* subtype II was identified in the pericardial fluid.

Case presentation

A 31-year-old man, native from Senegal and living in Spain for one year, came to the emergency room reporting non-productive cough, asthenia, evening fever and profuse sweating of one month duration, with progressive dyspnea limiting ordinary activity from the day before admission.

Patient's condition met the Beck's triad including arterial hypotension (a blood pressure of 85/65 mmHg), muffled heart sounds and mild jugular engorgement.

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Chest X-ray (Fig. 1) and computed tomography (Fig. 2) revealed a significant increase in the cardiac silhouette with bilateral pleural effusion and without pulmonary lesions. The electrocardiogram showed a heart rate of 100 beats per minute, with low voltage, a right bundle branch block and electrical alternans.

Transthoracic echocardiography described severe pericardial effusion with echocardiographic signs of hemodynamic compromise, right ventricular diastolic collapse, and right atrium systolic collapse, as well as a dilated inferior vena cava and global hypokinesia that conditioned a severely depressed left ventricular ejection fraction (30%) (Fig. 3).

To investigate the etiology of pericardial effusion and cardiac tamponade, an ultrasound-guided percutaneous puncture pericardiocentesis and pericardial biopsy with a pericardioscope through the subxiphoid route were performed. Pericardial effusion had serohematic appearance and the cytochemical and cytological study showed increased cells, predominantly lymphocytes and macrophages, with elevated adenosine deaminase levels (120,2 U/L). Conventional bacteriologic cultures of pericardial effusion were negative. Acid-alcohol-fast bacilli were not observed in the Ziehl-Neelsen stain. The pericardial sample was processed for culture in liquid medium (Bactec MGIT 960) and in enriched solid medium (Coletsos and Löwenstein-Jensen). Since only one sample was available for all microbiological processes, direct PCR and liquid culture were performed from the same sample. The direct MTBC PCR (FluoroTypeMTB-Hain) from the pericardial effusion was negative. Liquid medium culture was positive for

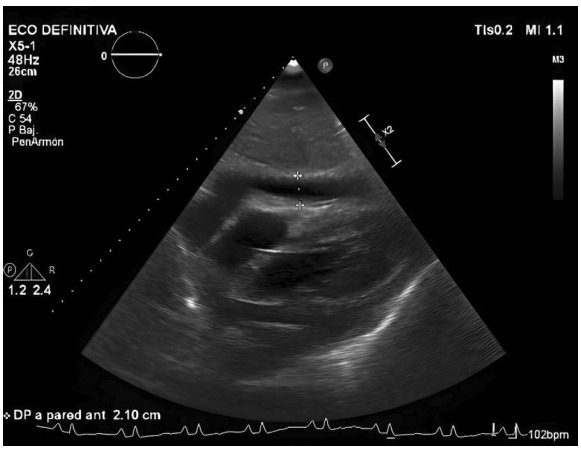

Fig. 3 Transthoracic echocardiography showing a massivepericardial effusion

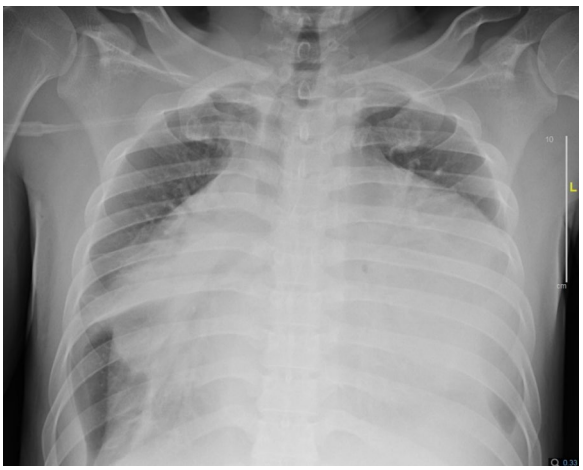

Fig. 1 Chest x-ray showing a significant increase inthe cardiac silhouette with bilateral pleural effusion without pulmonarylesions

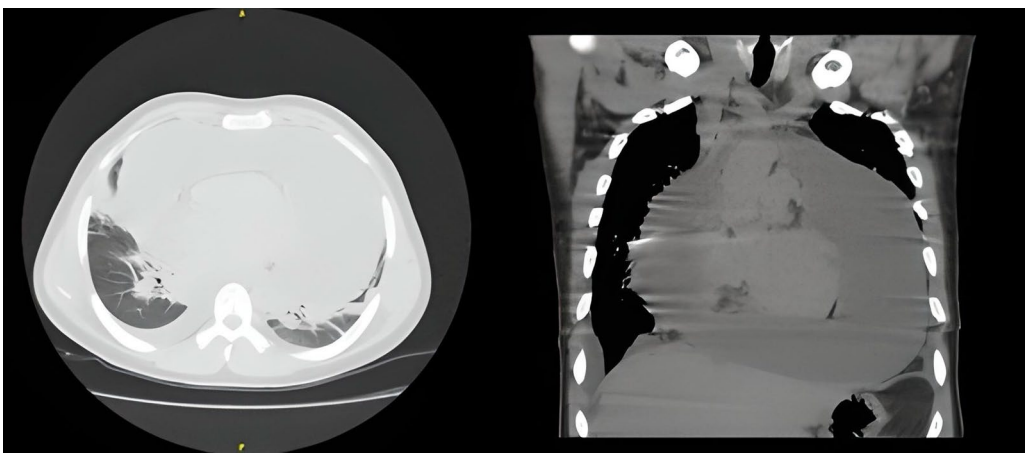

Fig. 2 Chest computed tomography showing a massivepericardial effusion

mycobacteria after seven weeks of incubation, and PCR performed at this moment from this liquid medium was also positive for MTBC. Rapid confirmation of presumptive positive liquid cultures of Mycobacterium tuberculosis, based on the detection of the MPT64 antigen, was negative from the liquid medium, but positive from direct colony.

The strain was sent to the Mycobacteria Laboratory of the National Center for Microbiology (Carlos III Health Institute), where it was identified as *M. africanum*, and it showed to be sensitive to isoniazid, rifampin, pyrazinamide, streptomycin, and ethambutol.

Genomic epidemiologic analysis was carried out (Tuberculosis Genomics Unit of the Biomedicine Institute of Valencia) using the whole genome sequencing technique for a subsequent genomic analysis of single nucleotide point mutations (SNP). The species and lineage identified were *M. africanum* subtype *II.* The analysis of genetic distances showed it was a single sample, not belonging to any transmission group of the Valencian Community included in the Tuberculosis Genomics Unit's database. The strain was found at a distance greater than 300 SNPs from the closest strain. No specific SNPs were identified that confirmed resistance to the different first and second line antituberculosis drugs.

IFN-γ production was determined by *QuantiFERON-TB Gold Plus (QFT-Plus)* in the patient's blood using ESAT-6 and CFP-10 antigens and was negative.

Pericardial biopsy revealed non-necrotizing chronic granulomatous pericarditis.

The HIV serology test was negative.

Antituberculous therapy including isoniazid, rifampin, ethambutol, and pyrazinamide was started, as well as adjuvant treatment with corticosteroids.

The patient was switched to isoniazid and rifampicin after an initial two-month regimen with four drugs and completed 10 months of therapy, with a favorable outcome. The patient underwent periodic transthoracic echocardiograms. One month after hospital admission, the pericardial effusion had improved, and a preserved left ventricular ejection fraction was observed.

Discussion and conclusions

Pericarditis is a rare manifestation of tuberculosis that carries high morbidity and mortality despite proper diagnosis and treatment. Tuberculous etiology represents less than 4% of all cases of pericarditis in developed countries [12]. The pericardium is affected by contiguity from the peritracheal, peribronchial and mediastinal nodes, or by the hematogenous route from pulmonary tuberculosis.

Although pulmonary and extrapulmonary tuberculosis caused by *M. africanum* have been reported, this is the first ever-reported case of pericardial involvement, causing tuberculous pericarditis with cardiac tamponade. *M. africanum* infrequently causes tuberculosis infection in Spain. Tuberculosis disease caused by *M. africanum* is more frequently associated with elderly patients, severe malnutrition, HIV infection and with severe abnormal radiological findings in the X-ray [13]. *M. africanum* induces similar clinical manifestations to the rest of mycobacteria belonging to the MTBC, although it has lower virulence and lower rate of progression to active tuberculosis than *M. tuberculosis* [14]. *M. africanum* lineages show microaerobic growth and are usually associated with extrapulmonary disease, which suggests a preference for regions with low oxygen [15].

Crucial virulence mechanisms have been shown to be altered in *M. africanum* infection, including an attenuation of T-cell responses to the mycobacterial-secreted antigenic and virulence factor ESAT-6, that could impair the accuracy of interferon-gamma release assays (IGRA) [16]. This would explain the negative results of the *QuantiFERON-TB Gold Plus* test observed in our patient.

Interferon-gamma release assays have recently shown promising results in diagnosing active extrapulmonary tuberculosis. The T-SPOT.TB has shown a high sensitivity and specificity on tuberculosis pericardial effusion [17]. Therefore, these tests appear to be a promising rapid diagnostic method with high diagnostic accuracy for diagnosis of tuberculous pericarditis [18].

M. africanum grows more slowly than *M. tuberculosis*; it can take up to 10 weeks to yield growth in cultures [19].

Regarding treatment, *M. africanum* infections respond to regular tuberculosis treatment. Adjuvant steroid treatment has been associated with a decrease in the incidence of pericardial constriction and hospitalization in mycobacterial pericarditis [20].

In conclusion, *M. africanum* can cause pericardial disease and must be considered in patients from endemic areas presenting with pericardial effusion. The diagnosis may be challenging due to the longer growth time than *M. tuberculosis* and the fact that the disease is less likely to have a positive IGRA result. These difficulties become more relevant in areas where there is a greater distribution of *M. africanum* and sometimes with fewer available resources, as in the case of Africa.

Abbreviations

MTBC: *Mycobacterium tuberculosis complex*; *M. africanum*: *Mycobacterium africanum*; PCR: Polymerase chain reaction; SNP: single nucleotide point mutations; IGRA: interferon-gamma release assays.

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Author contributions
Preparation of the manuscript (PM, MM, FG, ADLR, MRG, SP, JGA, AB, JL). All authors have read and approved the manuscript to be published. ADLR and MRG contributed to the analysis and identification of *M. africanum*. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
The treatment for the patient is performed under the tenets of the Declaration of Helsinki.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report.

Competing interests
The authors declare that they have no competing interests.

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