

Electronic Cardiovascular Device-associated to Infective Endocarditis Caused by *Mycobacterium Mageritense*

Silvia Tützer¹, Tamara Posse¹, Roxana Paul², Johana Monteserin², Hector Pérez³, Sara Kaufman^{1*}

1. Section of Clinical Microbiology, Hospital Juan A. Fernández, Buenos Aires, Argentina.

2. Mycobacteria Section, ANLIS INEI Dr. Carlos G. Malbrán, Buenos Aires, Argentina.

3. Infectious Diseases Department, Hospital Juan A. Fernández, Buenos Aires, Argentina.

*Corresponding author. Email address: sarackaufman@gmail.com

Abstract: Rapidly growing non-tuberculosis mycobacteria are a rare cause of bacterial endocarditis. During the last decades, there has been an increase in infections due to rapidly growing mycobacteria, especially after trauma and postoperative procedures, both localized and disseminated, as well as nosocomial outbreaks due to contamination of medical equipment. Routine acid-fast staining for blood culture bottles is not always performed. However, the microbiologist should be aware of potential RGM infections especially when gram-positive bacilli are observed. We describe a case of endocarditis caused by *mycobacterium mageritense* in a patient with an autologous pericardial patch and a pressure catheter in the left auricle. The bacterial species was identified as *mycobacterium mageritense* by mass spectrometry (MALDI-TOF MS), score 2.3, and confirmed by 16S rRNA analysis with 99.8 and 100% agreement, respectively.

Key words: infective endocarditis; electronic cardiovascular device; *mycobacterium mageritense*; mass spectrometry

1. Clinical Case

A 40-year-old woman from Paraguay, negative for HIV, with a history of atrial septal defect correction, autogenous pericardial patch and placement of a pressure-measuring catheter in the left atrium in 2008.

In 2010, she presented a retromammary abscess, which was drained, and the subcutaneous fragment of the catheter was removed. She was hospitalized in July 2013 in Asunción (Paraguay) for suspected infective endocarditis associated with a cardiovascular electronic device. The reference laboratory in Asunción reported *mycobacterium smegmatis/goodii/mageritense* complex in blood cultures, obtained by the PRA molecular method (analysis of the restriction fragments of the 440 bp amplicon of the *hsp65* gene, amplified by PCR) [10]. The patient received intravenous antibiotic treatment with amikacin plus vancomycin for 26 days and was discharged with doxycycline.

She consulted a hospital in the city of Buenos Aires in October 2013 due to the onset of fever during antibiotic treatment. A transthoracic echocardiogram was performed, which showed vegetation in the tricuspid leaflet measuring 1 × 1.5 cm and 0.5 cm at the tip of the catheter. Serial blood cultures were taken: Aerobic Plus/F, Anaerobic Plus/F and Myco/F

Lytic (Becton Dickinson, USA). Empirical treatment with meropenem (1 g/8 h) and ciprofloxacin (400 mg/12 h) was started; the patient remained afebrile.

At 48 hours, blood cultures were positive, Gram stain showed rod-shaped Gram-positive bacilli, and a rapid growing mycobacterium (RCM) was suspected. The Kinyoun stain, a cold variant of the Ziehl-Neelsen stain for acid-fast bacteria, was performed (Fig. 1). We proceeded with a direct extraction from the blood culture bottle to be analyzed by MALDI TOF MS mass spectrometry (Bruker, Bremen, Germany) according to the HF protocol (handmade procedure) recommended by Cattani et al [2], resulting in *M. mageritense* with a score of 2.3 (a score or identification score ≥ 2 confirms the genus and species). Mycobacteria develop in 48 hours from blood cultures on Columbia agar with 5% sheep blood (bioMérieux, L'Étoile, France), as shown in Figure 2.

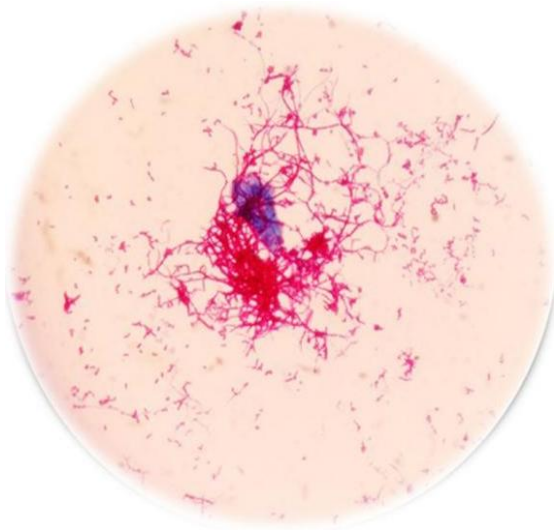


Figure 1. Direct Kinyoun staining of positive blood culture.



Figure 2. Appearance of *M. mageritense* colonies on 5% sheep blood agar.

The strain was sent to the National Tuberculosis Reference Laboratory INEI ANLIS Dr. Carlos G. Malbrán for sequencing of the 16S rRNA gene, which confirmed identification to species level with 99.8% identity.

Definitive identification of RCM isolates is difficult. MALDI-TOF MS analysis combined with DNA sequence analysis is a promising technique for rapid identification of RCMs, which is very important for understanding the epidemiology of these pathogens and their role in human infections. In a study conducted in Argentina, MALDI-TOF MS identified 61% of nontuberculous mycobacteria, which are low prevalent in clinical infections and could not be identified to species level by other methods [9].

The patient completed intravenous treatment for 10 weeks. As a manifestation associated with endocarditis, she presented splenomegaly with hypersplenism and splenic infarction, so spleen exeresis was performed. After 10 weeks of treatment, the transesophageal echocardiogram showed resolution of vegetations and negative blood cultures. Due to the good evolution and taking into account the results of the minimum inhibitory concentrations for the different antimicrobial agents tested (table 1), the regimen was rotated to ciprofloxacin (500 mg/12 h) plus trimethoprim-sulfamethoxazole (160/800 mg/12 h), to continue on an outpatient basis while awaiting surgical resolution.

Table 1. Sensitivity of mycobacterium mageritense

Antibiotic	MIC (µg/ml)
Amikacin	128
Tobramycin	> 64
Clarithromycin	> 256
Cefotaxime	> 256
Cefoxitin	32
Coccycline	> 32
Ciprofloxacin	0.25
Sulfamethoxazole	4
Trimethoprim-sulfamethoxazole	0.094
Linezolid	< 0.5
Meropenem	0.5

MIC: minimum inhibitory concentrations.

2. Introduction of RCMs and Focus on *M. mageritense* and Its Treatment Challenges

RCMs are widely distributed in water, soil, birds and other animals. They are able to form biofilms and survive in the absence of nutrients [3]. An increase in RCM infections, especially post-traumatic and post-surgical device-associated infections, both localized and disseminated, has been reported. RCMs also cause nosocomial outbreaks due to contamination of medical equipment [1, 3, 5, 10]. More than 170 species have been described so far, and more than half of them have been associated with human infections [6].

M. mageritense was first isolated in Spain in 1987 and was described as a new species by Domenech et al. [4], but was only associated with disease in 2002 in the USA [13]. The most frequent RCM in human infections are mycobacterium chelonae, mycobacterium abscessus and mycobacterium fortuitum. *M. mageritense* belongs to the latter complex, biovariety 3, sorbitol-positive [11]. *M. mageritense* is isolated infrequently from cardiovascular device-related bacteremia [6, 13]. A case of prosthetic endocarditis has been described in which a pigmented strain was isolated [8]. Most documented human infections are associated with postsurgical infection, catheters and sinusitis [13].

M. mageritense is generally resistant to certain antibiotics, including amikacin and clarithromycin, drugs with good activity against most RCM [12, 14]. In our case, the patient was first treated in Paraguay with antibiotics to which the microorganism was resistant, so we believe it is essential to correctly identify the RCMs and determine their sensitivity [14]. Mass spectrometry of the positive blood cultures yielded an accurate result in 20 min.

Treatment against this pathogen, which is time-consuming, also includes the removal of any device (catheter, pacemaker, prosthesis), since due to their ability to form biofilms, RCMs may persist despite adequate treatment [7].

M. mageritense is a low virulence RCM that is usually not associated with clinical disease. Our case, together with other reported clinical infections [6-8], shows the pathogenic potential of this microorganism. It is important to suspect the presence of a RCM, since by Gram staining these germs can be confused with the corynebacterium, actinomyces or nocardia genera.

We believe that the laboratory's contribution to determine the different RCM and their antibiotic resistance is substantial. It should be emphasized that antibiotic treatment should be prolonged and should include the removal of catheters/devices.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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