Case report

*Mycobacterium farcinogenes* osteomyelitis of the proximal tibia: A case report

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**ABSTRACT**

Non-tuberculous mycobacteria (NTM) are an unusual cause of osteomyelitis. *Mycobacterium farcinogenes* is an uncommon cause of human disease. We describe here the first case of *M. farcinogenes* osteomyelitis in a 49-year-old man who underwent left knee anterior cruciate ligament and medial meniscal repair which was complicated by recurrent septic arthritis and surgical site infection. As a consequence, he underwent multiple surgical debridements. Ultimately, left proximal tibial osteomyelitis was diagnosed and *M. farcinogenes* was recovered from the tissue biopsy culture. Clinical improvement was achieved following surgical removal of the prosthesis along with prolonged combination antimicrobial therapy.

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**Background**

*Mycobacterium farcinogenes* was first described in 1973 as a causal agent of bovine farcy in east and central Africa [1]. Bovine farcy is a chronic suppurrative granulomatous inflammation of the skin and lymphatics of cattle and is seen mostly in sub-Saharan Africa [2]. Cases of human infection were rarely reported. We report here the first case of *M. farcinogenes* osteomyelitis of the proximal tibia post knee anterior cruciate ligament (ACL) and medial meniscal repair.

**Case report**

A 49-year-old man, diabetic and hypertensive, underwent left knee ACL and medial meniscal repair in India in September 2019. Two months later, he developed septic arthritis of the left knee which was managed by joint washout and empirical antibiotic in a regional hospital. He did not show good clinical response and underwent multiple joint washout and received multiple courses of antibiotics. All microbiological cultures were negative. In January 2020, he presented to Sultan Qaboos University Hospital (a tertiary care center in Oman) with pus discharge at the surgical site. He was afebrile and his inflammatory markers were within normal. Wound debridement was done and necrotic tissue was found. *Pseudomonas stutzeri* was isolated from the wound swab and tissue cultures. Ciprofloxacin was started based on the susceptibility results. Two weeks later, he developed a sinus tract at proximal tibia site around 4 cm below the knee joint line corresponding to the ACL graft tibial fixation. Examination of the site revealed mild erythema, sinus tract with minimal pus discharge, no significant swelling or tenderness and no restriction of movement. Magnetic resonance imaging (MRI) showed hyperintense T2 signal surrounding the tibia screw with post contrast enhancement suggestive of osteomyelitis and intraosseous collection as well. Further exposure history revealed limited contact with animals; cows and goats in his farm and consumption of unpasteurized camel milk. He did not travel again after the first surgery in India. Last travel history before that was to Egypt two years ago.

He underwent tibial screw and ACL graft removal in addition to irrigation and debridement. Multiple tissue samples were obtained from the knee joint for culture, and extended incubation of the culture plates was requested. After 4 days of incubation, scanty growth of white colonies was observed on routine culture media in three out of four samples (Fig. 1-A), which was identified as *Mycobacterium farcinogenes* using matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry (Bruker) with a score of 1.99. In the mycobacterial reference lab, direct Acid

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http://dx.doi.org/10.1016/j.idcr.2021.e01194

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Fast Bacilli (AFB) stain from the biopsy samples was negative, but mycobacterial culture was positive at 8 days and 25 days by Middlebrook 7H9 Broth (BD BACTEC MGIT) and Lowenstein-Jensen (LJ) culture respectively. The identification was confirmed by rpoB gene sequencing. The PCR amplified products of fragment of rpoB gene was sequenced by Sanger Sequencing and BLAST search was carried out with NCBI database. The results revealed sequence similarity (99.5%) with M. farcinogenes (GenBank accession no. KY_40066411). The phylogenetic relationship of 9 strains which showed more close identity with the resulted sequence (as per NCBI BLAST) is shown in Fig. 2.

The patient showed clinical improvement post-operatively, so ciprofloxacin was continued, and doxycycline was added as empirical treatment pending susceptibility results. The isolate was sent to Biomnis Eurofins labs in France for susceptibility testing. The commercial microplate dilution method for rapid growing mycobacteria (Sensititre RAPMYCOI, Thermo Scientific™) was used. Antimicrobial drug susceptibility results were interpreted according to the CLSI M62 guidelines [3]. The results, detailed in Table 1, showed that M. farcinogenes was only susceptible to amikacin and clarithromycin (day-3 reading). Since the patient had dramatically improved clinically and he tolerated the treatment, it was decided to continue ciprofloxacin and doxycycline. The patient completed a 6-month course of treatment. At a follow-up visit 10-months after treatment completion, there was complete clinical resolution without disease recurrence.

**Discussion**

Non-tuberculous mycobacterial (NTM) disease has been steadily increasing globally owing to a growing population of immunocompromised, complex surgical procedures, as well as increased diagnostic capabilities [4]. M. farcinogenes has been rarely implicated as a human pathogen, one case has been reported.
Table 1
Antimicrobial sensitivity of Mycobacterium farcinogenes.

| Antibacterial drugs        | MIC (µg/mL) | Results |
|----------------------------|-------------|---------|
| Trimethoprim sulfamethoxazole | ≥8/152     | resistant |
| Ciprofloxacin              | >4          | resistant |
| Mosfloxacin                | 8           | resistant |
| Cefoxitin                  | 32          | intermediate |
| Amikacin                   | 8           | susceptible |
| Doxycycline                | >16         | resistant |
| Tigecycline                | 0.5         | -        |
| Linezolid                  | 16          | intermediate |
| Imipenem                   | 16          | intermediate |
| Cefepime                   | >32         | -        |
| Amoxicillin-clavulanate    | >64/32      | -        |
| Ceftriaxone                | >64         | -        |
| Minocycline                | >8          | -        |
| Clarithromycin at 3 days   | 0.25        | susceptible |

Note: - No Breakpoint in CLSI M62.

Fig. 2. Phylogenetic tree for tested strain; CPHL1437 Mycobacterium spp. (Sequences Alignment and construction of tree were carried out using Phylogeny.fr).

of hip prosthetic joint infection [5] and it has also been isolated from sputum samples of pastoralists of the Hamer Woreda tribe in southern parts of Ethiopia; these people presented with clinical signs of tuberculosis [6], although the authors of both reports expressed a degree of uncertainty about the accuracy of species identification. Although M. farcinogenes was originally described as a slow-growing mycobacterium [1], numerical taxonomy studies [7] and 16S–23S intergenic spacer sequence analysis further revealed that M. farcinogenes is closely related to Mycobacterium fortuitum complex; rapid growing mycobacteria (RGM) [8]. Time to positivity in our case for both liquid and solid mycobacterial primary culture was more than 7 days. However, standardized growth test [9] using 0.5 McFarland suspension of the organism inoculated on a solid LJ medium and incubated at 37°C resulted in mature colonies developing by day 4, which classifies the organism as a “rapid grower”.

The close relationship of molecular sequencing between M. farcinogenes and M. fortuitum complex, lack of incorporation of new taxa into classification databases, and the low discrimination between different RGM using 16S rRNA sequencing are all factors that make identification of RGM challenging [10]. In this case report we used two different methods of identification: MALDI-TOF with a score of 1.99, which is considered as high-confidence identification level for mycobacteria [11], and rpoB gene sequencing which has a higher discrimination power [10]. We believe that this growth was clinically significant because it grew from multiple joint-tissue biopsies, the patient had the right predisposing factors, and the clinical progress was suggestive. It was probably missed in previous cultures because culture plates were only incubated for 48 h due to a low index of suspicion of fastidious organisms or mycobacteria (i.e. routine lab procedures were followed).

Because there has only been limited experience with this organism and no specific treatment guidelines exist, we based our antimicrobial management on the available guidelines for NTM infection treatment on M. fortuitum group [12]. The patient was on ciprofloxacin to cover the previously isolated Pseudomonas stutzeri, so ciprofloxacin was continued, and doxycycline was added as a second agent for empirical anti-mycobacterial cover. Surgical debridement and removal of prosthetic materials played a major role in clinical improvement. Unlike M. fortuitum which is usually susceptible to multiple oral antibiotics [12], our isolate showed resistance to multiple agents with limited antibiotic options. Despite susceptibility to clarithromycin at day 3, the potential for development of resistance through an inducible erythromycin methylase erm gene [12] (which can be detected by incubation of the mycobacterial isolate in the presence of a macrolide for 14 days) could not be excluded because this result was not provided by the lab. In our case, antibiotics were continued based on clinical response.

Conclusion

M. farcinogenes may be an occasional cause of human infections. High index of suspicion and close collaboration with microbiologists is required to reach the correct diagnosis. Doing extensive surgical debridement is a key in reducing infection burden and eliminating the offending pathogen. Broader access to newer diagnostic methods will continue to improve recognition of NTM disease. In our case, molecular techniques confirmed the accuracy of MALDI-TOF mass spectrometry in identifying this emerging mycobacterial species.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Not applicable.

Consent

Informed consent was obtained from the patient for publication of this case report.
Author contribution

Al Farsi, F. contributed to literature review and manuscript drafting. Al Adawi, B. contributed in editing of the manuscript. Adikaram, C. contribute in phylogenetic analysis. All other authors critically reviewed the manuscript and approved the final version. Ba Taher, H, Al Busaidi I and Al Mutani, M treated patient.

Declaration of Competing Interest

All authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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