Case report

Mycobacterium farcinogenes infection after fracture repair of the tibia and fibula

Eriko Kashihara [a,b,c,*], Kohei Fujita [a,d], Hiroshi Yamamoto [e], Takao Odagaki [a,b]

[a] *Department of Infectious Diseases, National Hospital Organization Kyoto Medical Center, Kyoto, Japan*
[b] *Department of General Internal Medicine, National Hospital Organization Kyoto Medical Center, Kyoto, Japan*
[c] *Department of General Internal Medicine, Tenri Hospital, Nara, Japan*
[d] *Division of Respiratory Medicine, Center for Respiratory Diseases, National Hospital Organization Kyoto Medical Center, Kyoto, Japan*
[e] *Department of Orthopedics, National Hospital Organization Kyoto Medical Center, Kyoto, Japan*

A B S T R A C T

Mycobacterium farcinogenes is the causative agent of bovine farcy. *M. farcinogenes* shares common properties with rapidly growing mycobacteria, and distinguishing between *M. farcinogenes* and *M. fortuitum* is reportedly complex and challenging. Moreover, few studies have isolated *M. farcinogenes* from human clinical samples.

A previously healthy 37-year-old male construction worker presented to the emergency department after a severe injury and was diagnosed with a Gustilo-Anderson type IIIA fracture. After an uneventful postoperative period of two months, he experienced pain and serous discharge from the upper shin and lower calf region. Frequent debridement provided no relief, and the pathology cultures of the tissue were negative. However, *M. farcinogenes* was isolated from the fluid of the wound. The patient's symptoms gradually improved with anti-mycobacterial drug treatment.

Nontuberculous mycobacterial infections, including those caused by *M. farcinogenes*, should be considered in patients developing soft tissue infections despite negative pyogenic bacterial cultures several months after sustaining an open fracture.

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Introduction

Mycobacterium farcinogenes is the main causative agent of bovine farcy, a chronic progressive disease of the skin and lymphatic system of zebu cattle. It was initially thought to be caused by *Nocardia farcinica.* [1,2] Chamoiseau *et al.* first identified *M. farcinogenes* and *M. senegalense* as the causal agents of bovine farcy in 1973. Since then, this infection has rarely been reported [3]. *M. farcinogenes* and *M. senegalense* share common properties with rapidly growing mycobacteria, namely, the *M. fortuitum* complex (*M. fortuitum*, *M. houstonense*, *M. peregrinum, M. porcinum, M. septicum,* and *M. neworleansense*) [4]. *M. fortuitum* causes infections of the skin, soft tissue, and bone after trauma and surgery in immunosuppressed patients. However, it rarely causes infections among humans [5]. Only a few studies have isolated *M. farcinogenes* from human clinical

samples [6,7]. We report a rare case of *M. farcinogenes* soft tissue infection after fracture repair of the tibia and fibula.

Case report

A previously healthy 37-year-old male construction worker presented to the emergency department with severe left-sided lower extremity pain. His leg was injured after a piece of concrete fell on it while he was working outside. He was brought to the hospital 2 h after the injury. The clinical and radiologic evaluations revealed a Gustilo-Anderson type IIIA fracture (Fig. 1). Closed interlocked nailing was performed for the fracture one week after the injury. Although the patient had an uneventful postoperative period of two months, he complained of serous discharge from the upper shin and lower calf during the third month of his treatment course. Soft tissue infection and osteomyelitis were suspected.

Debridement was performed every two weeks, and the patient received antimicrobial therapy with cefazolin. Although the microbiological and pathological tissue cultures were negative for pyogenic organisms, the patient's clinical symptoms did not improve.

Fig. 1. Radiographic images of the left lower extremity shows fractures of the tibia and fibula.

Debridement was continued, and pathological cultures were taken every one to two weeks. About six weeks after the initiation of debridement, i.e., four months after the operation, the C-reactive protein levels increased, and gram-positive bacilli that were phagocytosed by neutrophils were observed on Gram-stained smears of the fluid of the wound. These findings suggested the presence of *Mycobacterium* species. The fluid was sent for a *Mycobacterium* culture, and *M. farcinogenes* was identified by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) and 16S ribosomal DNA (rDNA) internal transcribed spacer sequences. The patient was HIV-negative, and he did not have diabetes mellitus or other diseases associated with an immunocompromised state.

The probe-to-bone test was negative, and enhanced magnetic resonance imaging revealed minimal changes in the osseous signals on both T1-weighted (Fig. 2A, B) and short tau inversion recovery imaging (Fig. 2C, D). These findings indicated bone marrow edema, and the diagnosis of osteomyelitis was not confirmed. The patient was diagnosed with a soft tissue *M. farcinogenes* infection. The result of formal antimicrobial sensitivity test is shown in Table 1, and he received combination therapy with levofloxacin, amikacin, and rifampin. His symptoms and serum infection markers improved after the initiation of treatment.

The local inflammation improved with continuous antimicrobial therapy and debridement every two to three weeks for more than 12 months.

Discussion

We report a rare case of *M. farcinogenes* infection of the soft tissue in a previously healthy 37-year-old man, who underwent a fracture repair. Only two studies have isolated *M. farcinogenes* from human clinical samples. Both studies reported *M. farcinogenes* infections of the skin, soft tissue, and bone [6,7]. *M. farcinogenes* is challenging to distinguish from *M. senegalense* based on the histopathological findings and 16S rRNA sequence data [8,9]. A previous study showed that the ^{16}S–^{23}S rDNA spacer could distinguish between the two species [9]. Despite the lack of studies supporting its application to identify *M. farcinogenes*, the MALDI-TOF MS method was reportedly valuable for detecting and identifying *Mycobacterium* species [10]. In the present case, the MADI-TOF MS and 16S rDNA

data were used to confirm the causative mycobacteria. It shared common properties with *M. fortuitum*, an environmental mycobacterium, causing infections through contaminated tap water [11]. There have been no reports on the isolation or detection of both *M. farcinogenes* and *M. senegalense* from environmental samples. The present case suggested that *M. farcinogenes* can be isolated from environmental samples [4].

The patient had an uneventful period of two months, and the interval between the operation and biological diagnosis spanned almost four months. Wong et al. reported a case of *M. farcinogenes* infection of implants six months after total hip arthroplasty [6]. Isozaki et al. reported osteomyelitis, caused by *M. farcinogenes*, in a 66-year-old man, who underwent osteosynthesis for a compound fracture in the left lower thigh five months prior [7]. In both cases, the definitive diagnosis was achieved after about one year, and the patients successfully recovered with independent ambulation after discharge. In a case series of skin and soft tissue infections due to rapidly growing mycobacteria, Uslan et al. reported that the median duration between the recorded onset of symptoms and diagnosis by detecting the causative organism was 86 days [12]. Therefore, infections caused by rapidly growing mycobacteria should be considered in patients presenting with non-healing wounds after an uneventful postoperative period. A definitive diagnosis and appropriate treatment are necessary in these cases. Moreover, environmental exposure suggests possible infection.

The choice of antibacterials depends on the susceptibility of microbes. There is limited information on the antibiotic selection for *M. farcinogenes* infections. In this case, we chose the current treatment based on previous reports as well as the susceptibility. Wong *et al.* used ciprofloxacin and doxycycline, while Isozaki *et al.* used levofloxacin only [3,4]. Surgical debridement with removal of infected hardware, followed by combination antibiotic therapy, was reportedly effective in treating nontuberculous mycobacterial soft tissue infections, and it prevented resistance development [13]. Kasperbauer et al. suggested that *M. fortuitum* was more manageable than the other rapidly growing mycobacteria, such as *M. abscessus* and *M. chelonae*. Moreover, patients with skin and soft tissue infections, caused by *M. fortuitum*, should receive at least two active agents [14]. In cases involving abscess formation or those refractory to pharmacologic therapy, the duration of treatment should be at least four months. This should be increased to six months for cases with bone involvement [14]. As seen in the two previous reports on *M. farcinogenes*, the duration of treatment for *M. farcinogenes* infection was based on the treatment for *M. fortuitum* due to their similar characteristics.

In conclusion, nontuberculous mycobacterial infections, including those caused by *M. farcinogenes*, should be considered in patients developing soft tissue infections despite having negative pyogenic bacterial cultures several months after sustaining an open fracture. Since there are only few reports of *M. farcinogenes* infection, and the optimal treatment and duration of treatment have not been determined, the accumulation of similar cases is awaited.

Ethical approval

Not applicable.

Consent

We obtained written informed consent form from the patient.

Competing interest

We have no conflict of interest to declare.

Fig. 2. A–D: Enhanced magnetic resonance imaging revealed minimal change of osseous signal on both T1-weighted (A, B) and short tau inversion recovery images (C, D). However, edema and fluid retention were noted in the soft tissues around the bone. This finding suggests possible soft tissue infection.

Table 1
The drug susceptibility of *Mycobacterium farcinogenes*.

Drug	MIC
Faropenem	16
Imipenem/Cilastatin	≤ 2
Meropenem	16
Amikacin	≤ 4
Tobramycin	8
Clarithromycin	64
Azithromycin	≥ 64
Doxycycline	16
Levofloxacin	≤ 1
Moxifloxacin	≤ 0.25
Sulfamethoxazole-Trimethoprim	9.5
Rifampicin	8
Linezolid	8
Ethambutol	128
Sitafloxacin	0.25
Rifabutin	2
Clofazimine	0.5

MIC = minimum inhibitory concentration.

CRediT authorship contribution statement

EK and **KF** designed the case reports and drafted the manuscript. **EK** and **HY** diagnosed and treated the patient. **TO** managed the patient's treatment. **KF** advised on the treatment of mycobacteriosis in this patient. **EK, KF, HY,** and **TO** revised the manuscript. All authors have approved this manuscript for submission.

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