

***Mycobacterium marinum* infection successfully treated with oral administration of minocycline and thermotherapy**

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ABSTRACT

We report a case of a woman presenting with an erythematous finger nodule, with a history of exposure to tropical fish. The erythematous nodules subsequently spread proximally from the finger. Initial treatment with oral amoxicillin-clavulanate was unsuccessful, and she developed a drug eruption. Treatment with oral minocycline and thermotherapy was initiated, as we suspected infection with *Mycobacterium marinum* (*M. marinum*) from her history and clinical features. A culture from a skin biopsy from the finger grew *M. marinum*, confirming the diagnosis. There is no established treatment regimen for skin infections caused by *M. marinum*. In this case, it took time for cultures to confirm the diagnosis of non-tuberculous mycobacterial infection. While it would be ideal to await culture results, we felt it was better for the patient to initiate treatment, and in *M. marinum* infections, minocycline is considered particularly effective. However, it was envisaged that this would result in a prolonged treatment course, leading to potential resistance. Thermotherapy was added in an attempt to shorten the treatment period. This regime was successful, and the patient has remained free of recurrence since. The early initiation of treatment for cutaneous non-tuberculous mycobacterial infection requires aggressive suspicion. Also, testing, including adequate sampling and culturing, is essential for an accurate diagnosis. Slow-growing mycobacteria may take several months to be definitively diagnosed, as they grow only under certain conditions. Therefore, thorough clinical history-taking and information sharing with the microbiology team are essential. Our case illustrates this, and we believe this has important educational value.

Keywords: minocycline, *Mycobacterium marinum*, thermotherapy, non-tuberculous mycobacteria

Abbreviation:

M. marinum: *Mycobacterium marinum*

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CASE

A 47-year-old woman presented in April with a swollen erythematous nodule on the right index finger. She was treated with oral amoxicillin-clavulanate, but there was no improvement. On the 10th day of the treatment, erythema was observed on the entire body. The treatment was discontinued and the patient was referred to our clinic. She had a history of keeping tropical fish, and the tank was cleaned with bare hands.

Physical examination revealed an ascending array of erythematous nodules from the dorsum of the right hand to the forearm (Fig. 1A). She had a positive T-SPOT.TB.

Because of the time required for the culture and the identification tests, antibiotic therapy was started before the identification of the causative bacterium species. We felt this was possible because the clinical features, combined with a history of frequent exposure of the skin to a tropical fish tank, increased our suspicions specifically for *Mycobacterium marinum* (*M. marinum*). Furthermore, she had no history of recent close contact with *M. tuberculosis* or travel history, so we did not suspect tuberculosis as strongly as an infection with *M. marinum*. Since the patient had a history of drug eruption with amoxicillin-clavulanate, oral minocycline monotherapy (200 mg/day) combined with thermotherapy was started, taking into account previous reports. The thermotherapy regimen consisted of putting single-use hand warmers on the lesions for 2–3 hours each day. The area of erythema started rapidly shrinking and was cleared completely within

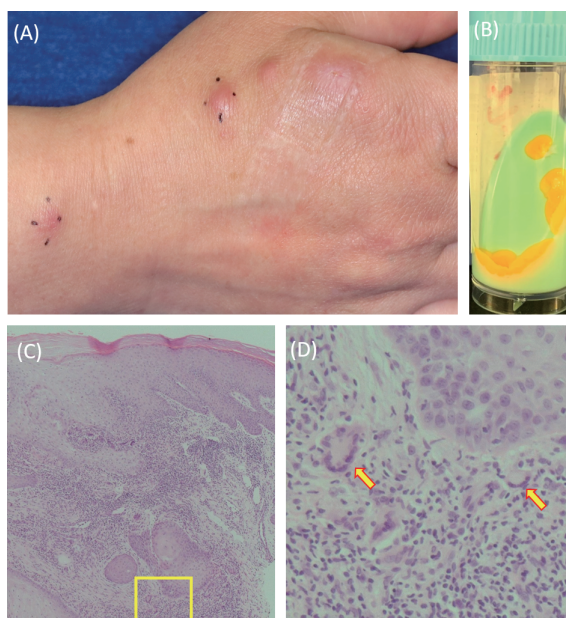


Fig. 1 Clinical and histopathological features of the skin lesions, and the nature of colonies of the causative *M. marinum*

Fig. 1A: The patient's clinical features at the initial examination. Several erythematous nodules were seen on the dorsum of the right hand and the right wrist.

Fig. 1B: Yellow colonies of *M. marinum* were formed in 2% Ogawa medium.

Fig. 1C-D: Haematoxylin-eosin staining of a skin biopsy specimen from a nodule on the right index finger revealed inflammatory granulation tissue formation and small epithelial granulomas. The yellow rectangle in (1C) is enlarged in (1D). Multinucleated giant cells are indicated with arrows.

M. marinum: *Mycobacterium marinum*

14 days following the administration of the treatment, before the identification of *M. marinum*.

Histological analysis revealed inflammatory granulation tissue formation, small epithelial granulomas, and multinucleated giant cells (Fig. 1C, D). No microorganisms positive for periodic acid-Schiff, Grocott or Ziehl-Neelsen stainings were seen in the biopsy specimen. Polymerase chain reaction (PCR) tests of the biopsy specimen were negative for *Mycobacterium avium-intracellulare* complex, as well as *Mycobacterium tuberculosis* complex. A culture taken from a skin biopsy specimen from a nodule on the right index finger grew colonies after 32 days' culture in liquid medium (30 °C), and the colony-forming bacteria were identified as *M. marinum* by Matrix-assisted laser desorption ionization-time of flight mass spectrometry (VITEK MS, bioMérieux Inc, ver 3.2 Knowledge Base). Yellow colonies with photochromogens were formed by culture in 2% Ogawa medium (Fig. 1B). The possibility of *Mycobacterium ulcerans* subsp. *shinshuense* was excluded by sequencing of 16S ribosomal RNA (rRNA) gene point mutations. The minimum inhibitory concentration (MIC) of minocycline for the causative *M. marinum* that came out later was 4 µg/mL, a level comparable to other reported strains,¹ and the nodules were completely resolved in three and a half months without additional treatments. There has been no recurrence after half a year of follow-up.

DISCUSSION

The majority of non-tuberculous mycobacterial infections of the skin are caused by *M. marinum*.¹ Naturally, *M. marinum* is widely distributed in saltwater and brackish water, and fish breeding-related infections are common.² Administration of antimicrobial agents, thermotherapy and surgical resection are adopted for *M. marinum* infections,³ although there is no universally established treatment regimen. Kim et al⁴ reported the efficacy of tetracyclines in 1974, and minocycline and other tetracyclines are often used as monotherapy or as one agent in combination therapy. From the standpoint of countermeasures against bacterial resistance and shortening the treatment period, it is desirable to use a multidrug regimen in which antibiotics are added according to their drug susceptibility, rather than a single antibiotic, and if the disease is refractory to multiple antibiotics, it is necessary to use thermotherapy or surgical resection. It is recommended that treatment should be continued for one to two months after the symptoms disappear completely.⁴⁻⁶ Aubry et al¹ reported that the median duration of antibiotic therapy was 14 weeks (range, 1–25 months). According to the report, the treatment duration was significantly longer in patients with deeper tissue infections than in patients with infections confined to the skin and soft tissues.¹

Since the present patient had a history of drug eruption and it took time to identify the causative bacteria, we treated the patient with minocycline monotherapy combined with thermotherapy due to strong clinical suspicion specifically for *M. marinum* as opposed to other mycobacteria. Awaiting culture results would have taken many weeks, and given the drug eruption history, it was safer to commence antibiotic monotherapy in this instance, as opposed to multiple therapy that is usually used in other mycobacterial conditions, such as rifampicin and clarithromycin. In addition, considering the remote possibility of a non-mycobacterial subcutaneous abscess as well as granulomatous conditions such as sarcoidosis, it was reasonable to commence minocycline monotherapy. In addition, we theorized that by shortening the treatment course through the use of thermotherapy, it would decrease the chances of developing antimicrobial resistance. This resulted in the improvement of the lesions within a short treatment period (3.5 months). The fact that the patient was not in an immunosuppressed state might be associated with the successful treatment outcome in the present case. As mentioned in the abstract, in order to treat non-tuberculous

mycobacterial infections of the skin, they need to be actively suspected. Investigations that include appropriate sampling and culturing are essential for an accurate diagnosis. Furthermore, slow-growing mycobacteria may take months to grow in specific conditions before the definitive diagnosis can be made. Hence, in order to initiate treatment early even in the presence of slow-growing mycobacteria, thorough clinical history-taking and information sharing with the microbiology team are essential. Our case illustrates this and has demonstrated a positive outcome, and we believe this has significant educational value.

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CONFLICTS OF INTEREST

The authors declare that we have no conflicts of interest.

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