

# *Sporotrichoid atypical cutaneous infection caused by *Mycobacterium marinum**

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## SUMMARY

A case of a sporotrichoid cutaneous infection caused by *Mycobacterium marinum* is reported. A 53-year-old male patient presented with red, partly purulent nodular lesions on the back of his left hand, forearm, and upper medial arm that had developed consecutively during the past 4 weeks. A mycobacterial infection with *M. marinum* was confirmed by molecular methods in a lesional skin biopsy. The patient was treated systemically with rifampicin (750 mg/day) and clarithromycine (1000 mg/day), and topically with sulmycin (gentamicin sulfate). After 12 weeks of treatment the nodules regressed, leaving behind erythematous patches. *M. marinum* is a waterborne mycobacterium that commonly infects fish and amphibians worldwide. Transmissions to humans occur occasionally, in most cases as a granulomatous infection localized to the skin, typically following minor trauma to the hands. For this reason, infections are especially common among aquarium keepers.

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## Introduction

*Mycobacterium marinum* is an ubiquitous waterborne organism that grows optimally at temperatures around 30 °C. It has a worldwide distribution and primarily infects fish that can secondarily contaminate aquaria, swimming pools, rivers, and seawater (1). When transmitted to animals such as amphibians, fish, mice, and bats, it can be highly prevalent in fish tanks and cause infections and death in various fish species. A vaccine against *M. marinum* infection in fish has been developed (2).

## Case report

A 53-year-old patient presented at the Department of Dermatology with reddish nodules and papulopustules up to the size of a cherry on the top of the left hand, forearm, and medial/lateral aspects of his upper arm following lymphatic drainage in a linear fashion. The most recent subcutaneous nodular lesions were located in the medial upper arm (Fig. 1). No other dermatological abnormalities were observed and other comorbidities were excluded by laboratory tests, X-ray, and abdominal ultrasound.

## KEY WORDS

swimming pool granuloma, mycobacterium marinum, sporotrichoid lesions

Eight weeks before first being seen at the Department of Dermatology, he had been treated successfully with Unacid PD (oral sulfamicillin 375 mg) for lymphangitis at the left palm and left middle finger that had developed from a cut. When asked about his hobbies, the patient mentioned an aquarium with ornamental fish in apparently good condition.

A biopsy taken from a nodule on the left upper arm showed necrotizing folliculitis and perifolliculitis with follicular rupture (Fig. 2). The nodular biopsy was subjected to microscopic, culture, and molecular analysis. Acid fast rods could not be observed by microscopic examination. The mycobacterial culture did not show any growth after an incubation time of about 10 weeks. Molecular diagnostics comprised a genus-specific PCR targeting the mycobacterial 16sRNA gene followed by automated DNA-sequencing (ABI Prism 310 Sequencer, Applied Biosystems). Results of the nucleotide BLAST search showed a 100% homology to *Mycobacterium marinum/ulcerans* (3–5).

Standard microbiological techniques including culture and common mycobacterial PCRs revealed no other pathogens from among the huge number of other mycobacterial species.

In view of the clinical pattern and the clinical findings, an atypical mycobacteriosis of the skin following a sporotrichoid pattern caused by *M. marinum* was diagnosed. The patient was started on long-term antibiotic therapy with rifampicin 750 mg/day and clarithromycin 1000 mg/day (500 mg twice daily) for 12 months and synchronous topical application of sulmycin. At the follow-up examinations after 4, 8, 12, and 22 weeks, a pronounced regression of the lesions was observed (Figure 3).

## Discussion

*M. marinum* can cause superficial infections and localized invasive infections in humans, with the hands being the sites most frequently affected. It can be observed in humans that are exposed to fish or fish tanks through their hobbies or occupations (6).

After exposure, symptoms usually appear within 2 to 4 weeks (7). However, there are some cases reporting an incubation time of 2 to 4 months and longer, with some cases reporting an incubation period as long as 9 months (8) due to the slow-growing nature of this bacterium.

In general, *M. marinum* infection in humans is comparatively rare; the approximate annual incidence in the US is 0.27 confirmed cases per 100,000 inhabitants. The temperature of human skin is advantageous for the establishment of superficial infection, which is commonly preceded by minor traumatic lesions. Following abrasions or superficial wounds, humans infected by

contaminated water develop purulent superficial or deep granulomatous skin infections (2). Single lesions consist of papulo-nodular, verrucous, or ulcerated granulomatous inflammation with minimal purulent secretions. Sporotrichoid lesions following the lymph drainage spread from the primary lesion, leading to linearly arranged, inflamed, pustular lesions resembling deep fungal infection with *Sporothrix schenckii* (Fig. 1 and 3).

Mycobacterial culture from smears and tissue biopsies is the most important diagnostic tool for detection of *M. marinum*. A positive culture significantly supports *M. marinum* as the causative agent for a nodular skin lesion and makes other infectious or neoplastic conditions less likely. In the case presented here, the mycobacterial culture specimen was cultivated at 30 °C in the liquid culture and at 37 °C in the fixed culture.

The culture was incubated at 30 °C, but remained sterile. The more sensitive sequence of PCR-product detected *M. marinum* and *M. ulcerans*. Possible reasons for this could be an irregular distribution in the material or perhaps the bacteria had already been damaged, so cultivation was impossible. Nevertheless, in the past decade molecular techniques have become highly relevant for mycobacteria detection and identification. The 16sRNA PCR protocol used here did not allow discrimination between *M. marinum* and *M. ulcerans* (9). Therefore, in this particular case, the patient could only be diagnosed with a *M. marinum* infection by evaluating anamnestic data, the clinical and dermatological presentation, the PCR/sequencing results, and the histomorphological analysis of skin biopsies.

The standard treatment generally includes various antibiotics as outlined below, with the treatment duration varying from as little as 2 weeks in some reports to as long as 18 months, depending on the extent and severity of the infection, the presence of underlying disorders, and the clinical response. For superficial infections, antibiotic therapy is usually given for between 6 weeks and 6 months, whereas deep infections are treated for as long as 6 to 18 months (10). Deeper infections may require adjunctive surgical debridement, in particular when there is evidence of therapy-resistant infection (11). Some reports demonstrate the successful use of excision, curettage, and cryotherapy (12). It is even stated that photodynamic therapy may be useful in the treatment of *M. marinum* infections, though more data are needed (13).

Antimicrobial therapy includes antibiotics such as cotrimoxazole, minocycline, doxycycline, trimethoprim/sulfamethoxazole, quinolones, ethambutol, rifampicin, and clarithromycin (6, 8, 11, 14, 15). At this point, a combination of ethambutol and rifampicin has been extensively used and is regarded as standard regimen, particularly for deep infections (10), but the potential for ocular toxicity has made this regimen unat-



**Fig. 1.** Subcutaneous nodular lesions located in the medial upper arm.



**Fig. 3.** Pronounced regression of the lesions at the follow-up.

tractive for treating less serious superficial infections. With no controlled clinical trials existing for the treatment of *M. marinum* infections because of the small number of affected patients, treatment success was seen with minocycline, particularly well-documented in the dermatology literature, even in cases complicated by delayed diagnosis and systemic immunosuppression (16). Reports suggest that minocycline may be the most effective treatment option, despite the underlying similarity in the mechanism and sensitivities of different second-generation tetracyclines (6).



**Fig. 2.** Necrotizing folliculitis and perifolliculitis with follicular rupture. (HE)

More recently, newer macrolide antibiotics such as clarithromycin have been shown to represent a treatment option for cutaneous *M. marinum* infection, especially if used in combination with rifabutin and ciprofloxacin (17). Although clinical experience is so far limited, clarithromycin is stated to have been used successfully alone and in combination with ethambutol and ciprofloxacin, thus being a promising therapy (10). Finally, in some recent reports the opinion is mentioned that clarithromycin is the optimal first agent in combination treatment of *M. marinum* (18, 19), assuming that ethambutol and rifampicin represent reasonable second line agents (11).

The type and duration of antimicrobial therapy varies considerably in the literature, with no single agent or combination of agents clearly shown to be the treatment of choice. The clinical response and the results of *in vitro* sensitivity tests should be used to guide any subsequent modification of the antibiotic regimen; therefore, a combined therapy is advised, particularly in deep infections like that of our patient (20).

## Conclusion

Infections due to *M. marinum* are uncommon, but not rare. An association of the infection with domestic tropical fish tanks or other aquatic exposures is known. The diagnosis requires both a detailed history as well as sophisticated microbiological and PCR-based investigations. No large systemic studies have been performed to determine the optimal treatment regimen. In most cases a combination of antibacterial drugs such as clarithromycin and rifampicin should be given as well as long-term therapy depending on the duration and severity of infection.

Fish-tank exposure is the source of most cases of cutaneous *M. marinum* infections and may be prevented by the use of waterproof gloves by persons with acute or chronic open skin lesions.

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