Answer to Photo Quiz: Coinfection with *Mycobacterium marinum* and *M. ulcerans*

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The patient’s pus stain showed unstained organisms in the Gram stain (see Fig. 1C in the photo quiz), which were positive by acid-fast staining (see Fig. 1D in the photo quiz). Tissue and pus specimens were cultured at 32°C by inoculating the sediment on LJ solid medium and in a mycobacterial growth indicator tube (MGIT) (Becton, Dickinson, Sparks, MD). The cultures grew acid-fast bacilli (AFB) after 4 weeks for the pus specimen and 8 weeks for the tissue specimen. Two groups of mycobacterial colonies were identified. The first group (at 4 weeks) contained colonies that were creamy in color and turned yellow when exposed to light (photochromogenic), while the second group of colonies (at 8 weeks) appeared yellow and rough, with a well-demarcated edge. The organisms were later identified as *Mycobacterium marinum* and *M. ulcerans*, respectively (1). DNA extracted from pus and tissue samples were evaluated by PCR targeting the 16S rRNA gene and by the IS2404 insertion elements. PCR targeting the 16S rRNA gene confirmed *Mycobacterium* species most closely matching *M. marinum* and/or *M. ulcerans*. The sequences of the IS2404 amplicon were identical to those from *M. ulcerans*. Coinfections due to *M. marinum* and *M. ulcerans*, thus, were diagnosed based on cultures (*M. marinum* and *M. ulcerans*) and PCR primers specific for *M. ulcerans*. *M. marinum* and *M. ulcerans* were subjected to antimicrobial susceptibility testing (AST) using a broth microdilution susceptibility test (2), and both organisms were susceptible to clarithromycin, doxycycline, moxifloxacin, and rifampin. The patient was empirically treated with rifampin, clarithromycin, and streptomycin together with multiple surgical debridements of his left index finger, which resulted in a significant reduction of the inflammation and resolution of the abscess.

Nontuberculous mycobacteria (NTM) are widely distributed in the environment, with high isolation rates worldwide. These organisms can be found in soil and water, including both natural and treated water sources. The most common clinical manifestation of NTM disease is lung disease, but lymphatic, skin and soft tissue, and disseminated diseases are also frequently described. *M. marinum* is the cause of “swimming pool granuloma” or “fish tank granuloma.” A systematic search of the literature found that exposure to a fish tank in a household with indoor or outdoor aquariums, death of the tank fishes, and injury from or contact with a fish spine or oysters were commonly identified risk factors (3). Infection is typically acquired from a soft tissue injury to the hand in an aquatic environment, usually without a history of direct contact with fish. *M. ulcerans* is widely dispersed in geographic areas in the watersheds of tropical rain forests, primarily in Africa, Southeast Asia, Australia, and South and Central America (4, 5). *M. ulcerans* causes indolent, progressive necrotic lesions of the skin and


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underlying tissue with indeterminate scalloped edges, known historically as “Buruli ulcers.” Infection is believed to occur through abraded or compromised skin after contact with contaminated water or soil (6). Our patient probably acquired the *M. marinum* pathogens while decorating coral without having direct contact with fish and acquired *M. ulcerans* pathogens by direct contact with soil and water during gardening. After the pathogens penetrated the skin via microtrauma, with tissue invasion precipitated by intraregional steroid injection, they caused superficial and deep tissue infections, resulting in necrotizing tenosynovitis.

Diagnostic tests of necrotizing skin and soft tissue infections to identify the causative agent should always be performed, including Gram staining and acid-fast staining with appropriate cultures from biopsy specimens, aspirates of abscesses, and/or surgical specimens. When available, PCR, especially quantitative real-time (multiplex) PCR (qPCR), should be performed to aid in rapid diagnosis. Other diagnostic tools, including histopathological examination and immunohistochemistry (IHC), may also be useful to help secure a diagnosis.

For treatment, by standard susceptibility testing, *M. marinum* isolates are generally susceptible to rifampin, rifabutin, and ethambutol, intermediate to streptomycin, and resistant to isoniazid and pyrazinamide. Clarithromycin and rifampin are usually the best choices for treatment of *M. ulcerans* infection (2). Debridement has been shown to reduce mycobacterial burden and mycolactone production, resulting in an improved cellular protective immune response. For *M. ulcerans* infection, the approach to treatment differs slightly, depending upon the size and stage of the lesion, as outlined by the World Health Organization (WHO) classification categories (6). In our patient, the lesion was categorized in WHO class II (i.e., ⩾5 cm) and failed to respond to initial antibiotic therapy, requiring multiple aggressive surgical procedures with debridement.

We herein report the first case of coinfection with *M. marinum* and *M. ulcerans*. Four months after treatment, the swelling and inflammation of the patient’s left index finger were markedly improved. His ESR was 5 mm/h after 6 months of antimicrobial treatment, and MRI of his left index finger showed near-complete resolution of the abscess and improvement of soft tissue inflammation.

REFERENCES