

Seroconversion of QuantiFERON-TB Gold Test due to *Mycobacterium marinum* Infection in a Patient with Psoriasis Treated with Adalimumab

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To the Editor;

Mycobacterium marinum (*M. marinum*) is a free-living mycobacterium species first isolated by Aronson in saltwater fish in 1926 (1). *M. marinum* causes disease in many fish species and infection in human following contact with infected fishes or contaminated water. *M. marinum* infections are rare with an estimated incidence between 0.04 and 0.27 cases per 100,000 persons annually (2). The first report of human disease caused by *M. marinum* was reported in 1951 in those using a contaminated pool in Örebro, Sweden (3).

A 44-year-old male of Caucasian origin was referred to the outpatient clinic of the Department of Dermatology in Malmö. He had a 20-year medical history of severe psoriasis and he had been treated for 2 years with adalimumab after insufficient results with methotrexate therapy. Before administration of adalimumab a QuantiFERON-TB Gold test was negative, and a chest X-ray did not reveal any radiographic evidence of active or prior *Mycobacterium tuberculosis* infection (MTB). The patient experienced good clinical response; however, 16 months later he developed asymptomatic erythematous

scaly nodular skin lesions in an irregular, roughly linear distribution localized on his left hand and underarm (Fig. 1A–C). No systemic symptoms were mentioned. The physical examination was otherwise unremarkable. The patient mentioned performing daily cleaning of a freshwater aquarium at home, often without gloves.

A skin biopsy of a nodule was taken and the histopathological examination showed necrotizing and granulomatous inflammation (Fig. 2). Furthermore, a skin biopsy culture from one of the skin nodules was positive for *M. marinum*. The QuantiFERON-TB Gold test was found to be positive and chest tomography was performed with normal findings. The diagnosis of fish-tank granuloma was made and the therapy with adalimumab was discontinued. Antibiotic treatment with ethambutol (1,200 mg/day) and clarithromycin (500 mg twice daily) was initiated. The nodular lesions went into regression (Fig. 1D, E) within 4 months; thereafter the antibiotics were discontinued. Adalimumab was reintroduced without any reactivation of the skin infection.

M. marinum is a non-tuberculous mycobacterium, whose natural habitat is fresh or saltwater, particularly enclosures of water that are not often replenished, e.g.



Fig. 1. (A–C) Multiple erythematous papules and nodules on the patient's left hand and underarm. (D, E) Regression of the lesions after the discontinuation of adalimumab and 8 weeks' treatment with clarithromycin and ethambutol.

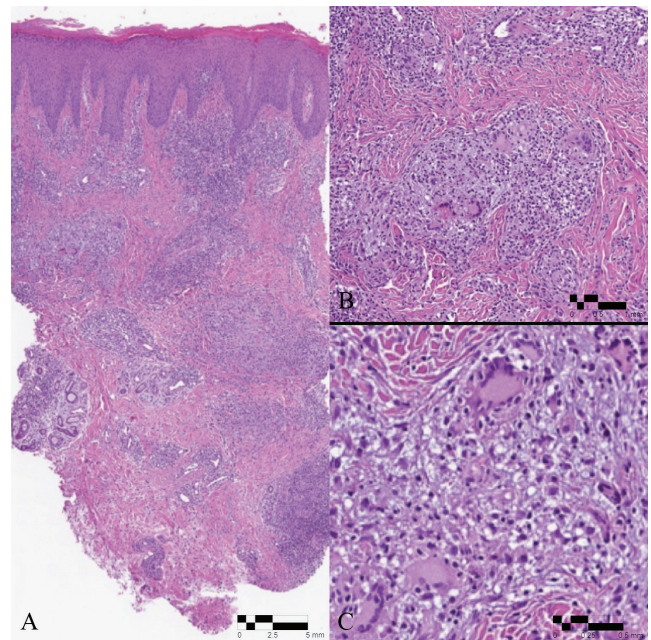


Fig. 2. (A) Granulomatous inflammation with numerous Langhans-type giant cells (H&E x10). (B) H&E x 40 (C) H&E x 100.

swimming pools and aquarium tanks. Human infection may be caused by direct injury by fish or occur after cutaneous trauma and exposure to contaminated water (2–4), manifests after an incubation time of 2–3 weeks, and is usually limited to the skin and soft tissues in immunocompetent patients. Slow-growing erythematous nodules, typically localized on the hands, elbows, or knees, and sometimes painful and ulcerated, can spread following the distribution of the lymphatic system (2–4). Disseminated cutaneous involvement has been reported in immunosuppressed individuals and in a child (4, 5).

Differential diagnosis includes sporotrichosis and leishmaniasis as well as other atypical mycobacterial infections. The diagnosis of *M. marinum* is often delayed due to insidious clinical presentation. A history of exposure to aquatic environments or marine animals in combination with the occurrence of single or multiple granulomatous skin nodules should raise suspicion of *M. marinum* infection, confirmed by performing a nonmotile acid-fast bacillus (AFB) culture of the tissue (2).

Tumour necrosis factor alpha (TNF- α) inhibitors are commonly used in the treatment of psoriasis and other inflammatory dermatoses. Adalimumab is a fully human IgG₁ antibody to TNF- α . One important concern with the use of TNF- α inhibitors has been the risk of reactivation of latent tuberculosis as well as other opportunistic infections, especially mycobacterial infections. Several cases of *M. marinum* infections have been reported in patients treated with various TNF- α inhibitors (6). It is therefore essential that before initiating TNF- α inhibitors, patients should be screened for latent TB infection with QuantiFERON Gold test or purified protein derivate (PPD) test.

The QuantiFERON-TB Gold test is an interferon-gamma (IFN- γ) release assay and considered a modern alternative to the tuberculin skin test (TST, PPD, or Mantoux). The antigens used in QuantiFERON-TB Gold test are ESAT-6 and CFP-10, both present in *M. tuberculosis*

but not in most non-tuberculosis mycobacteria, except for *M. marinum*, *M. kansasii*, and *M. szulgai* (7). In a study by Kobashi et al., the QuantiFERON-TB test was positive in 58% of patients with *M. marinum* infections (8).

The present case highlights the need for dermatologists to maintain a high degree of suspicion for atypical mycobacterial infections in patients treated with TNF- α inhibitors. Furthermore, *M. marinum* infection can lead to seroconversion of the QuantiFERON Gold test and this may be used in clinical praxis as a quick diagnostic tool.

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