

Why you should ask your patients about their fishing hobbies

C.V. Bakker¹, S.H. Kardaun^{1*}, K.R. Wilting², G.F.H. Diercks³, B. Horváth¹

¹Department of Dermatology, ²Department of Medical Microbiology, ³Department of Pathology, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands, *corresponding author: tel.: +31 (0)50-3612520, fax: +31 (0)50-3619247, e-mail: s.h.kardaun@umcg.nl

ABSTRACT

Patients who use immunosuppressive agents, in particular medication that blocks tumour necrosis factor- α , are at risk for mycobacterial infections. Besides the typical *Mycobacterium tuberculosis* infection, also atypical mycobacterial disease may occur. Here we demonstrate two patients with such atypical mycobacterial infection due to swimming and fishing water contact. We propose that patients, before starting with immunosuppressive therapy, are counselled about risk factors for mycobacterial disease.

KEYWORDS

TNF- α , ulcer, Mycobacteria

INTRODUCTION

Tumour necrosis factor alpha (TNF- α) antagonists, such as adalimumab, play a pivotal role in the treatment of various autoimmune and inflammatory diseases. The drawback is the increased susceptibility for mycobacterial infections. Patients are routinely screened for *Mycobacterium tuberculosis* before starting therapy. The increased risk for atypical (cutaneous) mycobacterial infections such as *Mycobacterium marinum*, however, should also be taken into consideration.^{1,2} We report two cases of *M. marinum* infection with an atypical presentation in patients on adalimumab.

CASE REPORTS

Case one, a 69-year-old male, treated for rheumatoid arthritis with methotrexate, prednisolone, and since one year also adalimumab, was referred with erythematous-

What was known about this topic?

Tumour necrosis factor alpha (TNF- α) antagonists are important in the treatment of various autoimmune and inflammatory diseases. Mycobacterial infection can complicate treatment and demand cessation of therapy.

What does this add?

Cutaneous mycobacterial infections in patients using TNF- α antagonists may present atypically. Asking about fishing hobbies and aquariums can be an important link to diagnosis. Despite adequate antibiotic regimens, reintroduction of the TNF- α antagonist can give rise to a relapse of infection.

livid (pustulo)papules and a few partly necrotic nodules on his right lower back, hand, and both legs (*figure 1*). He had a history of fishing in Dutch open freshwater and regularly cleaned his granddaughter's freshwater aquarium. Histology of a nodule showed a granulomatous infiltrate with acid-fast bacilli in the Ziehl-Neelsen and Wade-Fite stain; polymerase chain reaction (PCR) and culture were positive for *M. marinum* or *ulcerans*. *M. marinum* was suspected and adalimumab was interrupted, while ethambutol and clarithromycin were initiated. Four months later, when the patient was in clinical remission of the mycobacterial infection, etanercept was introduced because of rheumatoid arthritis disease activity, provoking a relapse. Etanercept was withdrawn and rifampicin was added.

The second case, a 55-year-old male, treated with adalimumab during the last year for psoriatic arthritis, presented with multiple small ulcers on his left calf.

Figure 1. *Mycobacterium marinum* infection. Clinical presentation of case 1. Multiple lenticular to nummular erythematous-livid papules and nodules (size 5-30mm) with central crusts, and few miliary to lenticular pustules (2-5mm) on the right upper and lower leg, left lower leg, right abdomen and right hand

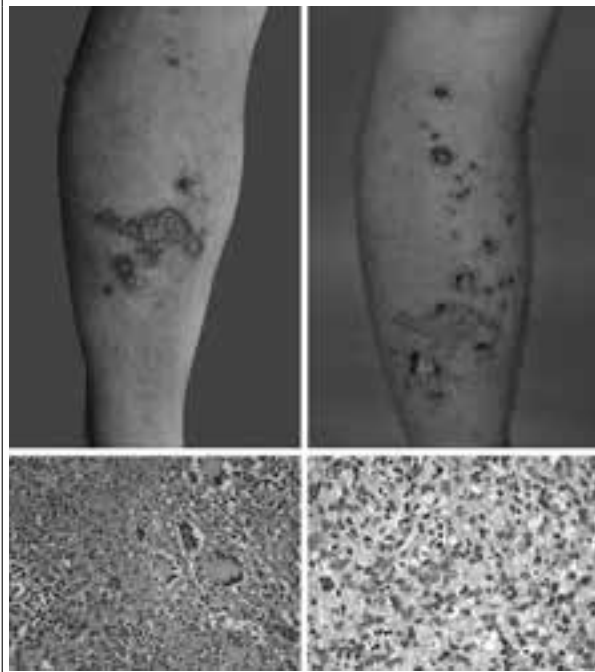


Because of positive bacterial swabs he was consecutively treated with three regimens of different antibiotics, not resulting in wound healing. Further history, specifically on contact with water prior to the appearance of the ulcers, revealed that he went bathing in the Dead Sea in Israel after a minor trauma on his left calf and, after returning to the Netherlands, had frequent contact with open freshwater while fishing. Histopathology (border ulcer) showed granulomatous infiltrates with acid-fast bacilli in the Ziehl-Neelsen and Wade-Fite stain (figure 2). PCR and culture of an ulcer indicated *M. marinum* or *ulcerans*; given the history, *M. marinum* was suspected. Following cessation of adalimumab and initiation of ethambutol and clarithromycin clinical improvement was achieved (figure 2). When adalimumab was reintroduced four months later, reactivation ensued. Adalimumab was therefore withdrawn indefinitely.

DISCUSSION

Cutaneous mycobacterial infections are usually self-limiting, showing one or a few nodules in a sporotrichoid pattern on the dorsal surfaces of hands or feet. In contrast, patients using TNF- α antagonists demonstrate a progressive course of disseminating ulcers and nodules, due to impaired granuloma formation.³ Various types of TNF- α antagonists have different pharmacological features and different risks of infections. Recently *M. marinum* infections were reported after the use of various TNF-inhibiting agents, but up to now adalimumab has only once been

Figure 2. *Mycobacterium marinum* infection. Clinical and histological presentation of case 2. Multiple disseminated ulcers (size 5-30 mm) with sharply defined violaceous borders on the left calf, and improvement of lesions during antibiotic treatment for *M. marinum*. Skin biopsy shows a granulomatous infiltrate with focal necrosis (HE stain, original magnification $\times 40$), while the Wade-Fite stain reveals numerous acid-fast bacilli (original magnification $\times 400$)



implicated.⁴ Reintroduction or switch to an alternative TNF- α antagonist under continued antibiotic regimen is not always successful as both our cases confirm.⁵ Despite antibiotic treatment as in immunocompromised patients, both cases developed a relapse after reintroduction of TNF- α blockade. Withdrawal of adalimumab had unfavourable effects on the patients' medical condition and quality of life: both experienced a disabling relapse of arthritis.

CONCLUSION

Our cases underline that patients' hobbies may carry a risk of infection with *M. marinum*. We propose that, before starting immunosuppressive therapy, patients are counselled about this risk, as mycobacterial infections not only require long-term antibiotic treatment, but also withdrawal of otherwise highly effective medication.⁶ The risk of relapse after reintroduction of TNF- α blockade emphasises the value of prevention.

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