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Case and Review

Ulcers as a Sign of Skin Infection with *Mycobacterium wolinskyi*: Report of a Case and Review of the Literature

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Keywords
Non-tuberculous mycobacteria · Rapidly growing mycobacteria · *Mycobacterium wolinskyi* · Skin and soft tissue infection

Abstract
Infection with *Mycobacterium wolinskyi*, if not detected, may cause severe skin and soft tissue infection with prolonged healing process and is therefore associated with high morbidity. Only about 20 cases of *M. wolinskyi* infections in humans have been described in the literature until now, none of them in Switzerland. We report a case of an infection in a 72-year-old male patient with recurrent subcutaneous abdominal wall abscesses and ulcer formation after insulin injection in the underbelly. A culture of skin biopsy tissue showed rapid growth of non-tuberculous mycobacteria (NTM), which were identified by 16S rRNA gene sequencing as *M. wolinskyi*. Surgical excision and primary closure of all abdominal ulcers in combination with antibiotic therapy, based on the antimicrobiotic susceptibility test results, were performed and resulted in complete resolution of the clinical symptoms and no recurrence of infection at a 6-month follow-up. The present case emphasizes the importance of accurate diagnosis and treatment of chronic infection with ulcer formation. In such cases, it is crucial to consider the presence of NTM, such as *M. wolinskyi*, in order to obtain rapid diagnosis, specific treatment and improved patient care.

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Case Report

A 72-year-old male patient with recurrent subcutaneous abdominal wall abscesses was referred to our dermatological inpatient unit at the University Hospital in Zurich, Switzerland. The abdominal skin problems had begun one and a half years before, after subcutaneous insulin injections in the underbelly region had been initiated. Within few days, the patient noticed a development of a small red indurated but indolent nodule in the right umbilical region. The patient's medical history included insulin-dependent diabetes mellitus type 2, atrial fibrillation with oral anticoagulation and a previous percutaneous coronary intervention due to a myocardial infarction. Five months later, local subcutaneous abscesses developed in the central abdominal wall region. The patient was referred to a nearby hospital for surgical wound debridement and received postoperative antibiotic treatment with oral amoxicillin and clavulanic acid. In the following months, there were several recurrences of abdominal wall abscesses turning into ulcers followed by repeated subsequent surgical debridements, excisions of abdominal wall fistulas, negative pressure wound therapies, as well as antibiotic therapies (amoxicillin and clavulanic acid).

As the abscesses with ulcer formation did not improve in the long term, the suspicion of pyoderma gangrenosum arose and the patient was referred to our clinic for further dermatological investigations. At hospital admission, the patient was in a good clinical condition, without fever or infection signs. Clinical examination revealed three 2- to 5-cm-large oval ulcers with granulation tissue on the lower right central abdominal area, with slightly erythematous but not undermined boarders (fig. 1a). Laboratory findings did not indicate a systemic infection with CRP 7 mg/l (range <5 mg/l), leukocytes 9 G/l (range 3.0–9.6 G/l). The differential diagnosis encompassed ulcers of either infectious, vasculitic or exogenous origin, open abdominal wall fistulas with ulcer formation as well as pyoderma gangrenosum.

Bacterial swabs from the ulcers showed only the presence of the commensal skin flora. Pathergy phenomenon could not be detected clinically. The patient had no personality changes that would imply an obsessive-compulsive disorder resulting in self-mutilation. Serological vasculitis screen with antinuclear antibodies, ANCA, rheumatoid factor, complement C3/4 fraction, and hepatitis B and C serology was negative. Imaging studies of the abdomen with contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) illustrated an abdominal subcutaneous fluid collection but no abdominal fistulas. A deep skin biopsy of the ulcers was performed and tissue culture started (for bacteria, fungi and mycobacteria). Histology revealed mixed inflammatory cellular infiltrates of neutrophils and histiocytes with granuloma and abscess formation in the dermis. No pathogen could be verified in different stainings (PAS, Grocott, Ziehl-Neelsen) (fig. 2). After 6 days of cultivation, skin biopsy tissue culture showed rapid growth of non-tuberculous mycobacteria (NTM), which were identified by 16S rRNA gene sequencing as *Mycobacterium wolinskyi.* The patient underwent surgical excision and primary closure of all abdominal ulcers with material being sent for further tissue culturing. The subsequent mycobacterial culture also yielded rapidly growing *M. wolinskyi.* Based on the antibiotic susceptibility test results (table 1), the patient was treated with intravenous amikacin (500 mg per day) for 1 month in combination with oral moxifloxacin (400 mg per day) and minocycline (100 mg twice a day) therapy for a total of 6 months. The patient responded well to this combination therapy with complete resolution of the clinical symptoms and no recurrence of infection at a 6-month follow-up (fig. 1b).

Discussion

M. wolinskyi belongs to NTM, which comprise over 140 different species. *M. wolinskyi* is ubiquitously distributed in soil and water. In the Runyon classification system, *M. wolinskyi* is a type IV mycobacteria and is also called rapidly growing mycobacteria (RGM), meaning that it has the ability to grow within 7 days in culture media [1, 2]. *M. wolinskyi* was first identified by Brown et al. [3] in 1999 using 16S rRNA sequencing. Among many species of RGM, *M. wolinskyi* belongs to the *M. smegmatis* group, which includes *M. smegmatis, M. wolinskyi* and *M. goodii*. Mycobacteria of the *M. smegmatis* group are predominantly associated with skin and soft tissue infections [1, 2].

Only about 20 cases of *M. wolinskyi* infections in humans have been described in the literature until now. These were mainly skin and soft tissue infections that arose following surgery (hip prosthesis implantation, peritoneal dialysis, organ transplantation, heart surgery, breast mammoplasty) and cosmetic procedures (filler injection and laser lipolysis) [1, 4, 5]. Typically, skin infection with *M. wolinskyi* became apparent months after surgery, often causing extensive pus production and in some cases deeper tissue destruction with involvement of adjacent bone.

Conventional histopathological methods, such as Ziehl-Neelson staining are not always able to detect this mycobacterium and are therefore not specific for the diagnosis of *M. wolinskyi*. The diagnosis of *M. wolinskyi* requires culturing of a tissue sample in an appropriate culture medium. Molecular detection and specification is performed using 16S rRNA sequencing [6, 7]. In our case, after culture results indicated the presence of acid fast bacilli, a commercial semiautomatic multiplex PCR assay (COBAS® TaqMan® MTB assay) combined with an in-house validated PCR assay to detect all *Mycobacterium* spp. [8] was performed in order to exclude *M. tuberculosis* complex. The results of the multiplex PCR indicated the presence of an NTM, which was further confirmed by 16S rRNA sequencing. The isolate was identified as *M. wolinskyi*, featuring a sequence identity of 100%.

Due to variability in antimicrobial susceptibility, there is no standardized antimicrobial regime or duration of therapy for *M. wolinskyi.* Minimal inhibitory concentration testing for susceptibility in culture medium enables a choice of the most suited individualized therapy [1, 9]. A combination therapy with at least 2 antimicrobial agents is preferred [9]. *M. wolinskyi* are typically susceptible to quinolones, doxycycline, linezolids and sulfamethoxazole, but resistant to tobramycin, imipenem and clarithromycin [10]. Surgical debridement combined with antimicrobial therapy contributes in general to the resolution of infection caused by *M. wolinskyi* [1].

Our case is the first report of *M. wolinskyi* infection described in Switzerland. The exact route of infection in this case remains unclear. An infection at the moment of surgery is unlikely, because the symptoms begun months before any surgical procedure was performed. There were also no known outbreaks during the time in the hospital, where the surgical revisions have been performed initially. It is more likely that the infection was associated with the insulin injections in the underbelly, with inoculation of these ubiquitously present mycobacteria in the soft tissue. Moreover, the diabetic background and associated immune suppression could have favored the propagation of these mycobacteria and the development of the clinically overt infection. However, past reports showed equal susceptibility to *M. wolinskyi* infection in immunosuppressed and immunocompetent patients [1].

The present case shows the difficulties and emphasizes the importance of accurate diagnosis and treatment in a situation with non-healing ulcers. Infection with *M. wolinskyi,* if not detected, causes severe skin and soft tissue infection with prolonged healing process and

is as such associated with high morbidity. Therefore, in case of chronic infection with ulcer formation, it is crucial to consider the presence of NTM, such as *M. wolinskyi*, in order to obtain rapid diagnosis, specific treatment and lastly improved patient care.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare no conflict of interest and no financial interest.

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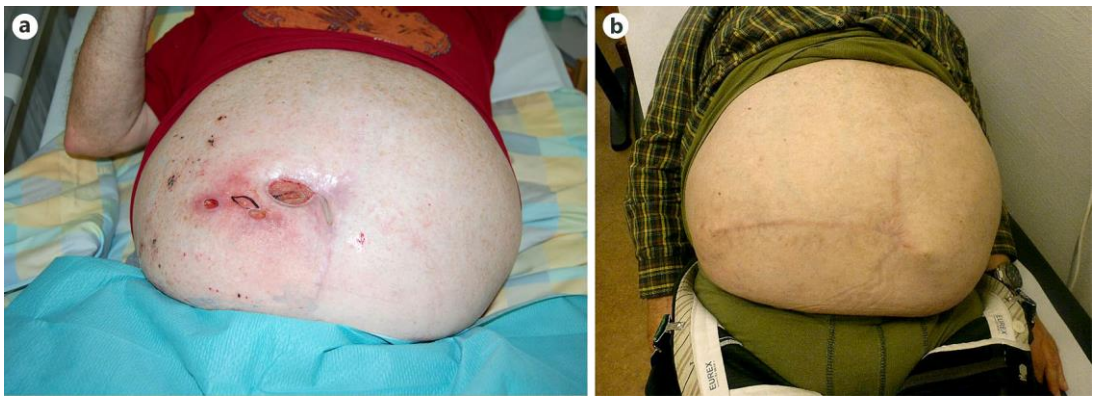

Fig. 1. **a** The patient's clinical appearance at hospital admission, showing multiple oval ulcers on the abdominal wall. **b** The patient's clinical appearance at the 6-month follow-up.

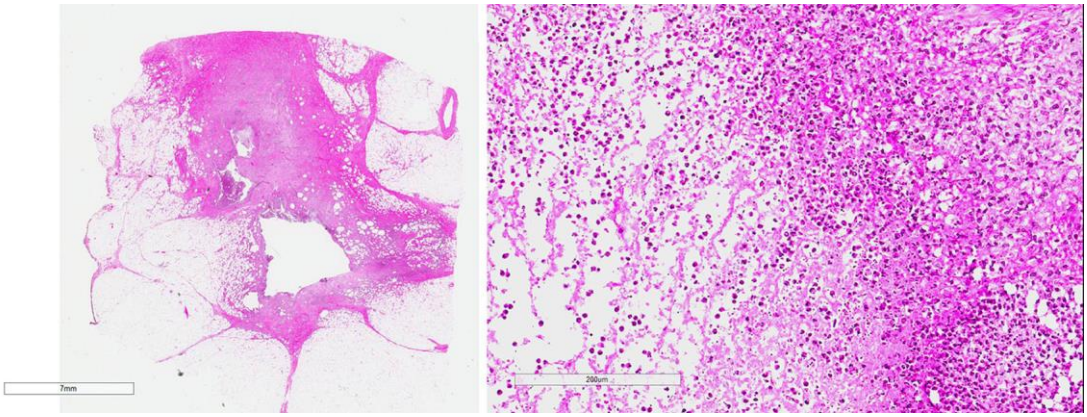

Fig. 2. Histology of abdominal wall biopsy. Left panel (×5 original magnification) shows substantial dermal inflammation, which on the right panel (×40 original magnification) reveals mixed inflammatory cellular infiltrates of neutrophils and histiocytes with granuloma and abscess formation. Hematoxylin and eosin stain.

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Table 1. Minimal inhibitory concentration breakpoints

Mycobacterium wolinskyi	Breakpoints		MIC result, mg/l
	S≤	R>	
Amikacin	16	64	
Tobramycin	2	8	64
Clarithromycin	2	8	>256
Linezolid	8	32	4
Doxycycline	1	8	32
Tigecycline	na	na	0.5–1
Minocycline	1	8	1
Ciprofloxacin	1	4	0.5–1
Levofloxacin	1	4	0.5
Moxifloxacin	1	4	0.5–1
Ethambutol	na	na	8
Imipenem	4	32	16–32
Meropenem	4	32	16–32
Cefoxitin	16	128	128
Clofazimine	na	na	<0.5

MIC = Minimal inhibitory concentration; S = sensible; R = resistant; na = not available.