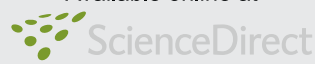


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CLINICAL REPORT

Upper extremity *Mycobacterium marinum* infection

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KEYWORDS

Mycobacterium marinum;
 Atypical mycobacteria;
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Summary *Mycobacterium marinum* is the cause of opportunistic infections in man. Although its clinical presentation is usually cutaneous, osteoarticular infections are not rare and should be rapidly diagnosed. Orthopaedic surgeons may have to manage a patient with this mycobacterial infection and should be able to make this diagnosis based on information about the patient's history and clinical criteria. Lesions develop from a skin wound, with a single nodule or a bright purplish-red patch with papules; they also may be inflamed or may abscess. Secondary lesions may develop as the disease progresses. Aquatic exposure is the most important factor to look for. We report three cases of this infection with a delayed diagnosis. Response to treatment and an absence of complications are correlated with an early diagnosis.

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Introduction

Mycobacterium marinum (*M. marinum*) is an atypical mycobacteria that causes dermatological and osteoarticular lesions. This infection usually affects adults without risk factors. Despite an increase in the number of cases in recent years, it often goes unrecognized and diagnosis is delayed, resulting in severe and sometimes lethal forms of the infection [1–6]. The source of contamination is usually contact with a marine animal or an aquatic environment [7–9]. In most cases, lesions develop near a skin wound,

which may even be quite old, and the infection may then spread up but may also descend towards the deep tissues [10–17].

Diagnosis should be suspected during the initial clinical examination based on questioning of the patient and the appearance of the lesions. Diagnosis can be confirmed if a specific request is made to the bacteriological laboratory to search for this mycobacteria so that appropriate measures can be taken for its incubation.

The aim of this study was to inform and familiarise the reader about this little known infection in order to minimise the risk of misdiagnosis and delayed treatment.

We also felt that it would be useful to mention the bases for the clinical and bacteriological diagnosis in the cases of three patients who were treated in our hospital after they had received initial inappropriate treatment.

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Table 1 Characteristics of the 3 patients.

	Case no. 1	Case no. 2	Case no. 3
Referral	Primary physician	Primary physician	Primary physician
Diagnosis suggested before cs	No	No	No
First cs in our hospital	Orthopedic surgery	Orthopedic surgery	Infectious diseases
Profession	None	Animal house	Engineer
Point of entry	Stuck by a rose right hand	Wound from coral right hand	Whitlow right hand
Cleaned aquarium	Yes	Yes	Yes
Incubation	3 weeks	3 weeks	3 weeks
Initial lesions	Inflamed nodule	Abscessed nodule	Inflamed nodule
Extension	Right hand Right forearm + Elbow bursitis Shoulder arthritis	Right hand	Right hand
Delay from first lesion to diagnosis	3 months	2 years	4 months
TTT received before cs in our hospital	Anti-staphylococcal ATB	Anti-staphylococcal ATB + Debriding of wound	Anti-staphylococcal ATB
Immediate diagnosis at cs	No	Yes	Yes
ATB treatment after diagnosis	4 months: clarithromycin + Rifampicin	2 months: clarithromycin + rifampicin + ethambutol 1 month: clarithromycin + rifampicin	5 months: clarithromycin + rifampicin
Bacteriology	Positive	Positive	Positive
Anatomopathology	Positive	Positive	Negative
Surgery	Yes	Yes	Yes

cs: consultation.

Patients

Case no. 1

A 60-year-old patient consulted her doctor for a skin wound from a rose bush on the dorsal surface of the third finger of the right hand (Table 1). Anti-staphylococcal antibiotic therapy was prescribed due to the suppurated point of entry but was not effective. Inflamed subcutaneous nodules developed on the dorsal surface of the right hand. Over the next three weeks, they gradually extended towards the forearm and were associated with bursitis of the elbow and infected epitrochlear lymph nodes. This patient was referred to us two and a half months later. The patient had no fever and tests for inflammation and radiological test results were normal. The contralateral arm was normal. The point of entry and the bursitis were debrided. Results of standard preoperative bacteriological tests were negative and the lesions persisted despite additional antibiotic therapy. The patient then developed homolateral arthritis of the shoulder and complained of paresthesia in the region of the homolateral ulnar nerve.

The patient was again questioned and several days after initially being wounded she remembered cleaning an aquar-

ium in which several fish had died. This suggested an atypical mycobacterial infection.

Excisional biopsy of the nodules and the epitrochlear lymph nodes was performed and a specific request was made to search for mycobacteria. The diagnosis was confirmed by bacteriological and anatomopathological results. Dual antibiotic therapy with clarithromycin and rifampicin was begun for 4 months, resulting in a cure.

Case no. 2

A 23-year-old man who worked in an animal house consulted for an abscessed nodule on the dorsal surface of the right hand. Standard clinical and bacteriological tests had been performed. Antibiotic therapy had been unsuccessful.

The patient consulted at our hospital in January 2008, due to persistent lesions and difficulty in performing his professional activities (Fig. 1). There was no fever, no associated adenopathy and articular range of motion was normal. Biological tests were inconclusive. During questioning, the patient mentioned that he been superficially wounded on the third finger of the right hand 2 years before while cleaning an aquarium. An excisional biopsy was performed and results of bacteriological and anatomopathological tests



Figure 1 Inflamed nodule with papules.

confirmed the diagnosis of *M. marinum* infection. The course of the lesion was favourable after treatment associating clarithromycin, rifampicin and ethambutol for 2 months, then clarithromycin and rifampicin for another month.

Case no. 3

A 41-year-old patient who was an engineer was referred to the infectious diseases consultation by his primary care physician in March 2006, for a persistent 7 month old whitlow on the third finger of the right hand which had not responded to treatment. The patient was in good general condition with no particular prior medical history. He also presented with a painless purplish red nodular lesion on the right hand which had developed 4 months before (Fig. 2). This nodule had developed approximately 3 weeks after the patient had cleaned his aquarium at home and had not responded to anti-staphylococcal antibiotic treatment.

A diagnosis of *M. marinum* infection was suspected and a sample was taken from the lesion for bacteriological analysis. Antibiotic treatment associating clarithromycin and rifampicin was begun one month later when bacteriological results confirmed the diagnosis. Because of the persis-



Figure 2 Purplish red nodule on the dorsal surface of the hand, and the scar from the whitlow on the third finger.

Table 2 Source of exposure to *Mycobacterium marinum* infection [24].

Source of contamination	Rate (%)
Aquarium	49.2
Direct contact with fish or shellfish	27.4
Contaminated salt water	8.8
Fresh water	7.8
Pool	2.6

tence of the nodule, treatment was continued for 2 months more, associated with surgical excision of the lesion. Anatomopathological results did not show tuberculoid granuloma. A cure was obtained.

Discussion and review of the literature

M. marinum is an acid-alcohol fast intracellular bacillus first isolated by Aronson in 1926 [18]. This atypical mycobacteria is a species in group I of the Runyon classification [19]. Linnel and Norden [20] first described "swimming pool granuloma" in 1954.

Considering the increase in aquatic tourism, domestic aquariums and immunosuppressant treatments, the yearly incidence of this infection is probably underestimated. According to Dobos et al. [21], 150 new cases are identified per year in the United States. According to a study by the National Reference Center for Monitoring Mycobacterial Infections and their Resistance to Antituberculins (*Centre national de référence pour la surveillance des infections à mycobactéries et de leur résistances aux antituberculeux*), the incidence is 0.09 per 100,000 inhabitants in France [22]. Contamination usually occurs through direct contact with a fish or with contaminated water [7–9], usually in the presence of a pre-existing skin wound. The point of entry is not identified in approximately 20% of cases [23]. Jernigan et al. [24] did not identify the probable source of contamination in nearly 72% of cases. When it was identified, an aquarium was the source in nearly half the cases (Table 2) while transmission from swimming pool water is now rare thanks to effective water chlorination. [25,26]. There is no contamination between humans [22].

The average incubation period is 2 to 3 weeks [22,24,27] but in fact it varies greatly, ranging from 5 to 270 days [24,28,29]. The delay between the first symptoms to diagnosis can also be several months [1–6]. Witteck et al. [6] emphasised two basic notions which should draw one's attention to this infection whatever the immune status of the patient: persistence or recurrence of skin lesions or of the soft tissue, and the notion of aquatic contact. In these cases, patient questioning is extremely important to identify exposure, even in the past, which s/he may have forgotten. The diagnosis was delayed in two of our patients in part because the lesions were old, but also because exposure to potentially contaminated water was not investigated. Once the diagnosis was confirmed, our patients received appropriate antibiotic therapy which was effective.

The infection is usually on the dorsal surface of the limbs near a skin wound even if it is old. It initially presents in the form of a red and/or purplish patch or a painless solitary,

Table 3 Therapeutic regimens.

	Molecule	Association	Duration	Additional surgery
Stage I	Cyclins	+ Clarithromycin	3.5 months	No
Stage II	Cyclins	+ Clarithromycin	3.5 month	+or – excision
Stage III	Rifampicin or ethambutol	+ Clarithromycin	>= 4 months	Yes; specific treatment

hard, subcutaneous nodule [23,30] which may later ulcerate or suppurate. Progression is often slow. In the sporotrichoid form, the nodules are distributed along dermal and subcutaneous lymphatics [31,32]. The upper limbs are more often infected than elsewhere [9,22,23,28]. The patient's general condition is usually good, but in certain cases, this infection may be fatal, [33,34] or require amputation [35–38].

Generally three clinical forms of the infection are described [39,40]. Stage I is a superficial papular or ulcerated skin lesion. Stage II is characterised by isolated or multiple subcutaneous granulomas that may fistulate, while in Stage III which is the most rare form, the infection extends deeper into the osteoarticular region, resulting in arthritis, osteomyelitis, tenosynovitis or bursitis [10–17].

The diagnosis of this zoonotic disease can be confirmed by a microbiological and anatomopathological test to search for atypical microbacteria which must be specifically requested from the bacteriologist. Otherwise, standard tests will result in a misdiagnosis, and a risk that the lesions progress. The infection was not suspected in one of our patients, so that only a standard bacteriological examination was performed resulting in a delayed diagnosis. Isolation of *M. marinum* is still difficult because the number of bacteria is limited in tissue samples. Direct examination by Ziehl-Neelsen is only positive in 10 to 22% of cases [23,41]. Isolation requires a specific culture medium (Löwenstein-Jensen, Middlebrook 7H11) and it is only positive in 60% of cases [23] 1 to 3 weeks later. According to Vincent et al. [42], cells should be cultivated at 30 °C and kept for 2 months before tests can be considered negative. The anatomopathological examination is very important if it shows a lymphoepithelioid or giant cell granuloma [10,12]. However, according to Streit et al. [43], this granuloma may be absent in recent lesions. This was true for one of our patients (case no. 3) whose lesion was 4 months old. On the other hand, a granuloma was identified in case no. 1 whose lesion was 3 months old. Molecular techniques such as polymerase chain reaction (PCR) proposed by Talaat et al. [44] are used increasingly frequently, resulting in a more rapid diagnosis [45–48].

The intradermal reaction to tuberculin is often positive because of genetic similarities and cross-reactions to the *Mycobacterium tuberculosis* [49]. There is no consensus for antibiotic treatment [50]. The most frequently used antibiotics are clarithromycin, minocyclin, trimethoprim-sulfamethoxazol, ethambutol and rifampicin [22,30,51,52]. The first three antibiotics can be administered alone for superficial skin lesions [30,52]. In fact, dual therapy is usually recommended because of the resistance of certain strains and the resulting dissemination of infection into the deep structures [22,30]. The most frequently prescribed associations are clarithromycin+rifampicin or clarithromycin+minocyclin. Dodiuk-Gad et al. [5] recommend empirical treatment with clarithromycin while waiting

for bacteriological test results. In severe or sporotrichoid forms, Rallis et al. [30] and Aubry et al. [22] suggest associating rifampicin–ethambutol. Antibiotic treatment is administered for an average of 3 months and a half when only soft tissues are involved, but can reach 25 months in the most severe forms of the infection [22]. In fact, in a review of the literature, antibiotic treatments vary greatly in terms of molecules, associations and duration. We recommend the same treatment regimen as the National Reference Center for Monitoring Mycobacterial Infections, and their Resistance to Antituberculous (Centre national de référence pour la surveillance des infections à mycobactéries et de leur résistances aux antituberculeux) [22] and Dodiuk-Gad et al. [5], which is set out in Table 3. Stages I and II respond well to antibiotic treatment alone [53]. Stage III lesions usually require surgery as well [2,22]. Simple preventive measures such as using gloves can reduce the frequency of this infection [54].

Conclusion

Diagnosis of an infection from *M. marinum* can be delayed by several months. Failure to identify the microorganism and an insufficiently detailed clinical examination are the main causes of delay. The orthopaedic surgeon may be the first to be consulted in these cases, and should be able to recognize the various clinical, bacteriological and anatomopathological signs as well as information from the patient's history to make the diagnosis. Questioning the patient about past exposure may be the key to making the diagnosis.

Because this organism requires a specific culture medium, the bacteriological laboratory should be informed that this is the suspected diagnosis. Better knowledge of this infection makes it possible to begin treatment early and reduces the risk of potentially severe regional or systemic spreading.

Information about simple recommendations such as wearing gloves should be widely circulated among professionals with exposure to products from the sea and aquarium owners.

Conflict of interest statement

None.

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