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Skin and soft-tissue infection caused by non-tuberculous mycobacteria in Taiwan, 1997–2008

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SUMMARY

The aim of this study was to investigate the clinical, microbiological, and pathological characteristics and the outcomes of skin and soft-tissue infection (SSTI) caused by non-tuberculous mycobacteria (NTM). Medical records of 50 patients with SSTI caused by NTM identified from 2005 to 2008 and 63 patients previously reported in a medical centre from 1997 to 2004 were reviewed. The annual incidence (per 100 000 outpatients and in-patients) ranged from 0·57 in 2005, 0·38 in 2007, to 1·1 in 2008, with an average of 0·62/100 000. From 1997 to 2008, the average incidence was 1·39/100 000 patients. The average annual incidence of SSTI caused by NTM was 0·62/100 000 outpatients and in-patients during 2005 and 2008. Of the total of 113 patients identified during the 12-year period, patients infected with *Mycobacterium fortuitum* and *M. marinum* were younger than those infected with *M. avium-intracellulare* complex (MAC) (36 and 44 years *vs.* 55 years, $P=0·004$ and $P=0·056$, respectively), and were more likely to have previous invasive procedures than those infected with MAC and *M. abscessus* (81·8% and 72·0% *vs.* 27·8% and 54·8%, $P=0·007$), and less likely to have associated immunosuppression (9·1% and 24% *vs.* 66·7% and 45·2%, $P=0·006$). Granuloma was more often observed in immunocompetent patients (60·1% *vs.* 40%, $P=0·019$), and in *M. marinum*-infected specimens (78·3%). There were significant differences in the demographic and clinical features of patients with NTM SSTI, including immunosuppression, trauma experience, and depth of tissue infections.

Key words: *Mycobacterium marinum*, *Mycobacterium avium-intracellulare* complex, non-tuberculous mycobacteria, outcome, rapidly growing mycobacteria, skin and soft-tissue infection.

INTRODUCTION

The pathogenic potential of non-tuberculous mycobacteria (NTM) has been recognized since the beginning of the last century [1]. Many large series studies have reported that NTM can be attributed to both pulmonary and extrapulmonary diseases, with increasing numbers in both HIV-positive and

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HIV-negative patients [1–4]. Of the extrapulmonary diseases caused by NTM, skin and soft-tissue infection (SSTI) was the most common [5–7].

NTM SSTI is often associated with surgical procedures or trauma [8–10] and tends to disseminate in hosts with immunosuppression [11, 12]. Immunosuppression defines patients who had chronic steroid use, immunosuppressive medications, or the following comorbidities, including diabetes mellitus, malignant neoplasms, chronic renal or hepatic disease, rheumatic disease, or AIDS. The clinical and histopathological presentations are diverse and not species specific [13]. In addition, no large-scale comparative clinical trials on the treatment of skin diseases caused by these organisms have been reported. Although the American Thoracic Society (ATS) and the British Thoracic Society (BTS) have issued guidelines on the diagnosis and management of NTM infections [4, 14, 15], the reported treatment regimens varied considerably.

In the current study, the clinical features and outcomes of patients with NTM SSTI in our institute from 2005 to 2008 were analysed together with information obtained from a previous study conducted during 1997–2004 [8]. The results may help to elucidate the spectrum of NTM SSTI.

PATIENTS AND METHODS

Study setting and NTM isolates

A retrospective study of patients with NTM SSTI was conducted for the period from 2005–2008 at the National Taiwan University Hospital (NTUH), a medical centre located in northern Taiwan. Cultures for mycobacteria were performed as described in our previous report [8, 16]. Briefly, the specimen was inoculated onto Middlebrook 7H11 by selective agar (BBL, Becton Dickinson, USA) and the fluorometric BACTEC technique (BACTEC MGIT 960 System; Becton-Dickinson Diagnostic Instrument Systems). Identification of the mycobacterial species was based on standard methods described previously [16].

Data collection

The medical records of patients with NTM SSTI were reviewed retrospectively with informed consent and approved by the Institutional Review Board of NTUH. Information was collected on demographic characteristics, clinical diseases, immune status, underlying medical conditions, predisposing factors (including prior trauma, marine animal exposure, or recent surgery), histopathological findings, antimicrobial treatment, surgical interventions, and outcomes. Chronic renal disease defined as a serum creatinine level $\geqslant 2$ mg/dl, and chronic steroid use as daily use of 20 mg prednisolone for at least 2 weeks. Patients with immunosuppression included those who had chronic steroid use, immunosuppressive medications (chemotherapeutic agents or radiotherapy for malignancy), or followed diabetes mellitus, malignant neoplasms, chronic renal or hepatic disease, rheumatic disease, or AIDS. Our previous data regarding SSTI due to NTM from January 1997 to December 2004 were also reviewed for comparison [8].

Diagnosis of SSTI and osteomyelitis caused by NTM

NTM SSTI was defined as culture of a wound discharge or biopsy specimen of a lesion involving skin, subcutaneous tissue, muscle, synovium or bone yielding NTM in the presence of a compatible syndrome. Two disease groups were categorized: localized skin infection and deep tissue infection. Localized skin infection included cellulitis, mass, nodule, pustules and subcutaneous abscess. Deep tissue infection consisted of tenosynovitis, osteomyelitis, deep neck infection, and paraspinal abscess.

Statistical analysis

Data were analysed using SPSS version 10.0 software (SPSS Inc., USA). Continuous variables were expressed as mean $\pm$ standard deviation. Comparisons between continuous variables were analysed using the Wilcoxon rank sum test or independent t test, as appropriate; for $\geqslant 3$ groups, Kruskal–Wallis one-way analysis of variance by ranks was used. Comparisons between or in categorical variables were tested by χ^2 or Fisher's exact test. A value of $P<0{\cdot}05$ was considered significant.

RESULTS

Secular trend of SSTI caused by NTM

During the 4-year study period, 50 patients with culture-proven NTM SSTI were identified and 64 cultures of 80 specimens collected from these 50 patients grew NTM. An average number of 12·5 cases each year was documented with an increasing annual trend

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in the number of cases. The average annual incidence was 0·62/100 000 outpatients and in-patients. The number of patients infected with rapidly growing mycobacteria (RGM) increased, while the number of patients infected with *M. marinum* and *M. avium-intracellulare* complex (MAC) remained the same. From 1997 to 2008, the average incidence of RGM infection was 1·39/100 000 patients. This incidence decreased during 2005–2008 compared to previous years (2·3–2·7/100 000 patients in 1999–2001 and 3·2/100 000 outpatients and in-patients in 2004 [8]).

Clinical characteristics

The clinical characteristics of the 50 patients with NTM SSTI during 2005–2008 are compared to those of patients identified during 1997–2008 in Table 1. The clinical characteristics of SSTIs caused by different NTM species are shown in Table 2. During 1997–2008, patients with *M. fortuitum* and *M. marinum* infections were younger than those with MAC (36 ± 16 *vs.* 55 ± 15, $P = 0{\cdot}004$; 44 ± 19 *vs.* 55 ± 15, $P = 0{\cdot}056$, respectively) and *M. abscessus* (47 ± 21) infections. The duration from symptom onset to diagnosis was also shorter for patients with *M. fortuitum* and *M. marinum* infections, and this difference was especially significant between *M. fortuitum and M. abscessus* infections (22 ± 27 *vs.* 80 ± 80 days, $P = 0{\cdot}01$). Patients with *M. fortuitum* and *M. marinum* infections were more likely to have previous invasive procedures or trauma than those with MAC (81·8% and 72·0% *vs.* 27·8%, $P = 0{\cdot}002$ and 0·006, respectively) and *M. abscessus* (54·8%, $P > 0{\cdot}05$) infections. However, immunosuppressed patients were more likely to have infections of the latter two organisms than the former two (66·7% and 45·2% *vs.* 9·1% and 24%, $P = 0{\cdot}006$) (Table 2). *M. marinum*-related SSTI mostly occurred over extremities (96%) which was less frequent in MAC- and *M. abscessus*-related SSTIs (50%, $P = 0{\cdot}001$ and 45·2%, $P < 0{\cdot}001$, respectively). *M. abscessus* was more likely to cause localized skin infection (OR 6·8, 95% CI 1·6–29·8, $P = 0{\cdot}012$) while MAC was more likely to cause deep tissue infection (OR 10, 95% CI 1·0–100·5, $P = 0{\cdot}05$).

Treatment and outcomes

The mean treatment duration of SSTI during 2005–2008 was 225·3 ± 249·9 days. Two patients died of causes unrelated to NTM infection. For RGM infections, clarithromycin and fluoroquinolones were most the often administered, to 24 (48%) and 15 (30%) patients respectively, 14 of whom received a combination of both drugs. Amikacin and imipenem were given to 11 (22%) patients with RGM SSTI.

The type of treatment is summarized in Table 1. Specific medications used and the response of SSTI caused by different NTMs during 1997 to 2008 are summarized in Table 3. The total treatment duration was 202·4 ± 207·3 days. Four (3·5%) patients died of causes other than NTM infections. Of the 65·5% of patients who underwent surgical debridement, 69·8% had localized cutaneous disease while 65·5% had disease over the extremities. Of the patients who received intravenous antibiotic therapy, 55·6% and 27·8% had disease located over the head/neck and trunk, respectively. In contrast, 72·6% of patients with infections over the extremities were treated with oral medication ($P < 0{\cdot}001$). Of the 15 patients who received surgical debridement, one had finger tenosynovitis and the rest had skin nodules or ulcers. All were cured without recurrence. The treatment duration was shortest in patients who received surgery only (55·5 ± 83·8, range 5–180 days) and longest in patients who received medical treatment only (227·8 ± 312, range 28–1400 days, $P = 0{\cdot}033$). Patients with localized cutaneous infections had a shorter treatment course (161·7 ± 121·2, range 5–540 days) than those with deep tissue infections (287·7 ± 307·8, range 7–1400 days, $P = 0{\cdot}026$).

Three patients had recurrent NTM diseases (Table 4). Case 1, a case of diabetes mellitus and sarcoidosis, had a positive culture for *M. gordonae* from nose biopsy. The lesion improved under initial treatment with rifampicinn, ethambutol and ciprofloxacin for 4 months but worsened 7 months later and repeated biopsy culture yielded MAC. The lesion resolved after discontinuation of systemic steroid combined with shifting of therapy to rifampicin, ethambutol, moxifloxacin and clarithromycin. Case 2 was treated with clarithromycin, ciprofloxacin and doxycyline for disseminated *M. fortuitum* infection for 1 year. However, para-spinal abscess and lumbar osteomyelitis caused by *M. marinum* was found 6 months after anti-NTM medication was stopped. The osteomyelitis persisted despite prolonged treatment study and the patient was finally lost to follow-up. Case 3 had persistent CD4 count $< 250/\mu$l following the diagnosis of HIV infection. A 1-year treatment plan with amikacin, ethambutol, clarithromycin, ciprofloxacin and rifabutin was initiated to treat MAC bacteraemia after culture was initially negative.

Table 1. *Comparison of the characteristics of patients with definite skin and soft-tissue infections at NTUH between 1997–2004 and 2005–2008*

	1997–2004 $n=63$ (%)	2005–2008 $n=50$ (%)	P
Age (years), mean (range)	47 (1–90)	47 (5–84)	0·87
Male/female	32/31	19/31	0·19
Underlying comorbidities			
Diabetes mellitus	7 (11·1)	9 (18)	0·42
Malignant neoplasm	2 (3·2)	8 (16)	0·022
Chronic hepatic disease	3 (4·8)	4 (10)	0·698
Rheumatic disease	4 (6·3)	5 (8)	0·506
AIDS	5 (7·9)	2 (4)	0·461
Chronic renal insufficiency	4 (6·3)	2 (4)	0·692
Previous trauma, surgery or foreign body-related infections	42 (66·7)	22 (44)	0·087
Receiving immunosuppressive treatment	8 (12·7)	7 (14)	0·27
Prednisolone	6 (9·5)	3 (6)	0·73
Others	2 (3·2)	4 (8)	0·40
Type of infection			
Cellulitis	22 (34·9)	7 (14)	0·008
Subcutaneous abscess	12 (19)	17 (34)	0·08
Nodule/mass/pustule	12 (19)	12 (24)	0·82
Tenosynovitis	9 (14·3)	9 (18)	0·61
Osteomyelitis	3 (4·8)	6 (12)	0·18
Deep tissue abscess	3 (4·8)	4 (8)	0·70
Catheter-related	1 (1·6)	1 (2)	1·00
Lymphadenitis	1 (1·6)	1 (2)	1·00
Sites of infections			
Upper extremity	28 (44·4)	16 (32)	0·24
Lower extremity	18 (28·6)	10 (20)	0·96
Head or neck	7 (11·1)	16 (32)	0·004
Trunk	10 (15·9)	5 (10)	0·84
Others	0	3 (6)*	
Interval between illness onset and diagnosis			
$\leqslant$7 days	8 (12·7)	9 (18)	0·12
7 days–1 month	14 (22·2)	16 (32)	0·11
>1–2 months	16 (25·4)	7 (14)	0·14
>2–3 months	9 (14·3)	6 (12)	0·577
>3 months	16 (25·4)	12 (24)	0·378
Treatment			
Nil	1 (1·6)	2 (4)	0·42
Antibiotics alone	18 (65·7)	13 (26)	0·24
Surgical intervention only	8 (12·7)	7 (14)	0·33
Antibiotics + surgical intervention	31 (47·6)	28 (56)	0·703
Outcomes			
Mortality	2 (3·2)	2 (4)	1
Complete recovery	54 (85·7)	39 (78)	0·58
Disease recurrent or worsened	0	3 (6)	0·48
Not available	7 (11·1)	5 (10)	
Pathological findings			
Granulomatous inflammation	32/54 (59·3)	31/63 (49·2)	0·84
Caseating necrosis	3/54 (5·6)	5/63 (7·9)	0·48
Presence of acid-fast bacilli	14/54 (25·9)	9/63 (14·3)	0·64

* Includes one case of multifocal osteomyelitis and paraspinal abscess, and two cases of generalized skin lesion and osteomyelitis.

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Table 2. *Clinical characteristics of 113 patients with skin and soft-tissue infections caused by non-tuberculous mycobacteria according to mycobacterial species*

Mycobacterial species	*M. abscessus*	*M. chelonae*	*M. fortuitum*	*M. avium* complex	*M. marinum*	Others
Patients, *n* (male/female)						
2005–2008	6/11	0/7	2/2	6/6	3/3	2/2
1997–2008	13/18	2/11	7/4	10/8	14/11	5/10
Age, years*, mean (range)						
2005–2008	49 (6–69)	47 (5–73)	49 (6–69)	58 (39–84)	32 (8–50)	52 (40–62)
1997–2008	47 (1–90)	40 (1–75)	36 (9–64)[c]	55 (33–84)	44 (8–78)	57 (33–76)
Patients with immunosuppression†, *n* (%)						
2005–2008	10 (58·8)	4 (57·1)	0 (0)	6 (50)	2 (33·3)	2 (50)
1997–2008	14 (45·2)	5 (38·5)	1 (9·1)[d]	12 (66·7)	6 (24·0)[e]	6 (40·0)
Previous trauma or surgery‡, *n* (%)						
2005–2008	9 (52·9)	4 (57·1)	2 (50)	3 (25)	2 (33·3)	2 (50)
1997–2008	17 (54·8)	10 (76·9)	9 (81·8)[d]	5 (27·8)	18 (72)[f]	5 (33·3)
Site of infection§, *n* (%)						
Deep tissue‖						
2005–2008	1 (5·9)	2 (28·6)	1 (25)	6 (50)	2 (33)	3 (75)
1997–2008	4 (12·9)	3 (23·1)	1 (9·1)	8 (44·4)	9 (37·5)	7 (47·8)
Extremities						
2005–2008	5 (29·4)	5 (71·4)	1 (25)	6 (50)	5 (83·3)	4 (100)
1997–2008	14 (45·2)[b]	8 (61·5)	6 (54·5)	9 (50)	24 (96)[g]	11 (73·3)
Head and neck						
2005–2008	9 (52·9)	1 (14·3)	3 (75)	3 (25)	0	0
1997–2008	9 (29)	4 (30·8)	2 (18·2)	5 (27·8)	1 (4)	2 (13·3)
Symptom duration¶ mean (range)						
2005–2008	67 (4–219)	60 (7–180)	149 (21–365)	46 (5–120)	47 (7–90)	297 (30–1095)
1997–2008	80 (4–365)[a]	82 (7–180)	22 (5–90)	147 (3–1460)	72 (7–150)	294 (14–1095)

* Significant difference in species, $P=0{\cdot}035$.
† Significant difference in species, $P=0{\cdot}006$.
‡ Significant difference in species, $P=0{\cdot}007$.
§ Significant difference in species, $P=0{\cdot}008$.
‖ Significant difference in species, $P=0{\cdot}038$.
¶ Significant difference in species, $P=0{\cdot}004$.
[a] Compared to *M. fortuitum*, $P=0{\cdot}01$.
[b] Compared to *M. marinum*, $P<0{\cdot}001$.
[c] Compared to *M. avium-intracellulare* complex, $P=0{\cdot}004$.
[d] Compared to *M. avium-intracellulare* complex, $P=0{\cdot}002$.
[e] Compared to *M. avium-intracellulare* complex, $P=0{\cdot}014$.
[f] Compared to *M. avium-intracellulare* complex, $P=0{\cdot}006$.
[g] Compared to *M. avium-intracellulare* complex, $P=0{\cdot}001$.

However, disseminated MAC infection was found in cultures several months later and therapy was switched to moxifloxacin, rifabutin and clarithromycin for 6 months. Five months later, MAC grew from cultures of the lower leg skin abscess and rifampicin, clarithromycin and ethambutol were restarted again. This patient's CD4 count progressively increased under HAART and was 1621/μl at the time MAC treatment was completed.

Pathological findings

Forty-one (82%) patients had at least one biopsy study during 2005–2008. Patients with

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Table 3. *Treatment and response of 113 patients with skin and soft-tissue infections caused by non-tuberculous mycobacteria according to mycobacterial species*

	M. abscessus $n=31$ (%)	*M. chelonae* $n=13$ (%)	*M. fortuitum* $n=11$ (%)	*M. avium* complex $n=18$ (%)	*M. marinum* $n=25$ (%)	Others* $n=15$ (%)
Treatment duration (days)						
Mean (range)	141 (5–495)	187 (35–373)	155 (28–540)	240 (60–740)	250 (7–1400)	257 (35–1020)
Surgical intervention	26 (83·9)	9 (69·2)	7 (63·6)	14 (77·8)	22 (88)	9 (60·0)
Antibiotic treatment						
Clarithromycin	24 (77·4)	10 (76·9)	4 (36·4)	10 (55·6)	13 (52)	7 (46·7)
Flouroquinolone	15 (48·4)	6 (46·2)	12 (45·5)	5 (27·7)	6 (24)	6 (40·0)
Minocycline	1 (3·2)	2 (15·4)	2 (18·2)	0	6 (24)	2 (13·3)
Co-trimaxazole	0	2 (15·4)	0	1 (5·6)	2 (8)	1 (6·7)
Rifampicin/rifabutin	3 (9·6)	1 (7·7)	0	10 (55·6)	7 (28)	7 (46·7)
Ethambutol	3 (9·6)	2 (15·4)	0	10 (55·6)	11 (44)	8 (53·3)
Amikacin	9 (29)	3 (23·1)	1 (9·1)	1 (5·6)	2 (8)	1 (6·7)
Imipenem	6 (19·4)	3 (23·1)	1 (9·1)	0	1 (4)	0
Mortality	3 (9·6)	1 (7·7)	0	0	0	0
Cure rate	23 (74·2)	12 (92·3)	9 (81·8)	16 (88·9)	24 (96)	9 (60·0)

* Includes *M. kansasii* ($n=5$), *M. haemophilum* ($n=2$), *M. gordonae* ($n=3$), *M. scrofulaceum* ($n=1$), *M. flavescens* ($n=1$), *M. arupense* ($n=1$), *M. terrae triviale* complex ($n=1$), unidentified NTM ($n=1$).

immunosuppression were less likely to develop granuloma at their infection sites (38·9% *vs.* 73·9%, $P=0·031$ during 2005–2008; 40% *vs.* 60·1%, $P=0·019$ during 1997–2008) and were older ($40\pm21·5$ *vs.* $55·3\pm13·2$, $P=0·007$) than patients without immunosuppression. Granuloma was also more often found in *M. marinum*-infected tissue (78·3%). Positive acid-fast stain was observed slightly more often in biopsy specimens from patients with immunosuppression (29·4% *vs.* 18·2%, $P=0·465$).

Differences in NTM SSTIs between 1997–2004 and 2005–2008

The interval between the recorded onset of symptoms and the day of culture-confirmed diagnosis was $87·7\pm163·5$ days (range 4–1095 days) in 2005–2008, which was shorter than that for 1997–2004 (average $131·8\pm236·8$). The percentage of immunosuppressed patients increased in the latter period from 31·7% to 48%, and fewer patients had previous experience of trauma, surgery or aquatic animal exposure (44% *vs.* 66·7%). RGM remained the most common pathogens but MAC-related infection increased and infection due to *M. marinum* decreased in the latter period (24% *vs.* 9·5%, 12% *vs.* 30·2%, respectively). Amikacin and imipenem use increased from 6·3% in 1997–2004 to 28% in 2005–2008 ($P=0·003$), while clarithromycin use increased from 48% to 74% ($P=0·007$).

DISCUSSION

This study investigated the clinical, microbiological, pathological characteristics and outcomes of 113 patients with NTM SSTI from 1997 to 2008. The average incidence was 1·39/100 000 outpatients and in-patients, and declined during the last 4 years (2005–2008). In an epidemiological study conducted in an urban community in the UK, 27% of 72 non-HIV patients with NTM disease had SSTIs [5]. This incidence was about 0·11–1·4/100 000. In another study in the USA, the incidence of NTM disease of any body site was 2·7/100 000 non-HIV patients and 18% of these patients had SSTIs [7]. However, it is difficult to compare our findings with previous studies due to the use of different epidemiological methods.

In a series of 125 cases of RGM infections, *M. fortuitum* was the most frequently isolated pathogen [10]. In two series of patients with cutaneous infection, *M. marinum* was the predominant isolated organism [13, 17]. In the current study, the most common microorganism was *M. marinum* from 1997 to 2004, and *M. abscessus* from 2005 to 2008. Although this study found a decreasing trend in cases of NTM SSTIs in patients with previous trauma experience and an increasing trend in cases in immunosuppressed patients, whether these trends were related to changes in the dominant causative NTM species remains unclear.

Similar to previous studies, the ages of our patients with *M. fortuitum* and *M. marinum* SSTIs were

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younger, and were often associated with previous invasive procedures or trauma, and less often associated with immunosuppressive comorbidities than those in patients with *M. chelonae*, *M. abscessus*, or MAC SSTIs [17–19]. Interestingly, we found that *M. abscessus* more often caused localized skin lesion and carried a higher risk of deep tissue involvement than MAC SSTIs. This could not be explained by the difference in percentages of immunosuppressed patients infected by the two species, since over half of the patients with *M. chelonae* and *M. abscessus* infections were immunosuppressed in this study, a similar percentage to those infected with MAC, nor was there any significant difference in the percentage of patients with previous trauma. Immunosuppressed patients with *M. abscessus* or *M. chelonae* SSTIs have been reported to present multiple skin lesions (>5) and disseminated skin lesions more often than those without any underlying diseases [11, 12, 18]. In previous studies, MAC mostly occurred in persons infected with HIV [20–22]. However, an increased incidence of MAC infection in non-HIV patients has been reported in several recent studies [5, 7], mainly in children with lung and cervical lymphadenitis.

The type and duration of antimicrobial treatment for NTM-related infections remains poorly established [4, 14, 15, 23, 24]. The treatment regimen for non-pulmonary disease caused by RGM (*M. abscessus*, *M. chelonae*, *M. fortuitum*) was suggested to be based on *in vitro* susceptibilities. For *M. abscessus* disease, a macrolide-based regimen was recommended. Surgical debridement may also be an important element of successful therapy [4]. In our previous study, amikacin was active against almost all RGM isolates [25]. Clarithromycin was usually active against *M. abscessus* (79–91% susceptible) and *M. fortuitum* (65% susceptible). *M. fortuitum* was highly susceptible to ciprofloxacin (62–83·3%) and imipenem (61–100%). However, the susceptibility of *M. abscessus* to imipenem varied widely in our previous studies (from 18% to 82%) [8, 25]. We treated our patients with RGM SSTI based on the susceptibility patterns determined in our previous study [25], and the resulting cure rate was 72–93%. These previous studies and the current study support the view that surgical debridement alone might be enough for patients with disease localized to skin and without any underlying comorbidities.

The combination of rifampicin and ethambutol or monotherapy with doxycycline, minocycline, or trimethorpim–sulfamethoxazole (co-trimoxazole) has

Table 4. *Characteristics of patients with recurrent skin and soft tissue infection caused by non-tuberculous mycobacteria*

Age/sex	Underlying disease	Previous disease/site	Recurrent disease/site	Microorganism initial/recurrence	Treatment/duration (days)	Outcome
55/F	DM, sarcoidosis under steroid	Nodule/nose	Nodule/nose	*M. gordonae*/MAC	CLA/RIF/EMB/MOX/ (160)	Cured
50/M	AS, SLE under steroid	Disseminated/bone, liver, lymph nodes	Osteomyelitis with paraspinal abscess/multiple bones	*M. fortuitum*/*M. marinum*	AMK/IMP/CIP then RIF/EMB/CLA/ (1400)	Lost
44/M	AIDS, low CD4	Disseminated/bone, liver, blood, skin	Skin abscess with osteomyelitis/right tibia	MAC/MAC	EMB/RIF/CLA/ (490)	Cured

DM, Diabetes mellitus; AS, ankylosing spondylitis; SLE, systemic lupus erythematosus; AIDS, acquired immunodeficiency syndrome; MAC, *M. avium-intracellulare* complex; CLA, clarithromycin; RIF, rifampicin; EMB, ethambutol; MOX, moxifloxacin; AMK, amikacin; IMP, imipenem; CIP, ciprofloxacin; MTB, *Mycobacteria tuberculosis*.

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been suggested for the treatment of *M. marinum* SSTI [24–28]. *In vitro* and *in vivo* susceptibility studies of *M. marinum* to clarithromycin have been previously reported [29–31]. Most of our patients with *M. marinum* SSTIs were treated with clarithromycin with or without ethambutol. Nearly half of our patients with MAC SSTIs received macrolide, rifampicin and ethambutol with or without surgical intervention as suggested by ATS/BTS guidelines [4, 14, 15]. Most of our patients were cured after 6–9 months of medical treatment except for HIV patients with low CD4 counts, which is consistent with the results of an animal study in mice which showed that CD4 cells could protect against dissemination of MAC from the intestine [32]. In this study, one HIV-infected patient had recurrent MAC infection; however, it was not determined whether these MAC isolates had different serotypes or pathogenicity as reported in other studies [33, 34].

In addition, previous studies of mycobacterial DNA in the cutaneous lesions of patients with sarcoidosis identified *M. avium* in 20–30% of patients [35, 36]. Furthermore, *M. avium* subspecies *paratuberculosis* (MAP), an emerging pathogen, has been suggested to play a possible role in the pathogenesis of sarcoidosis and Crohn's disease [37–39]. The agents that are referred to as anti-inflammatories, immunomodulators and immunosuppressants all cause dose-dependent inhibition of MAP in culture. The more potent anti-inflammatory agents, notably methotrexate and 6-mercaptopurine, caused dose-dependent inhibition of all mycobacterial strains (*M. avium* subspecies *avium* and *M. tuberculosis* complex) in previous studies [37, 38]. Although MAP was not identified in isolates from this sample of patients with NTM SSTI, further study using advanced laboratory methods is needed to better understand this uncommon aetiology.

In conclusion, the clinical presentation and treatment varied in SSTIs caused by different NTM species in this study. The recurrence of NTM SSTI is often related to immunosuppression.

DECLARATION OF INTEREST

None.

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