SCIENTIFIC ARTICLE

Nonmarinum, Nontuberculous Mycobacterial Infections of the Upper Extremity: A Multi-Institutional Descriptive Report

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Purpose We analyzed patient demographic factors involved in the development of nonmarinum, nontuberculous mycobacterial infections (NTMI) involving the upper extremity, and assessed diagnostic and prognostic values of commonly used preoperative laboratory and imaging studies, as well as factors related to recurrence of disease and patient outcomes.

Methods Patients from 2 academic, tertiary facilities with culture-proven, nonmarinum NTMI involving the upper extremity were reviewed. Patient-related factors and clinical outcomes were extracted. The analysis was based on pathogen identification (rapid- vs slow-growing subspecies) and immune status.

Results Our 76 patients had a mean age of 59 years, and 65% were male. Forty-eight percent reported an injury, and hands were frequently involved (58%). Forty-one percent were immunosuppressed (19% organ transplant recipients). The mean symptom duration prior to presentation was 203 days. The culture identification took a mean of 33 days, with 25 different species identified (subcategorized as rapid or slow growers). Seventy-seven percent had solitary lesions, with a cutaneous or subcutaneous location most common. Immunosuppressed patients were treated longer with antibiotics (243 vs 155 days in immunocompetent patients) and experienced higher rates of side effects, complications, and recurrence. All patients underwent debridement to control infection, including 4 individuals who required amputations. One-third experienced complications and/or recurrence, regardless of the organism type.

Conclusions Upper-extremity nonmarinum NTMI is often misdiagnosed, causing management delays. Early consideration in differential diagnoses of chronic, painful swelling, nodular or inflammatory lesions, or septic arthritis is crucial. Tissue biopsy with specimens for histopathology and microbiological analysis (mycobacterial smear, cultures, and broad range polymerase chain reaction) and early involvement with an infectious disease specialist are recommended. Empiric antibiotic therapy is not standard. Debridement and prolonged, directed combination antimicrobial therapy is required; however, adverse reactions are commonly encountered.

Type of study/level of evidence Prognostic IV. *(J Hand Surg Am. 2022;■(■):1.e1-e10.*

Key words Arm, hand, infection, mycobacteria, nontuberculous.

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Nonmarinum nontuberculous mycobacteria (NTM) species are ubiquitous in the environment and uncommonly cause human infections.[1] The most common slow-growing NTM species include *Mycobacterium avium* complex, *Mycobacterium kansasii*, *Mycobacterium xenopi*, and *Mycobacterium abscessus* are the most common rapid-growing NTM.[2] Although nontuberculous mycobacterial infections (NTMI) are not on the Centers for Disease Control and Prevention's reportable list, the estimated annual incidence is 30,000 cases in the United States.[3] A 2013 study found the incidence of cutaneous NTMI increased nearly 3-fold between 1980 and 2009.[4] They theorized that this increase may be due to increases in the average age and number of solid organ transplant recipients in the United States. Nonmarinum NTMIs account for 5% to 15% and 25% to 40% of all mycobacterial infections in the general population and in transplant recipients, respectively.[5–7]

A hallmark of skeletal NTMI is an indolent, progressive infection. Often confused for a noninfectious, inflammatory process, NTMI frequently delays diagnosis and treatment. The most common manifestations of NTMI are pulmonary disease and lymphadenitis, yet the wrist and hand are theorized to be the most common sites of extrapulmonary NTMI.[8–10] The majority of cases present as tenosynovitis.[10–13] Subsequently, corticosteroid injections are often used, which can exacerbate underlying NTMI.[14] Once a diagnosis is confirmed by tissue culture, a multidisciplinary treatment approach is indicated.

We present a retrospective study, spanning over an 8-year period, of NTMI of the upper extremity. We chose not to include *Mycobacterium marinum* infections because they have specific and unique risk factors, as well as classic clinical manifestations and standardized treatment regimens, that have been well described in the literature.[14–20] The purpose of this study was to describe patient factors, comorbidities, clinical manifestations, laboratory data, and histopathologic and microbiological information; to identify potential clinical features or risk factors; and to examine therapy-based outcomes when comparing infections caused by rapid- versus slow-growing organisms or when comparing infections in patients with and without clinical immunosuppression.

MATERIALS AND METHODS

This retrospective, descriptive study was approved by our Mayo Clinic institutional review board. The microbiology database from 2 referral centers of a large, tertiary-care hospital system was searched for the term "mycobacterium" between January 2011 and December 2018. From a comprehensive list of positive mycobacterial cultures, we included patients if they met the following inclusion criteria: age >18 years and NTMI involving the upper extremity (shoulder to fingertip).

For each patient, the inciting injury or event (if any) was categorized as a burn, crushing, gardening, or penetrating injury or as a medical procedure or intervention after which symptoms began. The duration of symptoms (time from onset to presentation at our institutions) was recorded in days. Pain, swelling, and constitutional symptoms, including night sweats, fever, and weight loss, were recorded. Unifocal or multifocal lesion locations (digit, hand, wrist, forearm, elbow, brachium) and characteristics (bone, tendon, synovium, joint, cutaneous, or bursal involvement and abscess formation) were noted. Interventions prior to surgical debridement, including antibiotic therapy, steroid injections, or wound care, were verified. Preoperative laboratory values consisted of the white blood cell count, erythrocyte sedimentation rate, and C-reactive protein. Underlying comorbidities were documented, including body mass index, diabetes mellitus and insulin dependence, and rheumatologic, autoimmune, and skeletal disorders. Immunosuppressive disorders and microbiological test data are shown in Table 1. Histopathology results from biopsy specimens were detailed, as were the duration and choice of antimicrobial therapy, adverse reactions, and complications.

Continuous variables were summarized with the mean, standard deviation, median, and range by organism type. Wilcoxon rank-sum tests were used to test the associations between continuous variables and organism types. Categorical variables are summarized as counts and percentages by organism type. To test the associations between categorical variables and organism types, chi-square or Fisher exact tests were used.

RESULTS

Patient demographics

A total of 76 patients with upper-extremity NTMI were identified during the study period. The mean age was 59 years (range, 18–89 years) and 65% of patients were male. The mean body mass index was 27.1 kg/m^2 (range, 18.5–52.4 kg/m^2). Pertinent comorbidities included diabetes mellitus (n = 23; 30%) and underlying immunosuppression (n = 31; 41%). Among immunosuppressed patients, 52 (71%)

TABLE 1. List of Included Immunosuppressive Disorders and Microbiological Test Data

Immunosuppressive Disorders	Microbiological Test Data
Hematologic malignancy	Acid fast smear (AFB stain)
Solid organ or bone marrow transplantation	Mycobacterial culture
Human immunodeficiency virus (HIV infection)	Broad-range PCR assay
Common variable immune deficiency	DNA probe
Immunosuppressive therapies at the time of NTMI acquisition: cancer chemotherapy, systemic corticosteroids (>20 mg/d of prednisone or equivalent for >1 mo), therapeutic interferon preparations, receipt of biologics (such as tumor necrosis factor and interleukin inhibitors), other disease-modifying antirheumatic drugs (such as azathioprine, methotrexate, calcineurin inhibitors, or mycophenolate mofetil)	

AFB, acid-fast bacteria; HIV, human immunodeficiency virus; PCR, polymerase chain reaction.

had an underlying autoimmune disorder, 84% were on active therapy with disease-modifying antirheumatic drugs, and 19% had undergone a solid organ transplant (Table 2).

Clinical characteristics

Clinical characteristics and outcomes are summarized in Table 3. Local symptoms of pain (75%) and swelling (96%) were documented more than systemic symptoms, such as fever or night sweats (13%) Additionally, isolated cutaneous or subcutaneous lesions were reported in 67% of cases, and the mean C-reactive protein value was 23 mg/L in patients with rapid-growing NTMI compared to 9 in patients with slow-growing NTMI.

Characteristics of pathogens and immune status

All patients had either an intralesional (debulking) or marginal excision (depending upon the anatomic location and proximity of neurovascular or other vital structures) of pathologic tissue visualized during the surgical debridement. No patients in this series were treated without surgery. There were 25 different species of NTM identified; organisms were subcategorized as rapid growers or slow growers (Table 4). The distinction between rapidly growing and slow-growing mycobacteria was made based on Runyon's classification, which allows grouping of mycobacterium based on the growth rate and certain phenotypic characteristics, such as pigmentation.[21,22] Notably, acid-fast bacteria stains were positive in 67% of patients, regardless of the organism type. Table 5 lists some of the differences in presentations and outcomes between immunosuppressed and immunocompetent patients.

Management and outcomes

Inadequate coverage and side effects were the most common reasons for a change in antimicrobial therapy, regardless of immune status. Thirty-three percent of all patients experienced complications, 67% of which were medical (nonsurgical). Medical complications were most commonly due to antibiotic-related side effects, and surgical complications most commonly involved wound-healing problems. Complications were seen more in immunosuppressed patients (55%) compared to immunocompetent patients (16%; $P < .05$). The 4 patients who underwent amputation (3 females, 1 male) had an average age of 71 years (range, 63−78 years). Three of these patients were immunosuppressed (rheumatoid arthritis, n = 2; transplant, n = 1) and 2 had insulin-dependent diabetes mellitus (1 with concurrent immunosuppression).

DISCUSSION

In the United States, the reported incidence of upper-extremity NTMI is increasing, but still may be underdiagnosed.[18] In 2018, a retrospective review of culture-positive tenosynovial or intraarticular NTMIs (including *M. marinum*) of the upper extremity found that patients saw an average of 5 physicians prior to receiving an accurate diagnosis, with a mean time to diagnosis of 10 months. Diagnoses of all NTMIs are often delayed because of a lack of awareness or knowledge of these pathogens, an indolent clinical course, and difficulty with inadequate testing and/or organism isolation.[10,20] In our cohort, an increased frequency of infection during the study period could be due to a combination of several factors: ours is a tertiary referral center with a large population of immune-compromised patients (solid organ, stem cell transplant) and an increasing numbers of patients on

TABLE 2. Patient Demographics and Clinical History

Characteristic	Organism Type		Total (n = 76)	*P* Value
	Fast Growers (n = 23)	Slow Growers (n = 53)		
Age				
N (missing)	23 (0)	53 (0)	76 (0)	.9
Mean (SD)	58.7 (16.39)	59.5 (15.09)	58.7 (16.21)	
Median	63.0	61.0	61.0	
Range	20.0–85.0	27.0–89.0	12.0–89.0	
Sex, n (%)				
Female	7 (30.4%)	20 (37.7%)	27 (35.1%)	.6
Male	16 (69.6%)	33 (62.3%)	49 (64.9%)	
Body mass index				
N (missing)	23 (0)	53 (1)	76 (1)	.8*
Mean (SD)	27.2 (5.29)	27.2 (6.00)	27.1 (5.79)	
Median	26.2	25.5	25.5	
Range	18.5–41.6	19.2–52.4	18.5–52.4	
Diabetes mellitus, n (%)				
No	18 (78.3%)	45 (84.9%)	63 (83.1%)	.5
Yes	5 (21.7%)	8 (15.1%)	13 (16.9%)	
IInsulin-Dependent DM, n (%)				
No	18 (78.3%)	48 (90.6%)	64 (83.1%)	.5†
Yes	5 (21.7%)	5 (9.4%)	13 (16.9%)	
HIV, n (%)				
No	23 (100.0%)	52 (98.1%)	76 (98.7%)	>.99†
Yes	0 (0.0%)	1 (1.9%)	1 (1.3%)	
Transplant, n (%)				
No	20 (87.0%)	50 (94.3%)	71 (92.2%)	.4
Yes	3 (13.0%)	3 (5.7%)	6 (7.8%)	
Autoimmune disease, n (%)				
No	16 (69.6%)	38 (71.7%)	55 (71.4%)	.8†
Yes	7 (30.4%)	15 (28.3%)	22 (28.6%)	
Injury or event, n (%)				
No	12 (52.2%)	28 (52.8%)	40 (51.9%)	>.99*
Yes	11 (47.8%)	25 (47.2%)	37 (48.1%)	
Injury or event type (gardening, trauma, other, etc.), n (%)				0.1.1*
Burn	2 (18.2%)	0 (0.0%)	2 (5.4%)	
Crushing	0 (0.0%)	2 (8.0%)		
Gardening	2 (18.2%)	4 (16.0%)	6 (16.2%)	
Medical	4 (36.4%)	5 (20.0%)	9 (24.3%)	
Penetrating	3 (27.3%)	14 (56.0%)		
Missing	12	28		
Location				
Digit, n (%)				.6*
No	15 (65.2%)	40 (74.1%)	55 (71.4%)	
Yes	8 (34.8%)	14 (25.9%)	22 (28.6%)	

(Continued)

TABLE 2. Patient Demographics and Clinical History (Continued)

Characteristic	Organism Type: Fast Growers (n = 23)	Organism Type: Slow Growers (n = 53)	Total (n = 76)	*P* Value
Hand, n (%)				.7*
No	20 (87.0%)	44 (81.5%)	64 (83.1%)	
Yes	3 (13.0%)	10 (18.5%)	13 (16.9%)	
Wrist, n (%)				.03*
No	23 (100.0%)	44 (81.5%)	67 (87.0%)	
Yes	0 (0.0%)	10 (18.5%)	10 (13.0%)	
Forearm, n (%)				>.99*
No	19 (82.6%)	44 (81.5%)	63 (81.8%)	
Yes	4 (17.4%)	10 (18.5%)	14 (18.2%)	
Elbow, n (%)				.1*
No	16 (69.6%)	46 (85.2%)	62 (80.5%)	
Yes	7 (30.4%)	8 (14.8%)	15 (19.5%)	
Brachium, n (%)				>.99*
No	21 (91.3%)	49 (90.7%)	70 (90.9%)	
Yes	2 (8.7%)	5 (9.3%)	7 (9.1%)	

DM, diabetes mellitus; HIV, human immunodeficiency virus.
*Fisher exact *P* value.
†Wilcoxon rank-sum *P* value.

novel biologics with expanding indications. Additionally, over the past 2 decades, novel molecular identification techniques have become available. Our practice has evolved to routinely send suspicious tissue specimens for bacterial, fungal, and mycobacterial cultures, and to obtain early infectious diseases consultations. We suspect that experience accumulated over the years by both hand surgeons and infectious diseases physicians at our institution has also contributed to better awareness and quicker diagnoses.

Nonmarinum NTM are also now recognized as notable pathogens in immunocompetent hosts. Hellinger et al[23] published 6 cases of localized soft tissue infection with *Mycobacterium avium* or *Mycobacterium intracellulare* complex (MAC) in immunocompetent patients, concluding that soft tissue inoculation of MAC can cause a localized infection and that degenerative changes associated with aging may be important in allowing the infection to progress (average age, 64 years). Other studies have also evaluated the environment (farmers, marine workers, aquatic exposure) and reported mechanism of injury as potential risk factors.[10,24] Forty-eight percent of patients in our study reported an initial injury. Among patients with an initial injury, 8 (22%) were infected with MAC, compared to 11 (28%) without a reported injury. We did note a higher incidence of injuries in immunocompetent patients, a finding also reported by Sotello et al.[15] Our study differed from this latter study because we did not include patients with *M. marinum* infections and all our patients underwent surgical debridement, whereas 50% of immunosuppressed patients did not have surgery in Sotello et al's[15] cohort. They also found similar treatment outcomes between immunocompetent and immunosuppressed patient groups, whereas we found a higher complication rate in immunosuppressed patients (55% vs 16% in immunocompetent patients). This may be due to greater virulence and more toxic antimicrobial side effects with treating nonmarinum NTMI in our group of patients.

In our study, the average symptom duration prior to presentation was 206 days. Kozin et al[11] analyzed 33 patients with culture-positive NTMI (including *M. marinum*) of the upper extremity, and found an average delay between symptom onset and correct diagnosis of 1 year (range, 1 month to 8 years). Anatomically, most reported NTMIs involving the hand present as tenosynovitis, fasciitis, septic arthritis, or localized cutaneous involvement, with tenosynovitis being most frequently reported.[11,23,25] Multiple case reports have been published that illustrate the various presentations of NTMIs, including indolent flexor tenosynovitis, osteomyelitis, abscess,

TABLE 3. Clinical Manifestations and Intraoperative Findings*

Symptom	Organism Type		Total (N = 76)	*P* Value
	Fast Growers (n = 23)	Slow Growers (n = 53)		
Night sweats, fever, weight loss, n (%)				
No	19 (82.6%)	48 (90.6%)	67 (87.0%)	.5†
Yes	4 (17.4%)	5 (9.4%)	10 (13.0%)	
Pain, n (%)				
No	5 (21.7%)	14 (26.4%)	19 (24.7%)	.8†
Yes	18 (78.3%)	39 (73.6%)	57 (75.3%)	
Swelling, n (%)				
No	0 (0.0%)	3 (5.7%)	3 (3.9%)	.6†
Yes	23 (100.0%)	50 (94.3%)	73 (96.1%)	
Single vs multifocal lesion, n (%)				
Multifocal	7 (30.4%)	11 (20.8%)	18 (23.4%)	.4†
Single	16 (69.6%)	42 (79.2%)	58 (76.6%)	
Abscess formation, n (%)				
No	12 (52.2%)	32 (60.4%)	44 (57.1%)	.6†
Yes	11 (47.8%)	21 (39.6%)	32 (42.9%)	
Bone involvement, n (%)				
No	17 (73.9%)	41 (77.4%)	58 (75.3%)	>.99†
Yes	6 (26.1%)	12 (22.6%)	18 (24.7%)	
Tendon or tenosynovial involvement, n (%)				
No	13 (56.5%)	21 (39.6%)	34 (45%)	.2†
Yes	10 (43.5%)	32 (60.4%)	42 (55%)	
Joint involvement, n (%)				
No	16 (69.6%)	37 (69.8%)	53 (70.1%)	>.99†
Yes	7 (30.4%)	16 (30.2%)	23 (29.9%)	
Cutaneous or subcutaneous involvement, n (%)				
No	5 (21.7%)	20 (37.7%)	25 (33%)	.3†
Yes	18 (78.3%)	33 (62.3%)	51 (67%)	
Bursal involvement, n (%)				
No	17 (73.9%)	40 (75.5%)	57 (75%)	>.99†
Yes	6 (26.1%)	13 (24.5%)	19 (25%)	
Compressive neuropathy, n (%)				
No	23 (100.0%)	46 (86.8%)	69 (90%)	.1†
Yes	0 (0.0%)	7 (13.2%)	7 (10%)	
ESR	n = 11	n = 22	N = 33	.97‡
N (Missing)	11 (0)	22 (0)	33 (0)	
Mean (SD)	15.5 (11.43)	21.3 (22.92)	19.3 (19.83)	
Median	10.0	21.0	15.0	
Range	2.0–36.0	2.0–99.0	2.0–99.0	
CRP	n = 12	n = 22	N = 34	.7‡
N (Missing)	12 (0)	22 (0)	34 (43)	
Mean (SD)	22.6 (40.02)	8.7 (11.52)	13.6 (25.76)	
Median	5.7	4.9	4.9	

(Continued)

TABLE 3. Clinical Manifestations and Intraoperative Findings* (Continued)

Symptom	Organism Type		Total (N = 76)	*P* Value
	Fast Growers (n = 23)	Slow Growers (n = 53)		
Range	3.0–141.2	3.0–55.2	3.0–141.2	
DMARDs or TNF, n (%)				
No	15 (65.2%)	35 (66.0%)		
Yes	8 (34.8%)	18 (34.0%)		

*Abbreviations: CRP, C-reactive protein; DMARDs disease-modifying antirheumatic drugs; ESR, erythrocyte sedimentation rate; TNF, tumor necrosis factor.
†Fisher exact *P* value.
‡Wilcoxon rank-sum *P* value.

and granulomatous synovitis.[1,8,11,23,26–36] In our study, cutaneous or subcutaneous lesions (68%) were most frequent, and most commonly involved the wrist, hand, and digit (n = 46; 58%), consistent with prior studies.[9,10] Although there is a wide spectrum of clinical presentations and no clearly defined pathognomonic findings, NTMI should be considered for an inflammatory-like process that persists after several weeks or months despite treatment.[10,12,13] There should be a low threshold for biopsy, atypical mycobacterial cultures, and polymerase chain reaction assay of a persistently painful, swollen lesion, particularly if the patient is immunosuppressed or has a history of penetrating trauma or other interventions. C-reactive protein is a very sensitive inflammatory marker and is often elevated in these patients. It was also noted to be higher in patients infected with rapid-growing subspecies (median, 5.7 vs 4.9 with slow-growing subspecies). We postulated that it might indicate a more aggressive inflammatory response in those patients; however, the erythrocyte sedimentation rate was higher in patients infected with slow-growing organisms (median, 21.3 vs 15.5 in rapid-growing organisms). Unfortunately, our small cohort size did not permit a statistical analysis of these differences. Once an NTMI is confirmed thorough debridement (if not accomplished at the initial biopsy procedure), appropriate antimicrobial therapy is required. Serial magnetic resonance imaging scans with intravenous gadolinium can also be helpful in identifying early recurrent bone, joint, or tenosynovial disease. These can be helpful in focusing redebridement, which may help improve antibiotic efficacy or support a change in the antibiotic regimen. Patients should be cautioned about a prolonged course of therapy (mean, 184 days), a high incidence of side effects (46%), the need to change antibiotic coverage (74%), a high rate of complications (32%), and a high rate of recurrent infection (31%).

In our study, tissue samples were sent for histopathology and bacterial, fungal, and mycobacterial cultures, as well as broad-range polymerase chain reaction. An infectious disease specialist was consulted before surgery, and directly supervised the flow of specimens. Interestingly, the most commonly isolated mycobacteria in our study were *Mycobacterium chelonae* and *M. abscessus* (23/77; 30%), both rapidly growing NTMs. There is little published information comparing clinical features and treatment outcomes of infections caused by rapid- versus slow-growing organisms. We were able to identify some differences in our study, although not with respect to disease recurrence or complication rates. Again, since these infections are uncommon, a relatively small cohort size did not allow for statistical analyses of some comparisons.

A multidisciplinary approach involving surgeons, infectious diseases specialists, and a microbiology laboratory with capability for growth and identification of mycobacteria is key to success. In our study, 62 patients (81%) had inappropriate treatment prior to presentation at our institution, including localized corticosteroid injections and antimicrobial therapy directed toward routine bacterial infections. Current recommendations for treatment of invasive NTMIs include a combination of debridement and antibiotics.[37–40] In our cohort, all patients underwent surgical debridement; of those, 4 ultimately underwent amputation for disease eradication. In 2017, Lopez et al[18] published a retrospective review of 34 patients with positive NTM cultures of the upper extremity, and all patients underwent surgical intervention and received antibiotic therapy for a mean duration of 5 months. In our cohort, immunocompromised patients were treated longer (mean, 243 days [8.1 months] with antimicrobial therapy versus 155 days [5.2 months] in immunocompetent patients).

Several institutions have described changes in their practices due to the increasing prevalence of NTMIs

TABLE 4. Characteristics of Pathogens

NTMI Classification	Mean/Median Time to Culture Identification (d)	Number/Percentage of Immunosuppressed Patients	Mean/ Median Duration of Symptoms (d)	Mean/ Median HbA1c	Prior Corticosteroid Injections at Site of Infection (Percentage of Patients)	Mean/ Median Duration of Treatment With Antimicrobials (d)	Histopathology		
							Incidence of Granuloma Formation (%)	Chronic Inflammatory Changes	Tissue Necrosis
Rapid-growing organisms (n = 23; 30%), *M. chelonae*, *M. fortuitum*, and *M. abcessus*	23/20	11/48	115/60	7.9/8.7	23	120/135	36	9	9
Slow-growing organisms (n = 54; 70%), *M. haemophilum* (n = 7), *M. kansasii* (n = 3), *M. avium* complex (n = 19), and other (n=25)	37/34	20/38	248/90	6.4/ 6.8	11	209/180	60	32	24
P value	<.05	.4	.8	.1	.3	.1	.3	.2	.4

HbA1c, glycated hemoglobin.

TABLE 5. Immune Status

Immune Status	Inciting Event or Trauma Reported, Number/ Percentage of Total	Single Lesion, Number/ Percentage of Total	Corticosteroid Injection at Site Prior to Infection, Number/ Percentage of Total	Complications, Number/ Percentage of Total	Hand Involvement, Number/ Percentage of Total	Duration of Antimicrobial Therapy, Mean/Median in d	Side Effects to Antibiotics, Number/ Percentage of Total	Recurrence Rate, Number/ Percentage of Total	Mean/ Median Patient Age at Diagnosis
Immunocompetent (n = 45)	31/69%	40/89%	10/22%	5/16%	12/27%	155/180	12/33%	7/21%	56/58
Immunosuppressed (n = 31)	6/19%	18/58%	1/3%	11/55%	1/3%	243/180	14/70%	9/47%	63/67
P value	<.05	<.05	<.05	<.05	<.05	.16	<.05	.07	.07

in the upper extremity, even in immunocompetent patients.[4,18] One group recommends a separate cutaneous biopsy for atypical mycobacterial tissue culture in patients who present with an upper-extremity lesion with atypical features or who have failed to resolve with appropriate antibiotic treatment for common skin organisms, arguing this facilitates a more timely diagnosis.[15] Another proposed a management algorithm that would start antimicrobial therapy immediately upon initial suspicion of infection from clinical symptoms or pathologic findings.[19,27] Given the need for a prolonged duration of combination antimicrobial therapy for NTMIs that differs based on the species, and due to accompanying side effects of such a therapy, we discourage empiric antimicrobial therapy; obtaining surgical or radiographically directed specimens for culture and histopathology is crucial before initiating antimicrobials. Rapid-growing mycobacteria, with their shorter replication half-life, tend to present in a more acute fashion, with a shorter latency compared to slowly growing mycobacteria. In our series, isolated cutaneous and subcutaneous lesions were more common with rapid-growing species. This, combined with a higher proportion of immunosuppression in patients with these rapid-growing species, may have led to earlier consideration of atypical pathogens and use of more invasive procedures to confirm a diagnosis. The shorter duration of therapy was likely based on the clinical response, combined with the adequacy of debridement when performed. Since there are no clear recommendations for the duration of therapy, management needs to be individualized.

Our study has several limitations. Since our study was retrospective, all aspects of the presentation, symptoms, and clinical course may not have been accurately captured, due to reliance on medical records that may not have been complete for every patient. This also prevented an *a priori* sample size estimate to determine the number of patients needed for many of the comparisons made in this study. Consequently, it is quite possible that a null hypothesis based on any comparisons is at risk for a type 2 error (false negative). It is quite possible that a larger cohort of patients could reveal significant differences ($P < .05$). Changes in laboratory techniques and NTM nomenclature may also have led to misclassification of certain species of NTM. We excluded *M. marinum* infections because these are known to occur often after a marine-related injury involving the hand; because of our geographical location, we do not see many of these patients. *Mycobacterium marinum* infections have been

abundantly analyzed in published studies with respect to causative and patient-related factors, as well as treatments.[14-20] Finally, any inciting injury or event, as well as the durations of symptoms that patients noted in our study, are susceptible to recall bias.

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