

Rheumatologic Perspective on Persistent Right-Hand Tenosynovitis Secondary to *Mycobacterium marinum* Infection

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Background: Rheumatologic conditions share many symptoms with infectious processes. The immunosuppressive therapies used in rheumatology unfavorably impact any underlying infection. Nontuberculous mycobacteria (NTM) are difficult to grow in culture media and may affect the musculoskeletal system, developing manifestations that may imitate rheumatic inflammatory arthritis. For this reason, surgical debridement and biopsy culture are essential in cases where suspicion remains high.

Case Presentation: We present the case of a patient with progressively worsening right-hand tenosynovitis who was evaluated for rheumatic conditions given initial negative

synovial tissue biopsy cultures. He was finally diagnosed with *Mycobacterium marinum* infectious tenosynovitis after repeated surgical debridement.

Conclusions: Our case reinforces the vital role of history gathering in establishing diagnoses and underscores the value of clinical suspicion in patients unresponsive to standard treatment for inflammatory arthritis. Tissue biopsy with culture for acid-fast bacilli is crucial for accurate diagnosis in NTM infection, which may imitate rheumatic inflammatory arthritis. Physicians should be keenly aware of this fastidious, indolent organism in the setting of persistent localized tenosynovitis.

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Rheumatologic conditions and infections may imitate each other, often making diagnosis challenging. Therefore, it is imperative to obtain adequate histories and have a keen eye for these potentially confounding differential diagnoses. Immunosuppressants used in managing rheumatologic etiologies have detrimental consequences in undiagnosed underlying infections. Consequently, worsening symptoms with standard therapy should raise awareness to a different diagnosis.

Nontuberculous mycobacteria (NTM) are slow-growing organisms difficult to yield in culture. Initial negative synovial fluid stains and cultures when suspecting NTM infectious arthritis or tenosynovitis should not exclude the diagnosis if there is a strong clinical scenario. The identification of *Mycobacterium marinum* (*M marinum*) infection in the hand is of utmost importance given that delayed treatment may cause significant and even permanent disability.

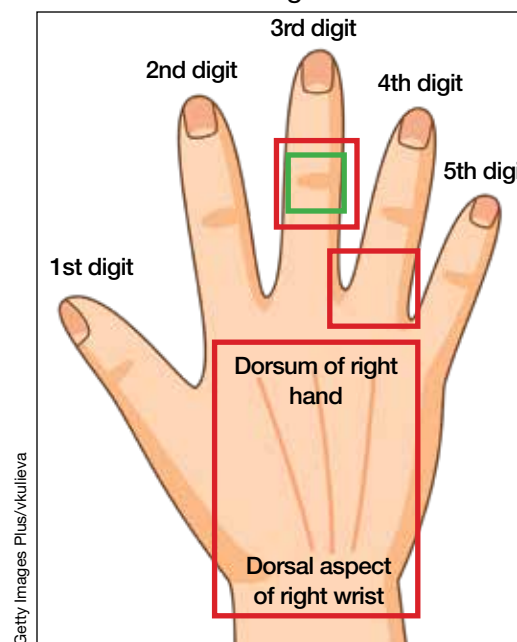
We present the case of a 73-year-old male patient with progressively worsening right-hand tenosynovitis who was evaluated for crystal-induced and sarcoid arthropathies in the setting of negative synovial biopsy cultures but was subsequently diagnosed with *M marinum* infectious tenosynovitis after a second surgical debridement.

CASE PRESENTATION

A 73-year-old male patient with history of type 2 diabetes mellitus, hypertension, hyperlipidemia, hypothyroidism, bilateral knee osteoarthritis, obstructive sleep apnea, and posttraumatic stress disorder presented to the emergency department (ED) with right wrist swelling and pain for 4 days. The patient reported that he was working in his garden when symptoms started. He did not recall any skin abrasions or wounds, insect bites, thorn punctures, trauma, or exposure to swimming pools or fish tanks. Patient was afebrile, and vital signs were within normal range. On physical examination, there was erythema, swelling, and tenderness in the dorsum of the right hand and over the dorsal aspect of the fourth metacarpophalangeal joint (Figure 1). The skin was intact.

Symptoms had not responded to 7 days of cefalexin nor to a short course of oral steroids. Leukocytosis of $14.35 \times 10^9/L$ (reference range, $3.90-9.90 \times 10^9/L$) with neutrophilia at $11.10 \times 10^9/L$ (reference range, $1.73-6.37 \times 10^9/L$) was noted. Sedimentation rate and C-reactive protein levels were normal. Right-hand X-ray was remarkable for chondrocalcinosis in the triangular fibrocartilage. Right upper extremity magnetic resonance imaging (MRI) revealed diffuse inflammation in the right wrist and

FIGURE 1 Dorsal Right Wrist and Hand



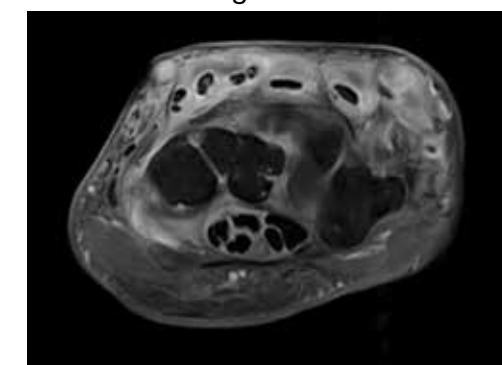
Red rectangles indicate the areas affected with swelling, erythema, and tenderness; green rectangle indicates the location of the tophi-like nodule.

hand (Figure 2). There was no evidence of septic arthritis or osteomyelitis. Consequently, orthopedic service recommended no surgical intervention. Additionally, the patient had preserved range of motion that further indicated tenosynovitis, which could be medically managed with antibiotics.

One dose of IV piperacillin/tazobactam was given at the ED, and he was admitted to the internal medicine ward with right hand and wrist cellulitis and indolent suppurative tenosynovitis. Empiric IV ceftriaxone and vancomycin were started as per infectious disease (ID) service with adequate response defined as a reduction of the swelling, erythema, and tenderness of the right hand and wrist. Differential diagnosis included sporotrichosis, nocardia vs NTM infection.

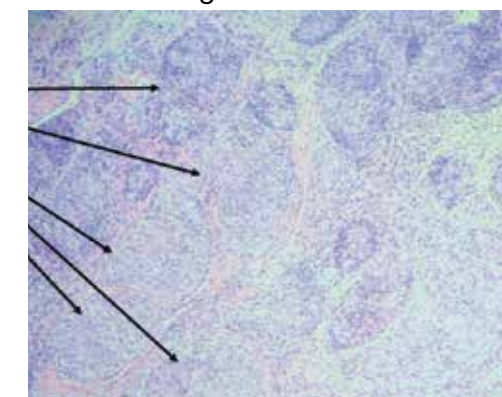
Interventional radiology was consulted for right wrist drainage. However, only 1 mL of fluid was obtained. Synovial fluid was sent for cell count and differential, crystal analysis, bacterial cultures, fungal cultures, and acid-fast bacilli (AFB) stains and culture. Neutrophils were 43% and lymphocytes were 57%. Crystal analysis was negative. Bacterial culture and mycology were negative. AFB stain and culture

FIGURE 2 Contrast Magnetic Resonance Image



Extensive edema and inflammation with tenosynovitis in extensor tendon can be seen.

FIGURE 3 Hematoxylin and Eosin Stain x40 Magnification

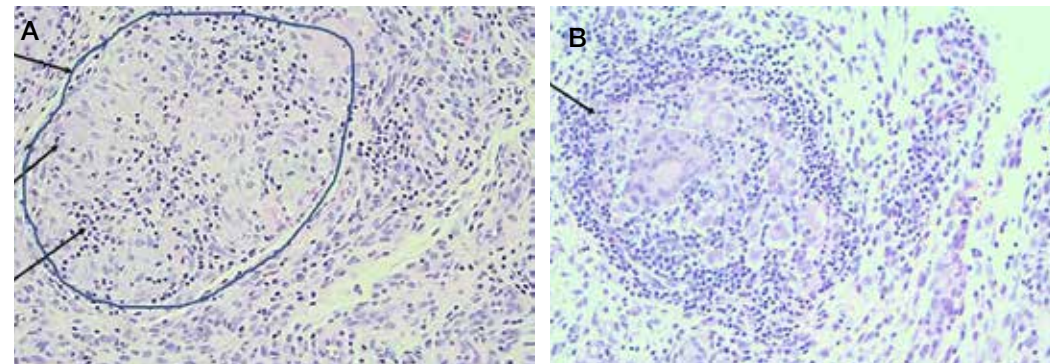


Arrows indicate multiple nonnecrotizing granulomata throughout the tissue.

results were negative after 6 weeks. Based on gardening history and risk of thorn exposure and low suspicion for common bacterial pathogens, ID service switched antibiotics to moxifloxacin, minocycline, and linezolid for broad coverage to complete 3 weeks as outpatient. The patient reported significantly improved pain and handgrip with notable decrease in swelling. Nonetheless, 3 weeks after completing antibiotics, the right-hand pain recurred, raising concern for complex regional syndrome vs crystalline arthropathy.

The patient was referred to rheumatology service for evaluation of crystal-induced arthropathy given chondrocalcinosis. Physical examination revealed right third proximal interphalangeal joint swelling and tenderness with overimposed tophillike nodule. No erythema

FIGURE 4 Hematoxylin and Eosin Stain ×200 Magnification



Arrows and circle indicate nonnecrotizing granuloma consisting of epithelioid histiocytes, some multinucleated, with scattered lymphocytes.

or palpable effusions were appreciated. Range of motion was preserved. Laboratory workup showed resolved leukocytosis and neutrophilia, and normal sedimentation rate or C-reactive protein levels. Antinuclear antibody panel, rheumatoid factor, and anti-cyclic citrullinated peptide levels were normal. Serum uric acid levels were 5.9 mg/dL. Chlamydia, gonorrhea, and HIV tests were negative. Short course of low-dose oral prednisone starting at 15 mg daily with tapering by 5 mg every 3 days was given for presumptive calcium pyrophosphate deposition vs gout. Nevertheless, right-hand swelling and pain worsened after steroids. Repeat right upper extremity MRI showed persistent soft tissue edema and inflammation along the dorsum of the hand extending to the digits, tenosynovitis, and fluid in the third metacarpophalangeal that could represent a superficial abscess. The patient was hospitalized given concerns of infection.

The relapse of tenosynovitis raised concerns for a persistent infection secondary to

a fastidious organism, such as NTM. Thus, inquiries specifically pertaining to any contact with bodies of water were entertained. The patient remembered that he had gone scuba diving in the ocean weeks before symptom onset. This meant scuba diving could then be the inciting event rather than gardening, which placed NTM higher in the differential. ID service did not recommend antibiotics until new cultures were available. Orthopedic service was consulted for surgical debridement. The right dorsal hand, wrist, and distal forearm tendon sheaths were surgically opened to obtain a synovial biopsy.

Synovial fluid was sent for fungal, bacterial, and AFB cultures, and synovial biopsy for AFB stains, PCR amplification/sequencing assay, and cultures. Results showed nonnecrotizing granulomas and all cultures were negative (Figures 3, 4). Rheumatology was again consulted for evaluation for sarcoidosis given negative cultures and noncaseating granulomas. Review of systems was completely negative for sarcoidosis. Computed tomography (CT) of the

thorax did not show any pulmonary abnormalities, lymphadenopathy, and hilar adenopathy. Serum calcium and angiotensin-converting enzyme levels were normal. ID service recommended against empiric antibiotics given negative culture. Given persistent pain, and reported cases of isolated sarcoid tenosynovitis, low-dose oral prednisone 20 mg daily was given after clearance by ID service. Nonetheless, the right wrist and hand swelling, erythema, and tenderness relapsed with 1 dose of prednisone, leading to a repeat right upper extremity synovial biopsy due to high suspicion for persistent infection with a fastidious organism. New synovial tissue biopsy revealed fibro-adipose tissue with prominent vessels and fibrosis, nonnecrotizing, sarcoidlike granuloma with giant cell granulomatous reaction. The AFB and Grocott methenamine silver stains were negative. PCR was negative for AFB. No crystals were reported. After 5 weeks, the synovial biopsy culture was positive for *M marinum*. Patient was started on oral azithromycin 500 mg daily, rifabutin 300 mg daily, and ethambutol 15 mg/kg daily. At the time of this report, the patient was still completing antibiotic therapy with adequate response and undergoing occupational therapy rehabilitation (Figure 5).

DISCUSSION

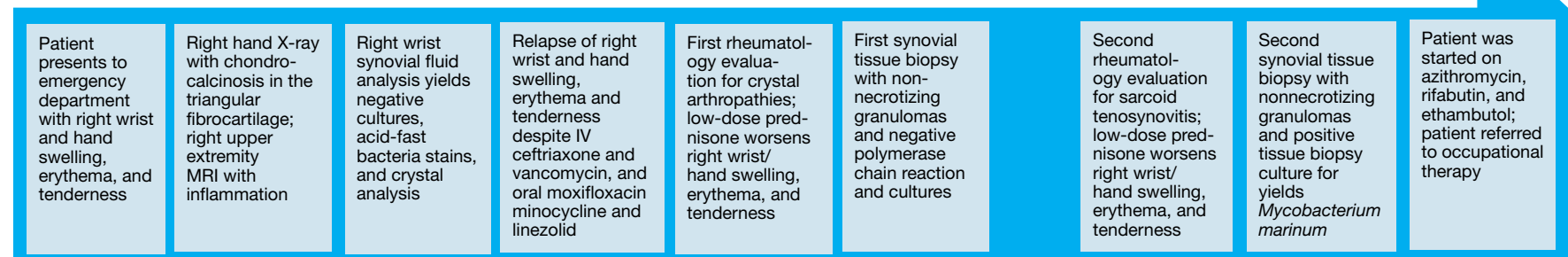
M marinum is an NTM found in bodies of water and marine settings. Infection arises after direct contact of lacerated skin with contaminated water. In a review article of 5 cases of *M marinum* tenosynovitis, they found that all individuals had wounds with exposure to fish or shrimp while in the water or while handling seafood.¹ The in-

cidence of this infection is infrequent, estimated to be 0.04 cases per 100,000, with only about 25% of these cases presenting as tenosynovitis.² The incubation period ranges from 2 to 4 weeks.³ Late identification of this organism is common because of its slow development. For example, presentation from first exposure to symptom onset may take as long as 32 days.¹ In addition, in the same review, surgical intervention occurred in 63 days.¹ It has been reported that AFB stains are positive in just 9% of cases, which confounds diagnosis even more.⁴ After synovial tissue culture is obtained, it takes approximately 6 weeks for the organism to grow. Moreover, diagnosis may take longer if it is not suspected.⁵

Four types of *M marinum* infections have been described.⁵ The status of the immune system plays a role in how the manifestations present. The first type is limited, which is seen in immunocompetent persons, characterized by skin involvement, such as erythematous nodular lesions, that may improve on their own in months or years.⁴ Conversely, in immunosuppressed patients, the second type of infection may cause sporotrichoid spreading described as following lymphangitic pattern. The third type presents with musculoskeletal findings, such as arthritis, tenosynovitis, bursitis, or osteomyelitis, as seen in our patient. The fourth type consists of systemic manifestations.⁵ Medications that lower the immune system, such as corticosteroids, chemotherapy, and biologic disease modifying agents, may increase the risk for developing this entity.⁴ Specifically, anti-tumor necrosis factor inhibitors have been historically associated with mycobacterium infections.⁶

Patients are frequently diagnosed with soft tissue infection, such as abscesses or cellulitis, as in our case. They may at times be found to have other musculoskeletal conditions such as trigger finger.¹ Other similar presenting entities are psoriatic arthritis, rheumatoid arthritis, and remitting seronegative arthritis.⁴ These clinical resemblances complicate the scenario, especially when initial cultures are negative, as the treatment for these rheumatic diseases is immunosuppression, which adversely impact

FIGURE 5 Case Events Sequence



the fastidious infection. In our case, the improved swelling and range of motion after the 3-week course of empiric antibiotics for suppurative tenosynovitis was initially reassuring that the previous infection had been successfully treated. Subsequently, the presence of chondrocalcinosis in the triangular fibrocartilage in the right-hand X-rays, persistent pain, and the tophi-like appearance of the right third proximal interphalangeal nodule raised concerns for crystalline arthropathies, such as calcium pyrophosphate deposition vs gout. Nonetheless, given the lack of response to low-dose steroids, an ongoing infectious process was strongly considered.

Sarcoidosis was a concern after the first synovial biopsy revealed noncaseating granulomas and negative stains and cultures. Sarcoid tenosynovitis is rare with only 22 cases described as per a 2015 report.⁷ Musculoskeletal involvement in sarcoidosis has been reported in 1 to 13% of sarcoid patients.⁷ Once again, unresponsiveness to steroids led to another synovial biopsy for culture due to potential infection. Akin to other cases, more than one surgical debridement was required to diagnose our patient.

CONCLUSIONS

Our case reinforces the vital role of history gathering in establishing diagnoses. It underscores the value of clinical suspicion especially in patients unresponsive to standard treatment for inflammatory arthritis, namely corticosteroids. Tissue biopsy with culture for AFB is crucial for accurate diagnosis in NTM infection, which may imitate rheumatic inflammatory arthritis. Clinicians should be keenly aware of this fastid-

ious, indolent organism in the setting of persistent localized tenosynovitis.

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The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner*, Frontline Medical Communications Inc., the US Government, or any of its agencies.

Ethics and consent

The patient provided signed informed consent. Patient identifiers were removed to protect the patient's identity.

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