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Full Length Article

Chronic tenosynovitis of the hand caused by *Mycobacterium heraklionense*

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ABSTRACT

Non-tuberculous mycobacteria are increasingly recognized as a cause of infection in both immunocompromised and immunocompetent hosts. *Mycobacterium heraklionense* is a recently described member of the *Mycobacterium terrae* complex. Herein we report a case of *M. heraklionense* chronic flexor tenosynovitis in the hand, managed with surgery and antibiotics.

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Case report

A 72-year-old man, with no notable past medical history was referred to our institution because for 9 months he had gradually worsening of right middle finger pain, swelling, and stiffness. He did not recall any trauma to his hand; however, he did report gardening and picking up golf balls as hobbies. Initial workup at another institution with magnetic resonance imaging done 7 months after the onset of symptoms showed notable inflammatory changes in the flexor tendon sheath. Rheumatoid factor and antinuclear antibody tests were negative. Cortisone injection was given to the affected finger, but produced only temporary symptomatic

improvement. Three months prior to his presentation to us he underwent surgical exploration of the inflamed tissue, and histologic analysis of the specimen showed tenosynovitis with granulation tissue formation. Bacterial, fungal, and acid-fast bacilli (AFB) stains were negative. All cultures, including bacterial, fungal, and AFB cultures did not grow any organisms.

Swelling and pain of the hand persisted. Two months later, the patient was seen by one of the authors who noted substantial swelling in the right middle finger extending from the proximal palm to the proximal interphalangeal joint flexion crease. There was a central wound over the proximal phalanx with granulation tissue visible. The patient underwent

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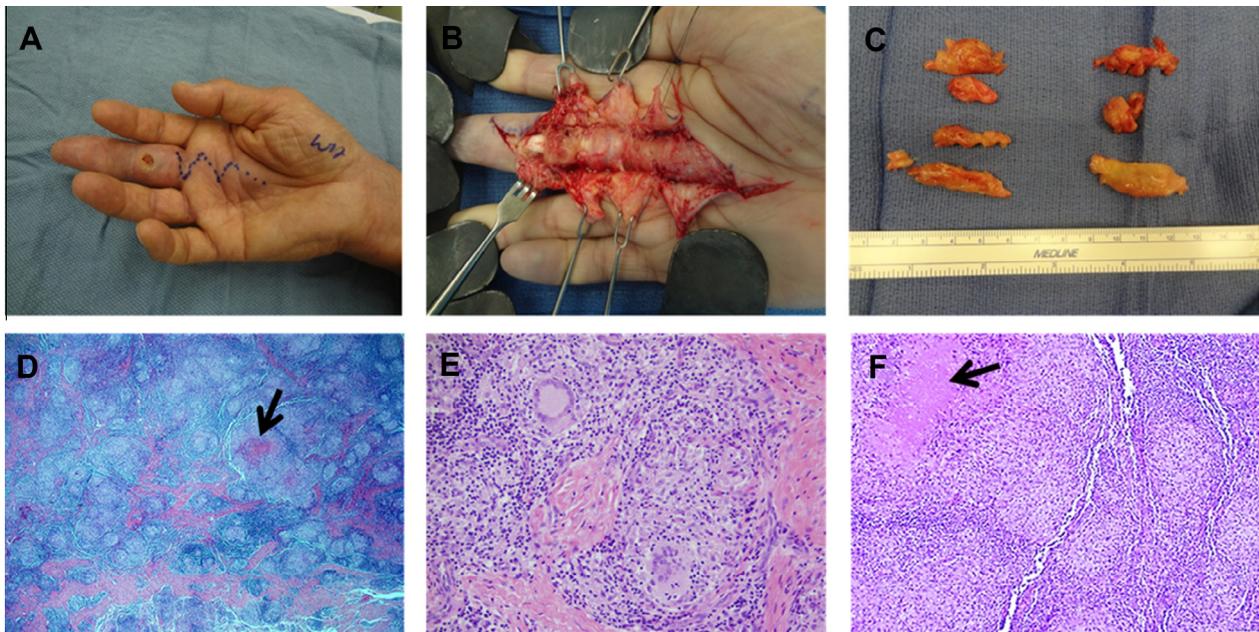


Fig. 1 – Gross images of right middle finger taken at surgery. (A) Preoperative appearance of the right middle finger; (B) exposure of flexor sheath of the right middle finger with thickened tenosynovium; (C) specimen from the right middle finger flexor tendons for submission to surgical pathology following tenosynovectomy. Representative histologic images of inflamed tenosynovium. (D) Numerous necrotizing (black arrow) and nonnecrotizing granulomas with associated chronic inflammation (hematoxylin-eosin, original magnification $\times 20$); (E) lymphocyte-rich epithelioid cell granulomas with Langhans-type giant cells and lymphocyte cuffing (hematoxylin-eosin, original magnification $\times 200$); (F) necrotizing (black arrow) and nonnecrotizing, epithelioid cell granulomas with chronic inflammation (hematoxylin-eosin, original magnification $\times 100$).

radical tenosynovectomy of the right middle finger (Fig. 1A–C) due to persistent symptoms. No bacteria were identified on gram-stained smears. Aerobic culture grew 1+ methicillin-sensitive *Staphylococcus aureus*. Occasional AFB were identified after extensive examination of Ziehl-Neelsen-stained smears done at the microbiology laboratory, but AFB did not grow (the sample was incubated at 31 °C and 37 °C using our standard protocol for plating tissue samples from extremities).

Histologic examination of the tissue showed intense chronic inflammation with numerous necrotizing and non-necrotizing granulomas with associated Langhans- and Touton-type giant cells and chronic inflammation (Fig. 1D–F). No fungal organisms were identified in a Gomori methenamine silver-stained tissue section. A fresh, frozen sample was sent to a reference laboratory at the University of Washington Medical Center, Seattle, WA, USA where DNA was extracted from the tissue. The sample tested negative for the *Mycobacteria tuberculosis* complex using primers for hsp65. A *Mycobacterium* species most likely related to *Mycobacterium heraklionense* DNA was detected using an rpoB primer set.

While awaiting the results of AFB culture and polymerase chain reaction, and considering that bacterial culture grew methicillin-sensitive *S. aureus*, the patient was started empirically on clarithromycin 500 mg twice a day and levofloxacin 750 mg daily. After a month of treatment, when polymerase chain reaction results became available, this regimen was changed to clarithromycin 500 mg twice a day, rifampin 600 mg daily, and ethambutol 1200 mg daily. Clarithromycin

was subsequently changed to azithromycin 500 mg daily because of gastrointestinal side effects. The patient improved gradually. On follow-up in our clinic 2 months later, the inflammatory changes appeared diminished. Three months after his initial surgery, the incision was well healed and the swelling had substantially improved. However, he still had diminished motion of his middle finger.

Discussion

Nontuberculous mycobacteria are increasingly recognized as a cause of infection in both immuno-compromised and competent hosts. *M. heraklionense* is a member of the *Mycobacterium terrae* complex that was described recently [1]. *M. heraklionense* can be associated with substantial morbidity and mortality [2]. However, until recently, there have been very few cases of infection caused by *M. heraklionense* reported in the literature. In most of the cases in a series by Neonakis et al. [2] the bacteria were isolated from patients' sputum or broncho-alveolar lavage specimens. The majority of these cases, however, were patients with serious underlying diseases, potentially obscuring or confounding a causal link with *M. heraklionense*.

There have been only a few recently reported cases of a *M. heraklionense*-associated hand tenosynovitis [3,4]. *M. heraklionense* has been one of the major causes of tenosynovitis/osteomyelitis in the US with little change over the past 20 years. However, it was only recently acknowledged as a substantial pathogen [4]. *M. heraklionense* is very difficult to

grow using standard methods for culturing mycobacteria. Using a molecular detection method is likely essential for making a correct diagnosis. *M. heraklionense* is susceptible to clarithromycin and ethambutol, and resistant to quinolones, rifampicin, sulfamethoxazole, and doxycycline [1]. Treatment guidelines, specifically the duration of treatment, however, have not been established. Once nontuberculous mycobacterial infection of skin and soft tissues is suspected, treatment should be started immediately after a tissue sample is obtained, because the results might not be available until days or weeks later. The most effective empirical regimen is a combination of rifampin, ethambutol, and macrolide (such as clarithromycin) [5]. Because of the diversity of mycobacterial species, accurate identification of the causal organism is very important to guide appropriate chemotherapy.

Abedalthagafi et al. [3] proposed a combination of azithromycin with rifampin and ethambutol for the treatment of their *M. heraklionense* tenosynovitis case. Surgical debridement of the infected area is widely utilized as well to successfully control infection. However, it is not clear if medical therapy alone could be enough to control the infection. More data are needed to clearly establish a role for surgery in the treatment of this infection.

Conflicts of interest

The authors declare no conflict of interest.

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