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Mycobacterium heckeshornense tenosynovitis: Case report and literature review

Mycobacterium heckeshornense should be considered in all patients who present with atypical joint infections, because most infections occur in immunocompetent patients and patients rarely report specific exposures.

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ABSTRACT: *Mycobacterium heckeshornense* is not a commonly isolated organism in British Columbia. We present the first known case of *M. heckeshornense* tenosynovitis in BC, in the hand of an immunocompetent patient. *M. heckeshornense* was identified using *hsp65* gene sequencing, and treatment consisted of surgery and multidrug antimycobacterial therapy. Nontuberculous mycobacteria should be considered as a potential cause of culture-negative tenosynovitis. Because the number of cases implicating *M. heckeshornense* continues to rise, it is important to correctly identify the organism and differentiate it from the phylogenetically related *M. xenopi*. More research and treatment experience are needed before a management guideline for *M. heckeshornense* can be developed.

Case data

A 91-year-old man was assessed by the infectious diseases service at Surrey Memorial Hospital after 3 months of swelling and erythema in the third digit of his left hand. He reported spontaneous development of a small papule that developed into an ulcerating lesion in the volar aspect of the finger around the distal interphalangeal and metacarpophalangeal joints. There was associated dactylitis. He was systemically well with no fevers or chills. He reported no trauma, animal bites or scratches, freshwater or saltwater exposure, or travel outside of Canada. His medical history included gout, diabetes, hypothyroidism, dyslipidemia, chronic kidney disease, congestive heart failure, benign prostatic hypertrophy, and right temporal stroke. His regular medications included insulin, atorvastatin, ferrous fumarate, levothyroxine, carvedilol, aspirin, and hydralazine. He had no known drug allergies.

The patient received courses of oral cloxacillin, intravenous cefazolin, and ceftriaxone for cellulitis and suspected septic arthritis. Joint aspiration revealed minimal fluid. Crystal analysis and cell count and differential could not be performed. Bacterial culture was negative. He was treated with steroids for a possible gout flare and seemed to have partial response.

The joint was re-aspirated 1 month later, which showed 278 000 × 10^6/L total nucleated cells with 92% neutrophils. Crystal analysis and bacterial cultures were negative. Given the subacute clinical presentation, fungal and mycobacterial cultures were obtained. They revealed 1+ acid-fast bacilli on auramine-rhodamine staining. Molecular testing for *M. tuberculosis* and *M. avium* complex were negative. The sample was inoculated on liquid and solid media for mycobacterial culture. Throughout the patient's presentation, his white cell count

and differential remained normal, and his C-reactive protein was only mildly elevated, with a peak of 22.7 mg/L.

The patient developed worsening seropurulent discharge from the affected finger and underwent incision and drainage. Operative cultures were positive for a few colonies of methicillin-resistant *Staphylococcus aureus*. The postoperative wound is shown in **Figure 1**. Histopathology showed granulation tissue and fibrinopurulent exudate, with negative periodic acid-Schiff and acid-fast bacilli stains. A deep wound swab was negative for acid-fast bacilli and had no growth in mycobacterial culture at 8 weeks of incubation. The patient received vancomycin, then subsequent daptomycin therapy for possible methicillin-resistant *S. aureus* tenosynovitis.

Despite 5 weeks of daptomycin therapy, the patient developed a new ulcerating lesion in the volar aspect of his finger, with surrounding hypergranulating tissue and serous drainage. Daptomycin was discontinued because there was no evidence of improvement, and repeat tissue cultures were obtained. Bacterial culture, acid-fast bacilli smear, and mycobacterial culture were negative.

The mycobacterial liquid culture (BACTEC MGIT 960 system) of the original acid-fast bacilli smear-positive aspirate flagged as positive at 5 weeks of incubation. Further incubation at 6 weeks demonstrated small yellow colonies on Löwenstein-Jensen solid medium, with short to medium acid-fast bacilli observed on smear. The organism was identified as *M. heckeshornense* using *hsp65* gene sequencing. Susceptibility testing results were obtained from the National Microbiology Laboratory in Winnipeg **[Table]**.

The patient underwent further debridement and left third-finger tenolysis for chronic flexor tenosynovitis. Operative samples were negative for mycobacteria at 6 weeks of incubation. Pathological review showed granulation tissue with abscess formation. Periodic acid-Schiff and acid-fast bacilli stains were negative, and the sample was negative for malignancy. The patient

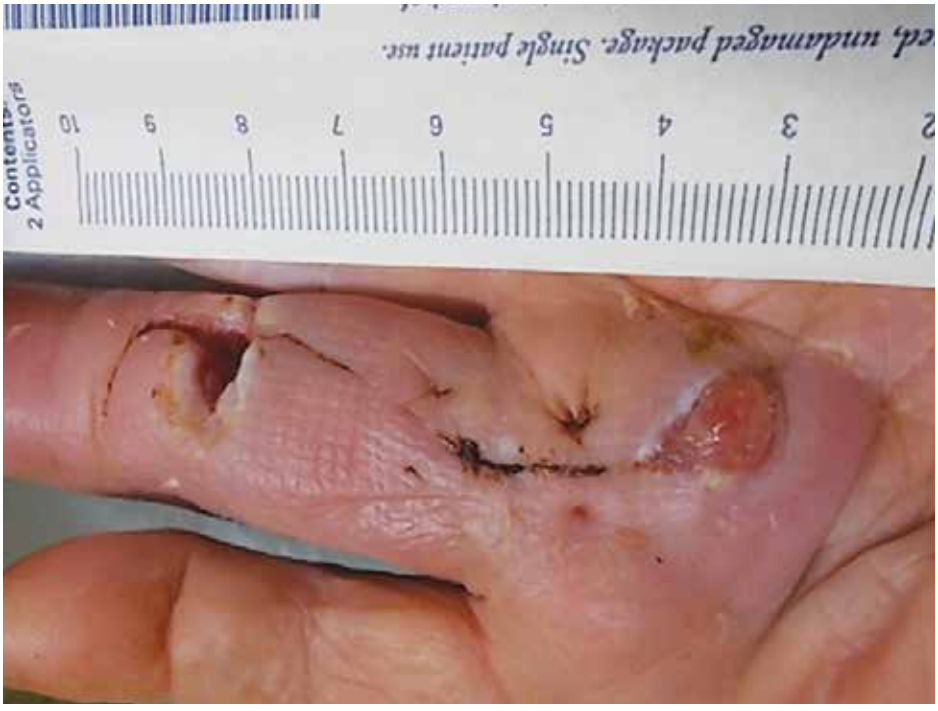

FIGURE 1. Post-debridement and tenolysis of left third finger.

TABLE. Antimicrobial susceptibility testing results of *Mycobacterium heckeshornense* isolated using broth microdilution minimum inhibitory concentration (MIC) panel.

Drug	MIC (µg/mL)	Interpretation
Amikacin	4.00	Susceptible
Clarithromycin	≤ 0.06	Susceptible
Linezolid	4.00	Susceptible
Moxifloxacin	1.00	Susceptible
Rifabutin	1.00	Susceptible
Trimethoprim/sulfamethoxazole	0.25/4.75	Susceptible
Doxycycline	4.00	No interpretation available
Ethionamide	1.20	No interpretation available
Isoniazid	0.50	No interpretation available
Streptomycin	16.00	No interpretation available
Ciprofloxacin	4.00	Resistant
Ethambutol	16.00	Resistant
Rifampin	2.00	Resistant

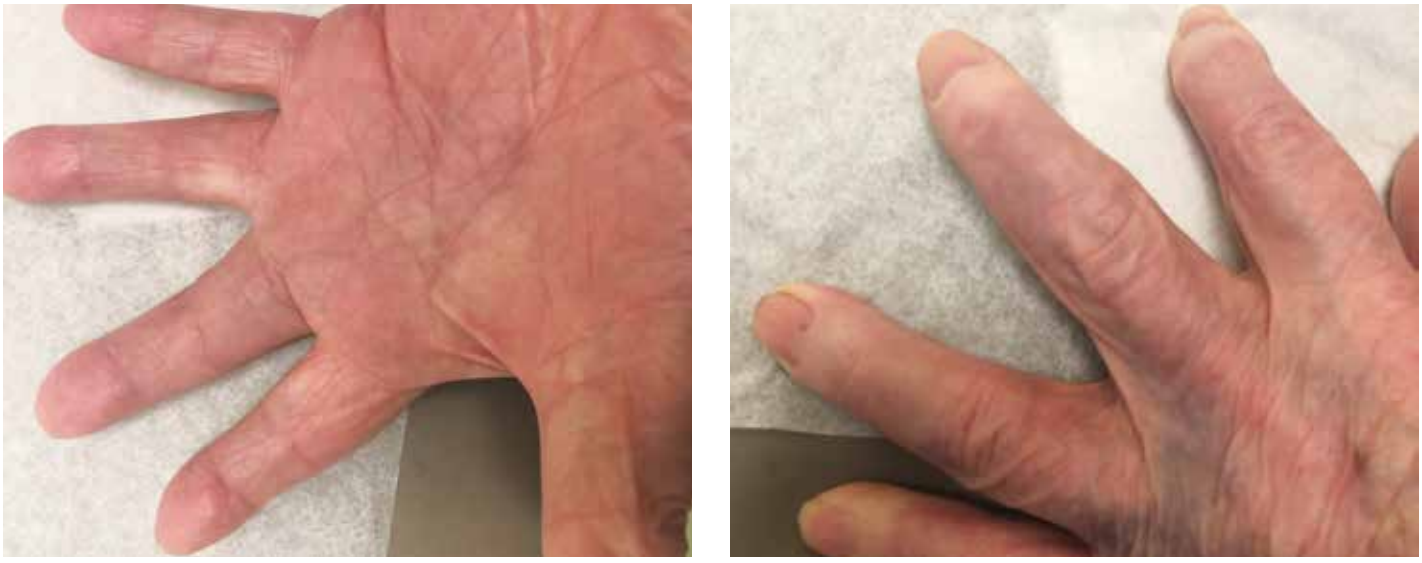

FIGURE 2. Left hand and third finger during follow-up after 3 months of antimycobacterial therapy.

was started on treatment with clarithromycin, moxifloxacin, and isoniazid based on susceptibility results.

The patient was reassessed in the outpatient infectious diseases clinic approximately 3 months after starting antimycobacterial therapy. The swelling had decreased, and there had been no recurrent ulcers since the last tenolysis **[Figure 2]**. The plan was to continue combination therapy for 9 to 12 months if there was ongoing improvement. If the patient had poor clinical response, further consideration would be given to digit amputation by plastic surgery. However, the patient presented to hospital the following month with an unrelated issue of subdural hematoma and died.

Discussion

Hands and wrists are common sites of nontuberculous mycobacterial infections due to a higher likelihood of penetrating injuries.[1] The most common species implicated are *M. marinum*, *M. chelonae*, *M. kansasii*, and *M. intracellulare*. Fifty-three percent of nontuberculous mycobacterial infections of the hand are initially misdiagnosed, leading to delayed treatment and potentially advanced infection by the time they are recognized.[1] Notably, serum inflammatory markers are usually normal, as described in our case. It is not known how our patient was exposed to *M. heckeshornense*.

M. heckeshornense is a rare nontuberculous mycobacterium that is phylogenetically related to *M. xenopi*.[2] It was first identified in 2000 at the Heckeshorn Lung Clinic in Berlin in respiratory mycobacterial cultures of an immunocompetent woman with chronic cavitary lung lesions.[2] Pulmonary and extrapulmonary infections by this organism have been described around the world, with varied clinical outcomes.[2-19] Extrapulmonary manifestations include peritonitis,[3] lumbar spondylodiscitis/osteomyelitis,[4-6] axillary lymphadenitis,[7] bacteremia,[8] and synovitis.[9] In the one published case of *M. heckeshornense* tenosynovitis, surgical treatment alone with flexor tenosynovectomy was effective.[10]

Most *M. heckeshornense* infections occur in immunocompetent patients. For this reason, *M. heckeshornense* and other nontuberculous mycobacterial infections should be considered in all patients who present with atypical joint infections. Patients rarely report specific exposures, which supports the theory that *M. heckeshornense* is widely distributed.

As with other mycobacteria, microbiological confirmation of *M. heckeshornense* infection may be challenging, because the organisms may not be found in all parts of the affected tissues (as evidenced by recovery of this organism in only one of the multiple specimens collected from our patient). Tissue or fluid, rather than swabs, are the appropriate sample types for mycobacterial smear and culture. *M. heckeshornense* is a slow-growing scotochromogen that is able to grow in temperatures ranging from 37 °C to 45 °C, but not at 30 °C.[2] Sequencing of both 16S rRNA and *hsp65* regions can be used to identify *M. heckeshornense*.[10] Granulomata, giant cells, rice bodies, and central necrosis are supportive histopathological clues. In our case, *M. heckeshornense* was ultimately recovered in the aspiration sample obtained after the patient had received a course of steroid therapy. Therefore, it is possible that initial treatment with steroids suppressed the patient's immune system sufficiently to create an environment suitable for this nontuberculous mycobacterium to flourish.

There are no established guidelines for the treatment of *M. heckeshornense*. The literature supports management with surgical source control and the use of combination antimicrobials.[3] It is important to consider in vitro susceptibilities, because *M. heckeshornense* has been found to have reduced susceptibilities to isoniazid and may acquire resistance to rifampicin with long-term treatment.[2] However, in vitro susceptibility results for nontuberculous mycobacteria do not have optimal correlation with clinical response. In many cases, despite the use of combination antimicrobials, definitive

adjunctive treatment with surgical source control is required for the resolution of symptoms. There is no consensus on the choice and duration of antimicrobial treatment for nontuberculous mycobacterial hand infections, which often ranges from 6 to 12 months but can sometimes be more prolonged.[1]

M. heckeshornense is not a commonly isolated organism in BC. Over the last decade, it has been confirmed in less than five cases per year, with most identified in respiratory specimens. The clinical significance of *M. heckeshornense* in these patients is unknown. Among clinically significant cases in BC that we know about, *M. heckeshornense* was described as a source of peritoneal dialysis–associated peritonitis in 2011, where source control with peritoneal catheter removal and fluid drainage alone was adequate for disease resolution,[3] and an unpublished case of a *M. heckeshornense* bacteremia in an immunocompromised patient was diagnosed in 2020.

Summary

We present a case of *M. heckeshornense* tenosynovitis in an immunocompetent patient. As the number of cases implicating *M. heckeshornense* continues to rise, it is important to correctly identify this mycobacterium and differentiate it from the phylogenetically related *M. xenopi*. More research and treatment experience are needed before a management guideline for *M. heckeshornense* can be developed. ■

Competing interests
None declared.

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