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# First Korean Case of *Mycobacterium arupense* Tenosynovitis

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*Mycobacterium arupense*, a slow-growing nontuberculous mycobacterium (NTM), was first isolated from clinical samples in 2006 [1]. It is a member of the *M. terrae* complex, which includes *M. arupense, M. engbaekii, M. heraklionense, M. hiberniae, M. kumamotonense, M. longobardum, M. nonchromogenicum, M. senuense*, and *M. terrae* [1-5]. Although the *M. terrae* complex is generally considered nonpathogenic [6], infections caused by the *M. terrae* complex have been reported [7-9]. The pathogenicity of *M. arupense* is debatable, but a few cases of *M. arupense* infection involving bacteremia, osteomyelitis, pulmonary infection, and tenosynovitis have been reported [10-14]. We report a case of *M. arupense* tenosynovitis in a patient with a history of puncture injury to the finger caused by a crab.

A 56-yr-old woman presenting with symptoms of redness, pain, and swelling in the second and fifth fingers of the right hand was admitted to our hospital. One year previously, the patient had suffered from a puncture injury to the right second finger caused by a crab; the injured finger showed swelling and redness 2 months later. She received antibiotics and corticosteroid injections at a local hospital, but the infected finger did not improve and the fifth finger of her right hand also began to show symptoms of infection.

The patient had a history of being treated for hypertension and had undergone trans-sphenoidal surgery 4 yr ago for a non-functioning pituitary adenoma. After the surgery, she was treated with prednisolone and levothyroxine, but prednisolone was stopped on the day after admission. On admission, her body temperature was 36.0℃, blood pressure was 117/79 mm Hg, pulse was 56/min, and respiratory rate was 20 breaths/min. Laboratory tests confirmed that the patient's electrolytes, liver function, hormones, and complete blood counts were normal, with the exception of an elevated erythrocyte sedimentation rate (43 mm/hr) and decreased thyroid-stimulating hormone level (0.12 μIU/mL). Magnetic resonance imaging of the right hand revealed synovial hypertrophy with enhancement along the flexor tendons, which was especially evident along the second and fifth flexor tendons.

Under suspicion of tuberculous tenosynovitis, her right hand was incised and drained. Histological examination of the resected tissue showed chronic granulomatous inflammation, but no organisms were detected on Gram and Ziehl–Neelsen stainings. Molecular analysis of the resected tissue for *M. tuberculo-*

*sis* and NTM by using the AdvanSure TB/NTM real-time PCR kit (LG Life Science, Seoul, Korea) showed a negative result, and direct cultures of the tissue sample for bacteria and fungi were sterile. After the surgical site had healed, the patient was discharged on cephradine.

The biopsied tissue was cultured for mycobacteria, and mycobacterial growth was observed on Löwenstein–Jensen medium 27 days later. The colonies were rough and unpigmented in the dark and after light exposure. The mycobacterium was identified as NTM by using the Seeplex MTB/NTM ACE Detection Kit (Seegene Inc., Seoul, Korea). For NTM identification, 16S rRNA and 65-kDa heat shock protein genes (*hsp65*) of this isolate were sequenced. The primers and PCR setting used to amplify the target regions were as previously described [15-17]. Sequences were analyzed by using an ABI PRISM 3730 series DNA Analyzer (Applied Biosystems, Foster City, CA, USA). For the first 500 bp of the 16S rRNA gene sequence, the isolate showed a 100% identity match with GenBank sequences NR_043588 (*M. arupense*), a 99.6% identity match with GU084182 (*M. heraklio-*

*nense*), and a 99.1% identity match with DQ058406 (*M. non-chromogenicum*). The 415 bp of *hsp65* showed a 100% identity match with AB239922 (*M. arupense*) and a 96.9% identity match with JX154109 (*M. engbaekii*). The phylogenetic tree of the *hsp65* showed that this isolate was most closely related to AB239922 (*M. arupense*) and was classified as *M. arupense* (Fig. 1).

After the identification of *M. arupense*, the patient was prescribed clarithromycin, ethambutol, and rifampin empirically. We used Clinical and Laboratory Standards Institute breakpoints for *M. kansasii* [18] to interpret the results of the drug susceptibility test (DST) performed by using the broth microdilution method, which indicated that the isolate was susceptible to clarithromycin, ethambutol, and linezolid, but resistant to amikacin, ciprofloxacin, moxifloxacin, rifampin, and trimethoprim-sulfamethoxazole (Table 1). Therapy was maintained and the patient was cured without further complications.

*M. arupense* was first described in 2006 by Cloud *et al*. [1] as a non-pigmented organism, negative for niacin accumulation
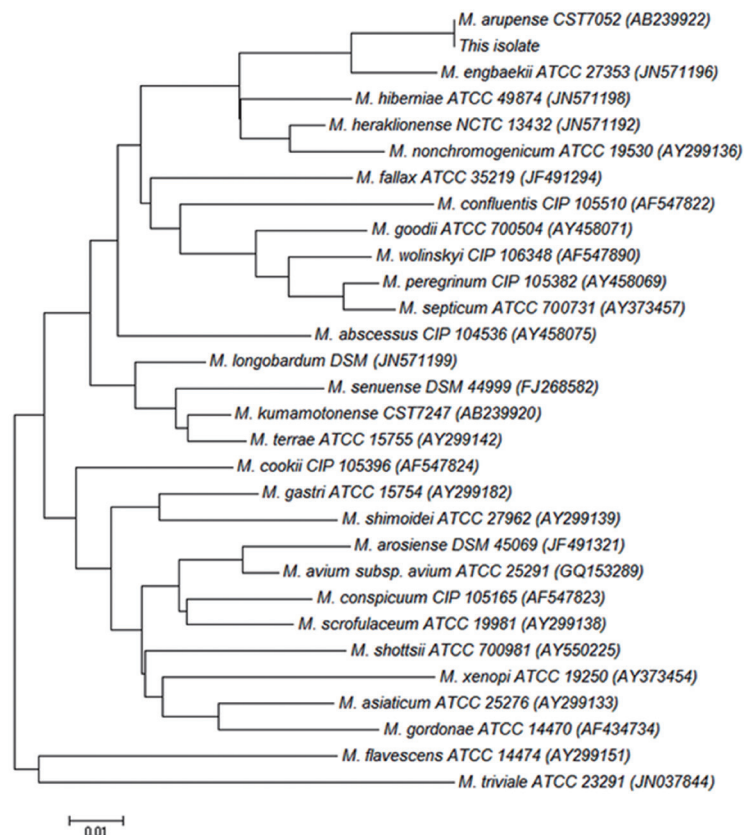


**Fig. 1.** Phylogenetic tree based on 65-kDa heat shock protein gene sequences constructed by using the neighbor-joining method. Nucleotide sequences were used to align the reference panels provided by the National Center for Biotechnology Information Reference Sequence (RefSeq) database. This isolate was identified as *Mycobacterium arupense*.

**Table 1.** Antimicrobial susceptibility testing results for *Mycobacterium arupense*

| Antibiotics | MIC (μg/mL) | Interpretation* |
|---|---|---|
| Amikacin | 64 | R |
| Ciprofloxaxin | 16 | R |
| Clarithromycin | ≤0.5 | S |
| Ethambutol | 2 | S |
| Linezolid | 16 | S |
| Moxifloxacin | >16 | R |
| Rifampicin | 4 | R |
| Trimethoprim/Sulfamethoxazole | 16/304 | R |

*Interpretations using breakpoints suggested by the Clinical Laboratory Standard Institute guidelines: antimicrobial susceptibility testing standards M24, 2011.
Abbreviations: MIC, minimal inhibitory concentration; S, susceptible; R, resistant.

and positive for 68°C catalase and hydrolysis of Tween 80. Although the clinical significance of *M. arupense* is controversial, infections caused by this organism are occasionally reported [10-14]. To date, only 6 patients, besides the present case, have been infected with *M. arupense*, although 1 pulmonary isolate from an immunocompetent patient was classified as colonization according to the American Thoracic Society criteria [6]. The cases include tenosynovitis of the hand (n=2), osteomyelitis of the wrist (n=1), pulmonary infection in an immunocompetent patient (n=1), pulmonary infection in an HIV-positive patient (n=1), and bacteremia in an HIV-positive patient (n=1). In all 4 extrapulmonary *M. arupense* infections in the immunocompetent patients, there was a predisposing factor such as corticosteroid injection or injury.

Accurate identification is important for the treatment of *M. terrae* complex infection, because a substantial number of patients infected with these organisms show persistent disease owing to misdiagnosis [7]. Using mycolic acid analysis by high-performance liquid chromatography, it is difficult to distinguish *M. arupense* from *M. nonchromogenicum* because of their similar mycolic acid patterns [1]. Thus, sequencing of the 16S rRNA gene, 16S–23S internal transcribed spacer region 1 region, and especially the *hsp65*, is useful for identifying *M. arupense* [1]. In our case, the *hsp65* showed better discriminatory power than 16S rRNA gene.

The present strain was susceptible to clarithromycin, ethambutol, and linezolid. Among the 8 isolates studied by Cloud *et al*. [1], all were susceptible to clarithromycin, ethambutol, and rifabutin, and 1 isolate was resistant to clarithromycin. However, the DST results for amikacin and trimethoprim-sulfamethoxa-

zole were variable, and all isolates were resistant to ciprofloxacin, linezolid, moxifloxacin, rifampicin, and streptomycin. Although the optimal therapy for *M. arupense* is not well established in the literature, a multiple antibiotic regimen including clarithromycin and ethambutol is a useful initial approach to manage these patients.

In conclusion, this is the first case of *M. arupense* tenosynovitis in Korea. Our findings indicate that *M. arupense* can be an opportunistic pathogen in patients with a history of corticosteroid injection or injury.

## Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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