Mycobacterium arupense Flexor Tenosynovitis: Case Report and Review of Antimicrobial Susceptibility Profiles for 40 Clinical Isolates

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We describe a case of chronic tenosynovitis in the hand of a 58-year-old cattle farmer. Surgical biopsy specimens grew Mycobacterium arupense. The patient responded to surgery and antimicrobial therapy based on in vitro susceptibility testing. The antimicrobial susceptibility profiles of the isolate from this patient and 39 additional clinical isolates are presented.

CASE REPORT

A previously healthy 58-year-old cattle farmer from Minnesota whose past medical history was significant only for hypertension and hyperlipidemia presented with a 2-year history of chronic swelling in his right hand. Initially, only mild swelling of his right fifth digit was noted in late 2011. He sought medical attention a few months later when the swelling progressed to involve the entire right hand, including all fingers and the wrist, with associated stiffness at the wrist and the metacarpophalangeal and proximal interphalangeal joints. He reported a distant history of blunt trauma to his right index finger but no recent injuries or fish tank exposure. His father had a history of deforming arthropathy, but no further information was available on the cause. His sedimentation rate, C-reactive protein level, HIV screen result, and autoimmune profile (comprising anti-nuclear antigen, anti-citrullinated protein antibody, and rheumatoid factor) were unremarkable. Plain films showed soft tissue swelling and tiny metallic fragments in the soft tissues of the distal-right long finger, suggestive of previous trauma. A seronegative, inflammatory arthropathy was suspected, and his local providers initiated him on oral corticosteroids, to which he had some response, although it was suboptimal. Methotrexate and subsequently adalimumab were added, but he failed to respond. He was referred to our institution for a second opinion in June 2013. At the time of evaluation, the patient had significant soft tissue swelling involving the whole hand, particularly the second and third digits, with evidence of flexor tenosynovitis of the fingers and swelling and tenderness of the right wrist (Fig. 1A and B). An infectious etiology was suspected due to the asymmetric involvement and the patient’s failure to respond to disease-modifying antirheumatic agents. Magnetic resonance imaging (MRI) showed diffuse severe tenosynovitis of the wrist and hand and innumerable enhancing loculations with hypointense foci suggestive of multiple “rice bodies” (1, 2). Pathology from a tenosynovial biopsy specimen showed marked chronic inflammation with no giant cells or granulomas. Gomori methanamine silver and acid-fast stains were negative for fungal and mycobacterial pathogens. Thirty-three days postbiopsy, a Middlebrook 7H10/S7H11 biplate (Becton, Dickinson, Franklin Lakes, NJ) grew a dry, nonchromogenic acid-fast bacterium which was identified as Mycobacterium arupense using 16S rRNA partial gene sequencing (478 bp, 100% match to M. arupense AR30097T, NCBI access number NR_043588.1). MGIT broth-based medium (BD) had no growth after 42 days of incubation. In addition to the biplate, a Middlebrook 7H10 plate supplemented with hemin was inoculated with the biopsy specimen and was incubated at 30°C. M. arupense also grew on this culture plate. The patient underwent formal tenosynovectomy of his right wrist, hand, and fingers, as well as dorsal wrist and hand tenosynovectomy. Rice bodies were seen intraoperatively (Fig. 1C and D) (1, 2), and M. arupense was again cultured from operative specimens after 29 days of incubation. He was empirically started on therapy with moxifloxacin, ethambutol, clarithromycin, and rifampin. This isolate was susceptible by a broth microdilution method (SLOMYCO plate; Trek Diagnostics, Inc., Cincinnati, OH) to rifabutin, ethambutol, and clarithromycin but resistant to ciprofloxacin, moxifloxacin, amikacin, trimethoprim-sulfamethoxazole, linezolid, and rifampin according to Clinical and Laboratory Standards Institute (CLSI) document M24-A2, which contains interpretive criteria for rifampin-resistant Mycobacterium kansasi (3). His therapy was adjusted to rifabutin, clarithromycin, and ethambutol, with resolution of his swelling and stiffness observed during follow-up at 7 weeks posttenosynovectomy. Repeat MRI of his forearm 6 months into treatment showed nearly complete resolution of the innumerable previously seen peripheral enhancing loculations in his flexor compartments of the right wrist, albeit with residual enhancement around the flexor tendons and carpus. The total planned duration of therapy is 12 months.

M. arupense was first described in 2006 by Cloud et al., who identified 8 isolates from sterile sites, including lymph node, lung biopsy specimen, pleural fluid, surgical tissue, and urine, in addition to 48 isolates from sputum/bronchial washings, 4 from stool or duodenum contents, and 5 from unknown sites (4). Interest-
ingly, in Cloud et al.’s study, the type strain of *M. arupense*, AR30097T, and a second isolate, AR30818, were isolated from a tendon and finger wound infection, respectively. *M. arupense* has been found in reclaimed and drinking water systems (5, 6), in African rodents and insectivores (7), and in bioaerosols in duck houses (8). Susceptibility data for eight isolates in the initial report by Cloud et al. (4) found *M. arupense* to be generally susceptible to ethambutol, clarithromycin, and rifabutin but resistant to rifampin, linezolid, and quinolones. Since its initial description, clinically significant diseases caused by *M. arupense* include three further cases of tenosynovitis (9–11), of which one was complicated by osteomyelitis (11), one case of pneumonia (12), and two cases related to AIDS/HIV infection (one pulmonary and one bacteremia case with dissemination) (13). Treatments in the reported cases differed in the combinations of antimicrobials used and, where data were available, in the durations of therapy, which varied from 6 to 14 months. Most of the reported cases recovered, except for the patient with HIV and disseminated *M. arupense* infection, who succumbed to his illness.

*M. arupense* is a slowly growing mycobacterium that is a member of the *M. terrae* complex, and the slow-growth characteristic often results in a long wait for reporting of antimicrobial susceptibility test (AST) results. There is no currently available correlation between AST results and clinical outcomes for *M. arupense*, and therefore, the optimal species-specific antimicrobial therapy is unclear. We reviewed AST results for 40 *M. arupense* isolates characterized and/or referred to our laboratories from 2007 until 2013 (all isolates identified by 16S rRNA sequencing). The study was approved by an Institutional Review Board of the Mayo Clinic. The specimen sources for these isolates (numbers of isolates are in parentheses) were bronchoalveolar lavage fluid (3), bronchial wash (6), sputum (23), mastoid portion of the temporal bone (1), synovial fluid (1), back (1), chest (1), finger (1), foot (1), wrist (1, this case), and tissue (nonspecified) (1). It was noted that two of the mature isolates reviewed were pigmented, which differs from the original description of *M. arupense*. After subculture, the growth of these two isolates appeared nonchromogenic until 3 to 4 weeks, when light-pink pigmentation was seen. Susceptibility testing was performed by the CLSI-recommended broth microdilution method using a SLOMYCO plate with cat-

![FIG 1 Clinical and intraoperative findings for our patient with Mycobacterium arupense tenosynovitis. (A) Dorsum view of hands; (B) ventral view of hands (note swelling, which is most prominent over the right index and long fingers); (C) rice bodies, which are rice-like intra-articular cartilaginous masses resulting from chronic synovial inflammation (black arrow; see references 1 and 2), noted on incision of volar surface of right wrist; (D) multiple rice bodies (black arrows) noted over grossly inflamed tenosynovium on deeper exploration.](http://jcm.asm.org/issue/v52/i7/p2707/)
ion-adjusted Mueller-Hinton broth supplemented with OADC (oleic acid-albumin-dextrose-catalase). Cumulative susceptibility data are presented in Table 1, for which we used the CLSI M24-A2 interpretive criteria (3) for M. kansasii, except with doxycycline and minocycline, for which we used the interpretive criteria for M. marinum in the absence of M. kansasii interpretive criteria.

The majority of isolates identified (97.5 to 100%) were susceptible to clarithromycin, ethambutol, and rifabutin and resistant (>78%) to ciprofloxacin, moxifloxacin, rifampin, and doxycycline. Amikacin, linezolid, trimethoprim-sulfamethoxazole, and minocycline had various susceptibility patterns (33% to 63% susceptible). Eight isolates were tested against the non-CLSI-standardized drugs isoniazid and streptomycin; these demonstrated high MICs: >8 μg/ml and 16 to >64 μg/ml, respectively.

M. arupense infection appears to present as several clinical syndromes: (i) tenosynovitis/extremity infections after traumatic injury and environmental contamination, which may be minor and underreported (9–11), with our case being the fourth reported case, (ii) pulmonary infection (12, 13), and (iii) disseminated infection in immunocompromised hosts (13). We believe that our data represent the largest series of M. arupense susceptibility results published to date, and based on our findings, empirical therapy with a combination of clarithromycin, ethambutol, and rifabutin would be most reliable while awaiting formal susceptibility test results.

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We declare no conflicts of interest.

REFERENCES