Cutaneous Mycobacterium shigaense Infection in Immunocompetent Woman, China

To the Editor: Mycobacterium shigaense is a novel, slow-growing, scotochromogenic mycobacterium (1), initially reported in 2012 as an opportunistic pathogen isolated from skin biopsy samples from a patient with a history of Hodgkin disease and severe cellular immunodeficiency. We describe the identification of this species in a chronic cutaneous infection in an immunocompetent woman.

A 56-year-old woman was admitted to our inpatient department in August 2011 with reddish papules, nodules, plaques, and scars on her face and neck (Figure, panel A) that had developed over >1 year, starting in June 2010. Initially, a few small papules appeared on her face; the primary papules gradually enlarged, spreading to the neck and developing into nodules, plaque, partly purulent lesions, and sometimes fistulas associated with moderate pain and scarring. The patient reported no history of trauma or surgical procedure and could not recall any potential inducement of the lesions or previous receipt of immunosuppressant therapy.

On physical examination, the patient was thin, with normal vital signs. Results of routine laboratory tests were unremarkable. Cephalic and cervical radiographs and computed tomography scans revealed lymphadenectasis of the neck only; a purified protein derivative test showed an erythema ≈8 mm in diameter on the forearm. Results of testing for HIV and human T-lymphotropic virus 1 antibody detection tests were negative. Cell-mediated immunity levels were detected by flow cytometry of peripheral blood cells; cell counts for CD3+, CD4+, CD8+ T-cells, and T-cell receptors and for CD19+ B-cells were within reference ranges.

Skin samples were collected from the face and neck of the patient and subjected to histopathologic examination, smear testing, and culture. Histopathologic examination showed a hyperplastic epidermis and noncaseating granulomatous infiltrates of lymphocytes, histiocytes, and multinucleate giant cells in the dermis (Figure, panel B). Results of Ziehl-Neelsen staining of smears for acid-fast bacilli and periodic acid–Schiff staining for fungi were negative; fungal and other bacterial cultures were sterile. Samples streaked on Löwenstein-Jensen medium at 32°C and 37°C for 4 weeks formed smooth, creamy, yolk yellow colonies (Figure, panel C); however, such colonies did not grow at 25°C and 45°C. Ziehl-Neelsen staining of samples from the colonies revealed acid-fast bacilli (Figure, panel D). Infection with a mycobacterium was suspected on the basis of these results.

The isolated bacilli were subjected to PCR restriction fragment-length polymorphism analysis and sequencing of the mycobacterial hsp65 gene to identify the bacteria and strain (http://app.chuv.ch/prasite/index.html) (2,3). However, a match for the restriction pattern or the sequence of the isolated organism and Mycobacterium spp. was not found. Therefore, complete DNA sequences of the 16S rRNA, hsp65, and rpoB genes and the 16S–23S rRNA internal transcribed spacer (ITS) region were determined by using primers and PCR protocols described previously (4–7). The sequences of 16S rRNA, rpoB and the 16S–23S rRNA ITS region were identical to those of the nontuberculous mycobacterium species M. shigaense; the hsp65 gene showed 94% similarity (online Technical Appendix, wwwnc.cdc.gov/EID/article/19/5/12-1022-Techapp1.pdf).

Results of biochemical tests of the isolate were positive for Mycobacterium spp. by a 2-week culture on MacConkey agar and a heat catalase test but
weakly positive by 3-day arylsulfatase and 2-week catalase testing (8). Results of nitrate reduction, semiquantitative catalase, growth in 5% NaCl medium, urease, and Tween 80 hydrolysis testing were negative. In vitro drug susceptibility was investigated by using the microdilution method, according to Clinical and Laboratory Standards Institute guidelines (9). The isolate was susceptible to moxifloxacin, amikacin, clarithromycin, rifampin, ethambutol, streptomycin, and ofloxacin.

The patient was treated with orally administered rifampin (450 mg 1×/d), moxifloxacin (400 mg 1×/d), and clarithromycin (500 mg 2×/d) for 6 months. The lesions subsided, leaving hyperplastic and atrophic scars (Figure, panel E). New nodules did not recur, and no notable side effects were found.

In general, culture-based identification methods using biochemical tests are slow and inadequate in differentiating species of mycobacteria. Laboratory methods with better performance, such as genetic investigations using nucleic acid amplification and sequencing, are increasingly used for identification. In this case, the complete gene sequences of 16S rRNA, complete 16S–23S rRNA ITS region, rpoB, and hsp65 of the isolate were used to find the most consistent and highest scoring match across all 4 loci in GenBank (www.ncbi.nlm.nih.gov/genbank).

In conclusion, our results strongly suggest that this chronic cutaneous infection in an immunocompetent patient was caused by M. shigaense. Our observations provide further evidence that this species should be classified as a nontuberculous mycobacterium that can cause disease in immunocompromised and immunocompetent patients. The isolate we identified was classified as clinically pathogenic because it was isolated from multiple lesions and at different times. The lesions improved after treatment with clarithromycin and moxifloxacin, and the bacterium was not detectable thereafter.

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References

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Technical Appendix

**DNA sequences for *Mycobacterium shigaense* genes**

All sequences are shown in a 5’→3’ orientation.

**16S rRNA (rrs) (1,346 bp)**

```plaintext
CGTGGGTAATCTGCCCTGCACATTCCGGAATAAGCCTGGGAACCTGGGTCTAATACCGG
ATAGGACCACCTTACGCGCATGGCTTTGTTGGTGAAAAGCTTTGCGGTGTGGATGGG
CGCGCTATACGCTTGTGTTGAGGGGTGACGCGCTACCAGAAGCCAGACGACCGG
CAGCAGTGGGGAATATTGCACAATGGGCGCAAGCCTGATGCAGCGACGCCG
CGTGGGGGATGGCGCTTCGGGTTGTAAACCTCTTTCAGCAGGG
ACGAAGCGCAA
GTGACGGTACCTGCAGAAGAACCGGCCAACTACGTGCCAGCAGCCGCGG
TAATTACGTAGGGTGCGAGCGTTGTCCGGAATTACTGGGCGTAAAGAGCTCGTAGGTGGTTT
GTCGCGTTGTCGTGAAACCCGGGGGCTTAACCCTCGGCGTGCGGGCGATACGGGC
AGACTGGAGTACTGCAGGGAGACTGGAATTCCCTGGTGTGATCGGTGGGAATGGCGCAG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
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AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
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AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
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AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
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AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGCGAAGCGGGGAGACGCAATTACGATCCCTTGCATTCCTGGGGATGCAACGC
ACCGGTGGGTAGTTGTTGAGGCAGATTTACCCTTTTGGGAATTCCGGCCTAGCTA
AACCGGCTGAACTTTTGGGGAGTCGAGCGGTAGTCCACGC
AGCCTGTTGTTGTTGAAACCCGGGGCTTAACCCTCGGCCTGGCCGCAGAGATGCCAAGCGG
ATATCAGGAGGAACACCCGGTGCGGAAGCGCGGTCTCTTGGGCAGTAACTGAGCGCTGA
GGAGC
```
16S–23S rRNA internal transcribed spacer region (197 bp)

TCTCCAATTTGTTGGGTTGTGAGCCGTGAGGGGGTTCTCGTCTGTAGTGGACGAGGGCC
GGGTGCACAACAGCAGGCAAATCGCCAGACACACTATTGGGCCCTGAGGCAACACT
CAGTTTCTTCGAGTGCTGTCCCTCCATCTTTGCTTGTTGGGTTGTTGTTGAGTATTG
GATAAGTGGTTGCAGCAGCATTCAATATA

rpoB (3,362 bp)

GCACCTAACCAGGTTTTCCTTTTGCAAGTTCGTCCGAACCCGCTTGAGGTTCGTTCCGGGCC
CTCGATGTGAGACACGACTCGTGTGGGCTGCCGTCCGCGGCTCAGGCTGCCGCGGCTTCA
CGACGCTGCGCACATGCCAGACTCTGTCTAGGCTGAGGCTGCCGCGCCGCTGCTGCTCA
AAGAAGGCCGAACAGGCTTACATGGGCGAGCTCCCGTGATGAGGCGAAGGGCAGCTCC
CTGACGAGCGCCGCGAGCGGCTGCTCAGCGACCTCCCGACATGAGCTCAGGCTGCCGCGG
CTGACTTCGAGTCCATCGA
CAAGTCGACCGAGAAACTGCTGCACAGCGTGAAG
GCGCCGAGGAGATCACGCGGGACATCCCGAACGTCTCCGACGAGGTGCTCGCCGACCTGGACGAGCGCGGCATCGTGCGTATCGGTGCCGAGGTCCGCGACGGCGACATCCTGGTCGGCAAGGTCACCCCGAAGGGTGAGACCGAGCTGACACCGGAGGAGCGGCTGCTGCGCGAGATCTTCGGTGAAAAGGCCCGCGAGGTCCGCGACACGTCGCTGAAGGTGCCGCACGGTGAGTCCGGCAAGGTGATCGGTATCCGGGTGTTCTCCCGCGAAGACGACGACGAACTGCCCGCCGGCGTCAACGAGCTGGTCCGGGTCTACGTCGCC

GAGACGCACCTGGGAGTGGTGCGGCAAGGCGGCTGGAACATCGAGGGCACCAGCCGACGCGGGCAAGGCGGACGCTGGGCGGCGAATCTGCCGGAGGACCTGCTGGCAGGATCGTCAAGGGCGAGAACATCCCAGAGCCGGGGATTCCCGAGTCGTTCAAGGTGTTGCTCAAGGAGCTGCAGTCGCTGTGCCTCAACGTCGAGGTGCTGTCGAGCGACGGTGCGGCGATCGAGCTGCGCGAGGGYGAGGACGAAGACCTCGAGCGGC

hsp65 (1,526 bp)

GCTCATGCCCCTTGCCGACGCGGTTAAAGGTGACGTTGGGGCCCAAGGGTCGCAACGTGTCCTGGAGAAGAAGTGGGGCGCTCCCACGATCACCAACGATGGTGTGTCCATCGCCAAGGAGATCGAGCTGGAGGACCCCTACGAGAAGATCGGCGCCGAGCTGGTC

GAAGTCGCCAAGAAGACCGACGACGTTGCCGGTGACGGCACGACGACGGCCACCGTGCTCGCTCAGGCACTCGTCAAAGAGGGCCTGCGCAACGTGGCGGCCGGCGCCAACC