

A Case of Subcutaneous Infection with *Mycobacterium mageritense* Identified by Matrix-assisted Laser Desorption/Ionization-time of Flight Mass Spectrometry

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Mycobacterium mageritense is a recently identified rapidly growing uncommon mycobacteria (RGM) (1). Only 9 cases of skin and soft-tissue infection with *M. mageritense* have been reported to date (1–7) (Table I). Although accurate identification of the pathogenic bacteria is mandatory for efficient treatment, using conventional methods for the identification of *M. mageritense* is complex and time-consuming. We report here a case of subcutaneous infection with *M. mageritense* that was treated successfully with antibiotics, in which matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) (8) enabled rapid identification of the species.

Table I. Summary of 9 cases of skin and soft tissue infection with *M. mageritense* reported

Sex/age, years	Surgical intervention	Antibiotics	Duration of treatment	Outcomes	Ref.
F/37	Yes	DOXY, CFPM	9 months	Cured	1
M/25	Yes	AMK, IPM/CS	N/A	Improved	1
F/43	Yes	TMP-SMX, LVFX	3 months	Cured	2
F/56	No	GFLX	2 months	Cured	2
M/48	Yes	N/A	12 months	Cured	3
F/59	Yes	CPFX, CAM	12 months	Cured	4
M/66	Yes	MLFX, CAM	4 days	Cured	5
M/52	Yes	CAM, LVFX	6 months	Cured	6
F/85	Yes	LVFX, IPM/CS, MINO	4 months	Cured	7
M/70	No	CAM, LVFX, MINO	7 months	Cured	This case

DOXY: doxycycline; CFPM: cefepime; AMK: amikacin; IPM/CS: imipenem/cilastatin; TMP-SMX: trimethoprim/sulfamethoxazole; LVFX: levofloxacin; GFLX: gatifloxacin; CPFX: ciprofloxacin; MLFX: moxifloxacin; CAM: clarithromycin; IPM/CS: imipenem/cilastatin; MINO: minocycline; N/A: not available; F: female; M: male.

CASE REPORT

A 70-year-old Japanese man developed subcutaneous abscesses in the periumbilical region within 2 weeks after a laparoscopic cholecystectomy. After unsuccessful treatments with antibiotics (cefamezin and vancomycin) and immunosuppressive agents

(prednisolone and azathioprine) for 1 year, he was referred to our hospital. On examination, a total of 80 reddish nodules intermittently excreting pus were observed on the abdomen (Fig. 1a). Histopathologically, the dermis and subcutaneous adipose tissue were prominently infiltrated with neutrophils (Fig. 1b, c). An

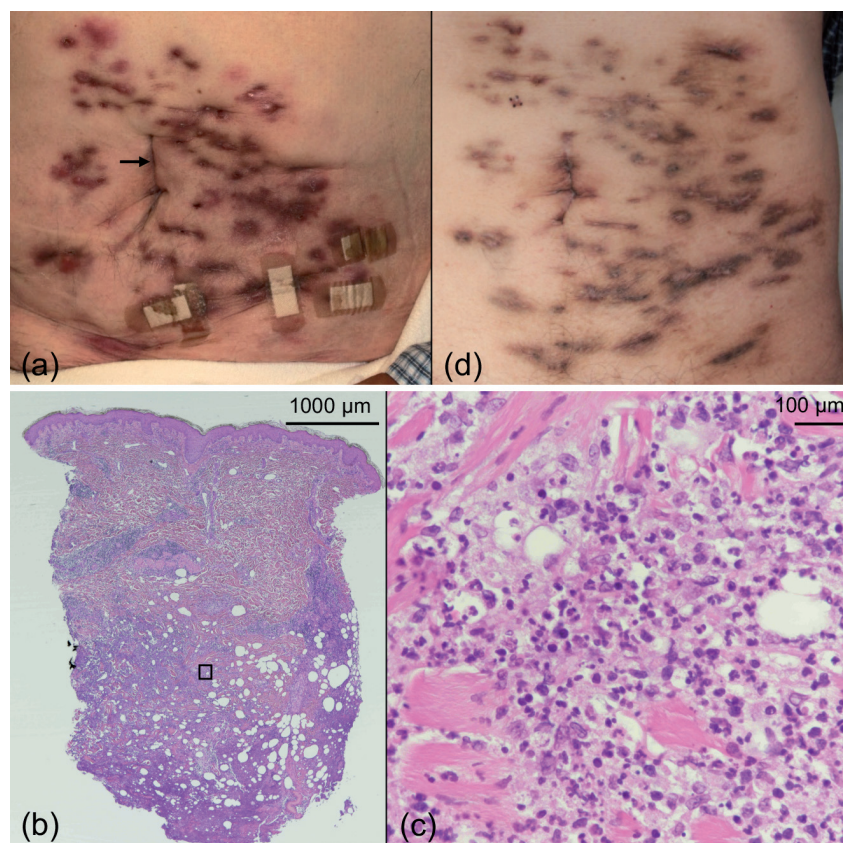


Fig. 1. Clinical pictures and histopathology. (a) A clinical picture before the treatment, showing reddish nodules on the abdomen. Arrow: scar from the laparoscopic cholecystectomy contiguous to the umbilicus. Histopathology: (b) low-magnification view showing a prominent infiltration of neutrophils in the deep dermis and subcutaneous adipose tissue. (c) High-magnification view of the rectangle in (b). (d) A clinical picture after treatment with antibiotics, showing post-inflammatory pigmentation.

acid-fast bacillus culture grown from the excreted pus at 37°C for 3 days revealed a *Mycobacterium* species. It was identified as *M. mageritense* using MALDI TOF-MS system (Microflex LT and MALDI Biotyper, Bruker Daltonics GmbH) with a score value of 2.26 according to the MycoEx extraction protocol (v.3.0) and Mycobacteria Library 4.0. In addition, full-length sequencing of the 16S rRNA gene confirmed this finding. Based on these results, the patient was given a diagnosis of subcutaneous infection with *M. mageritense*.

In advance of the species identification and drug-susceptibility tests, we empirically administered clarithromycin (800 mg/day), levofloxacin (500 mg/day) and minocycline (200 mg/day). After initiation of these antibiotics, no new lesions emerged and the pre-existing eruptions began to subside. Following the species identification, clarithromycin was stopped because *M. mageritense* is known for its resistance to macrolides (1). Consistently, drug-susceptibility tests later revealed that the isolate was sensitive to levofloxacin and minocycline and resistant to clarithromycin. Within 9 months after the initiation of the antibiotics, all of the subcutaneous indurations had diminished, leaving post-inflammatory pigmentation (Fig. 1d). After antibiotics were stopped, no recurrence was observed in 9 months of follow-up.

DISCUSSION

The standard treatment for non-tuberculous mycobacterial infections is a combination of antibiotics (9). The selection of antibiotics is usually based on drug susceptibility tests, yet the correlation between *in vitro* drug susceptibilities and *in vivo* treatment outcomes can be ambiguous for RGM infections (10). *M. mageritense* is known for its resistance to macrolides, which are often used for RGM infections; thus, an accurate identification of the bacterial species is mandatory for effective treatment of infections (1).

In general, the species within *Mycobacteria* are identified using PCR-based and/or DNA-DNA hybridization-based methods in a clinical laboratory (11). However, *M. mageritense* is not identifiable using commercially available kits; and the more robust identification methods (PCR restriction enzyme analysis, 16S rRNA gene sequencing, and high-performance liquid chromatography) are complicated and time-consuming, delaying the selection and administration of appropriate antibiotics. Recently, MALDI-TOF MS has been widely used for species identification, in which a colony is picked from a culture plate and is directly submitted to the analysis chamber after drying (8). Since the analysis processes of MALDI-TOF MS itself takes only a few seconds, MALDI-TOF MS enabled us to identify *M. mageritense* in a day from the initiation of the examination, providing a theoretical basis for the selection and long-term admi-

nistration of antibiotics. This patient's broadly distributed lesions were successfully treated using only antibiotics, although a surgical resection of remaining lesions is often required for the treatment of skin or subcutaneous tissue infections with *M. mageritense* (Table I). In addition, because of the paucity of evidence for the identification of the minor NTM, *M. mageritense*, by MALDI-TOF MS, we corroborated the result by the most robust method of full-length sequencing of the 16S rRNA. Further accumulation of data might certificate MALDI-TOF MS as a stand-alone method for the identification of *M. mageritense*.

This report describes the clinical course of a case of subcutaneous infection with *M. mageritense* showing a broad distribution of abscesses. MALDI-TOF MS enabled the efficient identification of *M. mageritense* and thus its effective treatment with a combination of antibiotics.

The authors have no conflicts of interest to declare.

REFERENCES

- Wallace RJ Jr, Brown-Elliott BA, Hall L, Roberts G, Wilson RW, Mann LB, et al. Clinical and laboratory features of mycobacterium mageritense. J Clin Microbiol 2002; 40: 2930-2935.
- Gira AK, Reisenauer AH, Hammock L, Nadiminti U, Macy JT, Reeves A, et al. Furunculosis due to mycobacterium mageritense associated with footbaths at a nail salon. J Clin Microbiol 2004; 42: 1813-1817.
- Appelgren P, Farnebo F, Dotevall L, Studahl M, Jönsson B, Petrini B. Late-onset posttraumatic skin and soft-tissue infections caused by rapid-growing mycobacteria in tsunami survivors. Clin Infect Dis 2008; 47: e11-e16.
- Fukunaga M, Goya M, Ogawa M, Fukuda K, Taniguchi H, Ando K, et al. Implantable cardioverter defibrillator infection due to Mycobacterium mageritense. J Infect Chemother 2016; 22: 180-183.
- Yonetani S, Kazumi Y, Araki K, Hiroi M, Okuyama T, Ida Y, et al. A case of surgical site infection by mycobacterium mageritense after gastrectomy. J Jap Soc Clin Microbiol 2013; 23: 34-38.
- Maruyama R, Matsumoto A, Kabumoto T. A case of cutaneous mycobacterium mageritense infection. Jap J Clin Dermatol 2015; 69: 722-726.
- Ogawa Y, Ito S, Nakano R, Kasahara K, Kuwahara M, Yano H, et al. Surgical site infection due to mycobacterium mageritense and literature review. J Infect Dis Ther 2016; 4: 283.
- Patel R. MALDI-TOF MS for the diagnosis of infectious diseases. Clin Chem 2015; 61: 100-111.
- Gonzalez-Santiago TM, Drage LA. Nontuberculous mycobacteria: skin and soft tissue infections. Dermatol Clin 2015; 33:563-577.
- van Ingen J, Kuijper EJ. Drug susceptibility testing of nontuberculous mycobacteria. Future Microbiol 2014; 9: 1095-1110.
- Domenech P, Jimenez MS, Menendez MC, Bull TJ, Samper S, Manrique A, et al. Mycobacterium mageritense sp. nov. Int J Syst Bacteriol 1997; 47: 535-540.