A first case report of nasopharyngeal *mycobacterium abscessus ssp. massilliense* infection

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Case report

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Abstract

Background

Mycobacterium abscessus ssp. massiliense is a non-tuberculous mycobacteriosis and was subdivided from *Mycobacterium abscessus* in 2006. There are no reports to date on nasopharyngitis caused by *Mycobacterium abscessus ssp. massiliense*.

Case Presentation

A 45-year old woman was referred to Yokohama City University Medical Center with an 18-month history of recurrent nasopharyngitis and presented with pain in the throat. Mycobacterial tissue culture and polymerase chain reaction testing revealed the presence of *Mycobacterium abscessus ssp. massiliense* in the nasopharyngeal tissue. This patient underwent surgery, followed by multiple rounds of chemotherapy with oral and intravenous antibiotic agents for four months. She has had no recurrence during the 8 months since treatment.

Conclusion

There are few reports on *Mycobacterium abscessus ssp. massiliense* infection in the head and neck region, and none in the pharynx. To our knowledge, this is the first report of a patient with a nasopharyngeal *Mycobacterium abscessus ssp. massiliense* infection. It is difficult to prove the presence of *Mycobacterium abscessus ssp. massiliense* in a pharyngeal “swab,” and tissue culture from a biopsy specimen is mandatory for the identification of the species. Currently, no definite treatment policy is available and only empirical treatment is applied. Further reports are needed to accumulate supporting evidence.

Background

Mycobacterium abscessus ssp. massiliense (referred to hereafter as *M. massiliense*) is a non-tuberculous mycobacterosis (NTM) and is included among the rapidly growing mycobacteria (RGM) [1]. It was subdivided from *Mycobacterium abscessus (M. abscessus*) in 2006 [2][3].

M. massiliense is rare species [4] described in only a few reports [5]. The *M. abscessus* complex, including *M. massiliense*, commonly causes skin, soft tissue as well as pulmonary infections [6]. Although there are reports of *M. massiliense* infection in the head and neck region, such as otitis media [7], there are no reports of nasopharyngitis caused by this pathogen.

It has been reported that the infections caused by *M. abscessus* complex usually follow accidental trauma or surgery [8]. On the other hand, multiple single cases of NTM disease which were caused by health care-associated outbreaks have been described in the last 20 years [1]. Most of the health care–associated mycobacterial outbreaks have involved RGM, especially *M. abscessus* complex and *Mycobacterium fortuitum* [9]. There are also reports of nosocomial infections in multiple countries such

as the United States, Hong Kong and Brazil [10]–[12]. While it may have been overlooked due to the low detection rate of the culture test, we here report, to our knowledge, the first case of nasopharyngeal *M. massiliense* infection.

Case Presentation

A 45-year old woman was referred to Yokohama City University Medical Center with an 18-month history of recurrent nasopharyngitis. She presented with pain in the throat. Nasopharyngitis had been identified on a previous visit to an otolaryngology clinic. It had been temporarily improved by antibacterial treatment and nasopharyngeal abrasive therapy, which involves rubbing the nasopharynx with a nasal swab or oral pharyngeal cotton thread soaked in zinc chloride solution or compound iodine glycerin [13]–[15]. The nasopharyngitis had, however, recurred within a few weeks. She was then referred to our hospital for further examination and treatment.

At presentation, she had infectious swelling of the adenoid remnant and pus on the lesion (Fig. 1a). Her physical examination was otherwise unremarkable and she had no other medical history including immunodeficiency.

The first pharyngeal swab culture test showed normal flora. Histopathological examination of a nasopharyngeal biopsy sample revealed the possibility of mycobacterial infection based on positive results for acid-fast bacillus and Ziehl-Neelsen staining. The first mycobacterial examination by pharyngeal “swab” mycobacteria culture was positive for smear dyeing of acid-fast bacillus stain, while the culture was negative. The second mycobacterial “tissue” culture of the biopsy specimen revealed the presence of *M. abscessus* complex. For differentiation of the *M. abscessus* complex, we requested polymerase chain reaction (PCR) testing by the National Institute of Infectious Diseases, and identified this species as *M. massiliense* (Fig. 2).

The patient underwent surgery to remove the inflamed adenoid tissue in the nasopharynx and washed the wound with saline. At the same time, she was treated with oral clarithromycin at 400mg/day, intravenous imipenem at 2g/day divided into four doses, and intravenous amikacin at 15mg/kg/day 3 times a week. She received multiple antibacterial therapy for 2 weeks in an inpatient setting. She was then treated with oral clarithromycin at the same dosage, and intravenous amikacin 2 times a week after discharge. The treatment courses are summarized in Fig. 3. She received this combination therapy with clarithromycin and amikacin for an additional four months. The mycobacterial “tissue” culture was negative 2 months after surgery. She is currently being followed up in our hospital, and has had no adverse event and no recurrence during the 8 months since the cessation of treatment.

Discussion And Conclusion

Regarding Mycobacterium massiliense

M. massiliense is a RGM[1]. The representative RGM, *M. abscessus*, was divided into three different species in 2006: *Mycobacterium abscessus ssp. abscessus*, *Mycobacterium abscessus spp. massiliense*, and *Mycobacterium abscessus ssp. bolletii* [2].

Due to the low incidence of mycobacterial infections, the statistical information often is found for the lung region but the incidence of mycobacterial infections in the head and neck region has not been reported. *M. massiliense* has been regarded as a rare species because the rate of *M. massiliense* infections in lung is about 0.6% of all NTM infections according to reports by Kurashima [3][4].

M. massiliense infections develop in the lungs and soft tissues [2], while a few cases have been reported in the head and neck region. As far as we are aware, this patient is the first case of pharyngeal *M. massiliense* infection.

It has been reported that infections caused by the *M. abscessus* complex usually follow accidental trauma or surgery [8]. On the other hand, multiple iatrogenic cases of NTM infection have been described in the past two decades [1], including cases resulting from cardiac surgery, injections, plastic surgery, liposuction, LASIK, dialysis-related outbreaks, long-term central intravenous catheters, middle ear tympanostomy tube replacement, and a variety of miscellaneous surgical procedures [1], [16]–[22]. Most of the health care–associated mycobacterial outbreaks have involved RGM, especially the *M. abscessus* complex and *Mycobacterium fortuitum* [9]. The common factor in health care–associated outbreaks is presumed to be exposure of a susceptible individual to an NTM-infected liquid, usually tap water [1]. Care must, therefore, be taken to prevent NTM infection during various medical procedures.

There are also reports of nosocomial infections in multiple countries such as the United States, Hong Kong and Brazil, etc. [10]–[12]. As it may have been overlooked due to a low detection rate in culture tests, although NTM infection is rare its possible presence must still be considered.

A route of infection

NTMs are widely distributed in the environment [23], [24], and it is considered that NTM infection in humans is caused by bacterium from the environment [4]. As NTMs originally have only weak pathogenicity in humans, it parasitizes and infects humans. Therefore, infections are caused by some trigger such as immunodeficiency [4]. On the other hand, some patients without obvious immunodeficiency develop NTM disease[25].

The *M. abscessus* complex is also frequently detected in water and soil, and, in general, there are many cases of skin and soft tissue infections associated with trauma or surgery [8], [26].

This case was a 45-year-old, previously healthy woman who was not immunodeficient. She should, therefore, be less likely to get infected. However, she had undergone an “operation;” i.e., nasopharyngeal abrasive therapy. The purpose of this therapy is sterilization and disinfection using a coating agent and phlebotomy[13]–[15]. It is said that the greater the degree of disinfection, the higher the amount of bleeding, but the more effective it is. It is possible that the patient, who was not immunodeficient, was

infected by *M. massiliense* because she had been repeatedly scratched around the nasopharynx with a machine using tap water.

Diagnosis

For the diagnosis and differentiation of NTM species, it is necessary to collect samples properly and perform genetic as well as culture tests. There are four important points: “avoiding potential sources of contamination, especially tap water”, “limiting antibiotic use during diagnostic evaluation of NTM diseases”, “collecting specimens as far as possible by needle aspiration or surgical procedures”, and “preserving the specimens, which should not be wrapped in gauze or diluted in liquid material” [27].

In this case, *M. massiliense* could not be identified by swab, and the biopsy could identify *M. abscessus* complex by culture examination. As NTM infections are very rare in the head and neck area, NTM infections are not often considered at the time of regular medical examination. There may be more cases of pharyngeal NTM infections involved with pharyngitis that is resistant to treatment. We recommend that tissue samples are collected actively for the assessment of pharyngeal NTM infections where possible.

Because of differences in antimicrobial susceptibility, determining treatment policy is problematic, and species-level identification of the NTM is becoming increasingly important on a clinical level [27]. The PRA (Polymerase Chain Reaction-restriction enzyme pattern analysis) method identifies many NTM species that are not identifiable by phenotypic or chemotaxonomic techniques alone[1].

Treatment

M. abscessus complex isolates are uniformly resistant to standard anti- tuberculous agents [28]–[30]. According to the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA), there is no reliable antibiotic regimen to produce a cure for the *M. abscessus* complex at present [1]. However, periodic administration of multidrug therapy, including a macrolide and one or more parenteral agents or a combination of parenteral agents over several months, may help control symptoms and the progression of *M. abscessus* complex disease[1]. In addition, it is reported that the only predictably curative therapy for focal *M. abscessus* complex disease is surgical resection combined with multidrug chemotherapy [1]. The treatment is limited to the current treatment policy for lung infections due to the problem with a lack of accumulated evidence.

The ATS/IDSA recommends the following chemotherapy for serious skin, soft tissue, and bone infections caused by the *M. abscessus* complex. Clarithromycin or azithromycin should be combined with parenteral medications (amikacin, cefoxitin, or imipenem)[29], [31]. The macrolides are the only oral agents found to be reliably active *in vitro* against the *M. abscessus* complex [29], [31].

The most active of the parenteral agents is amikacin [32]. Amikacin combined with high-dose cefoxitin is recommended for the initial therapy (minimum, 2 weeks) [28], [29], [33]. Therefore, hospitalization is recommended for a minimum of 2 weeks. However, limited cefoxitin availability may necessitate the

choice of an alternative agent such as imipenem [28], [29], [33]. For serious disease, a minimum of 4 months of therapy is necessary to increase the likelihood of a cure [1].

The clinical identification of *M. massilience* is significant due to the difference in therapeutic response between *M. massiliense* and other species [26]. A relatively large number of reports have described that even if treatment with the same treatment regimen is performed, the improvement rate in clinical findings, including imaging and physical findings, and symptoms are be better in *M. massiliense* than in other species [34]–[36]. The reason for the difference in response is the erm gene, which is a resistance-inducing gene for macrolide [37], [38]. Thus, it may take less time to cure *M. massiliense* infection than other species [35]. Also, such infections may be cured by treatment with oral medication alone, but due to insufficient data, there are many points regarding *M. massiliense* that remain unclear, such as detailed infectious factors, treatment regimen and required treatment period [26].

In this case, treatment was performed according to the ATS/IDMA. As the patient was exhausted by a few months of outpatient treatment, we had a discussion about the treatment policy with a doctor specializing in infectious diseases, including whether or not to switch to oral medicine. However, we decided to continue conventional treatment as far as possible. Eventually, the patient could not tolerate the outpatient treatment, and treatment ended after four months. It is possible to provide treatment that emphasizes the patient's quality of life if a shorter treatment period or an oral treatment regimen that is easy to continue is available that affords a better improvement rate in *M. massiliense* infections. The further accumulation of data is expected in the future.

We report the first case of pharyngeal *Mycobacterium massiliense* infection. There may be more cases of pharyngeal NTM infections among cases of pharyngitis that are resistant to therapy. This patient underwent surgery and the multiple rounds of chemotherapy with oral and intravenous agents for four months, and no recurrence has been observed for the past 8 months. There is currently no definite treatment policy, and only empirical treatment is used; therefore, further reports are needed.

Abbreviations

ATS/IDSA: American Thoracic Society/ Infectious Diseases Society; *M.abscessus*: *Mycobacterium abscessus*; *M. massiliense*: *Mycobacterium abscessus ssp. massiliense*; NTM: non-tubeculous mycobacteria; PCR: polymerase chain reaction; RGM: rapidly growing mycobacteria

Declarations

Ethics approval and consent to participate

Our institution’s Research Ethics Board does not require a review or approval for case reports.

Consent for publication

The patient consented to the publication of this case report and written informed consent was obtained from the patient.

Availability of data and materials

Not applicable.

Competing interests

Not applicable.

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Authors' contributions

Y.O., H.H., M.K., Y.I. and H.I. examined and treated the patient. Y.O. and H.H. wrote the manuscript and made all the figures.

J.T. and R.H. advised on treatment protocol. N.O. supervised the manuscript.

All authors have read and approved the manuscript for publication and the authorship.

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Figures

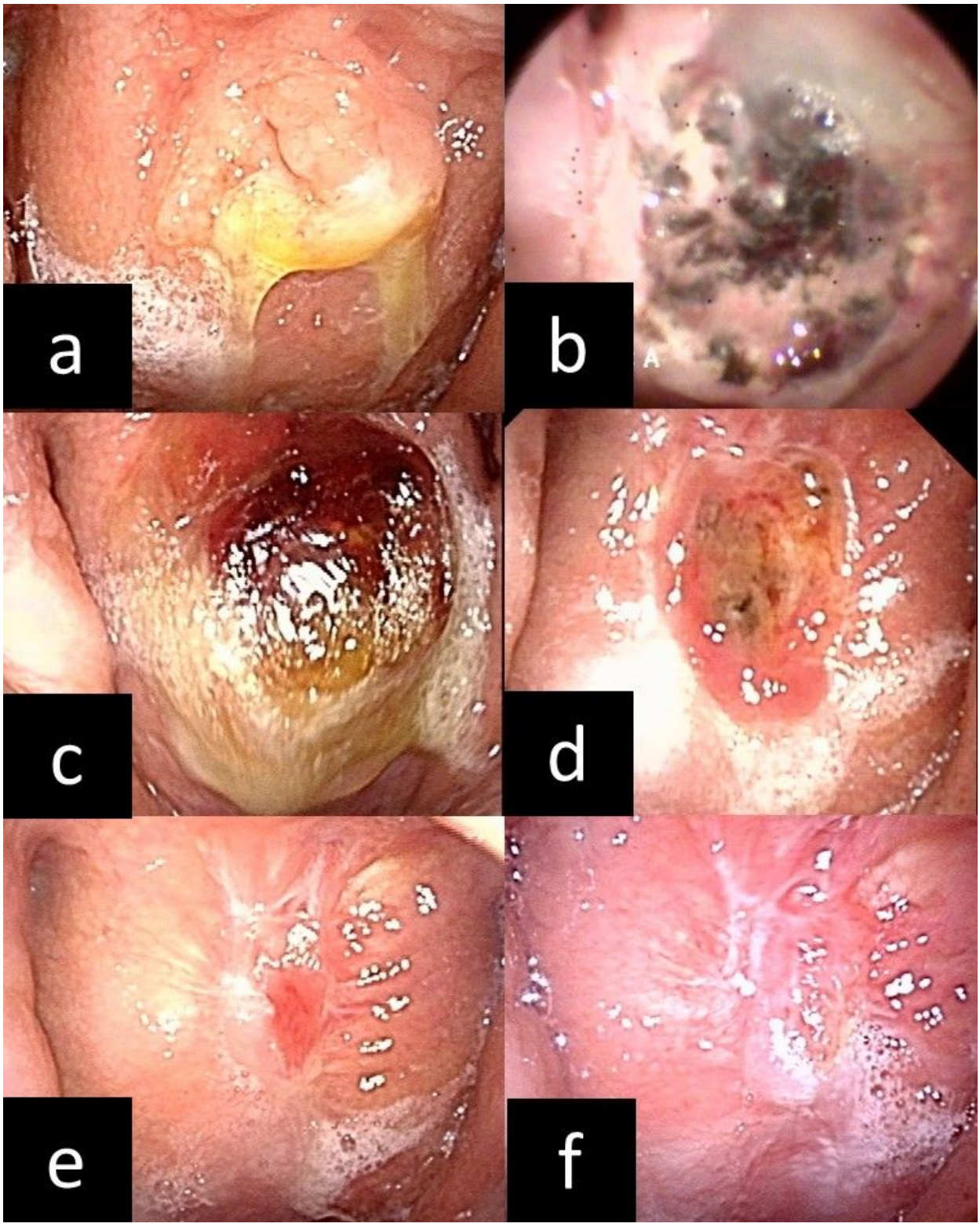

Figure 1

a. Findings of the nasopharynx before treatment. There were a raised nasopharyngeal lesion and a pus on the lesion. b. Findings of the nasopharynx after adenoidectomy. Fur and black scabs for hemostasis had been attached to the wound. c. 2 weeks later after surgery. There was a pus on the lesion. The pus on wound was appropriately removed by dealing and washed. d. 1 month later after surgery. There was

granulation rising in the wound. e. 3 months later after surgery. The granulation remained but the wound was smaller gradually. f. 5 months later after surgery. The wound is epithelialized and scarred.

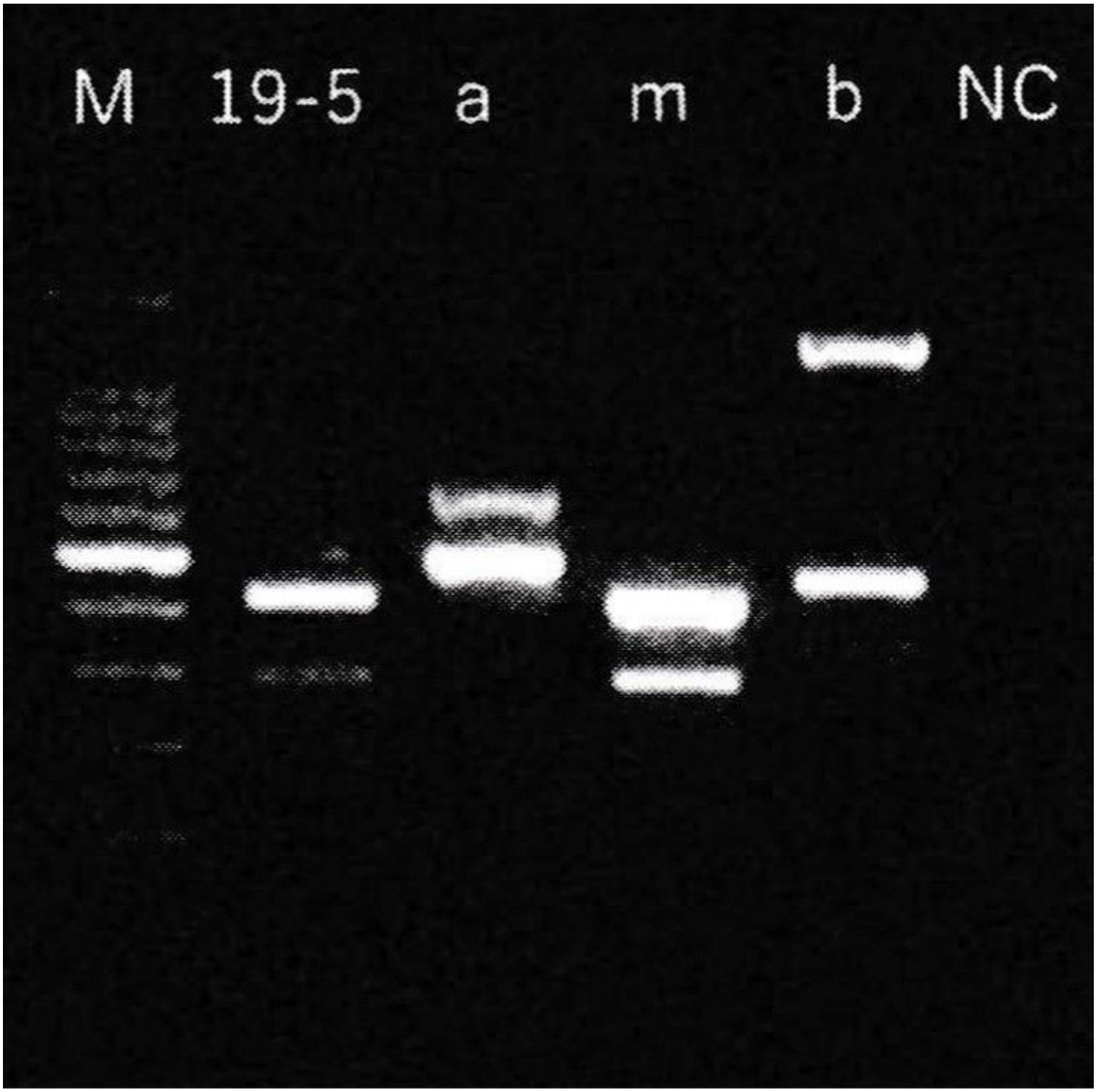

Figure 2

M: Ladder marker, 19-5: Sample of this case, a: Mycobacterium abscessus, m: Mycobacterium massiliense, b: Mycobacterium bolletii, NC: Negative Control The examination showed the disease as mycobacterium massiliense infection.

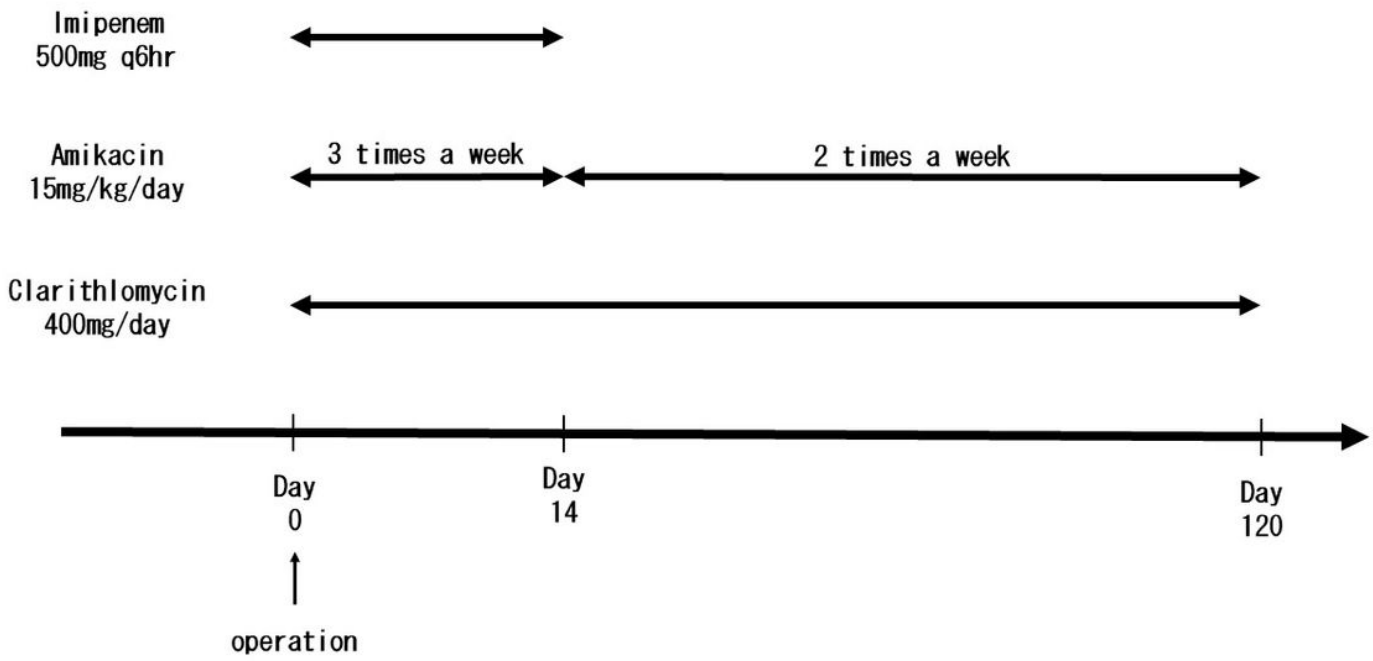

Figure 3

The patient was performed the operation, and at the same time, was treated with clarithromycin, imipenem and amikacin at intervals of 3 times a week. She was received with the multiple antibacterial drugs for 2 weeks. After two weeks of the hospitalization, she was treated with clarithromycin and amikacin at intervals of 2 times a week for 4 months.