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Case Report

# Chronic mycobacterial meningitis due to *Mycobacterium chelonae*: a case report

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SUMMARY

We report a case of chronic meningitis due to *Mycobacterium chelonae*. This organism is a rapidly growing Mycobacterium (RGM) and can be found worldwide in environmental sources such as soil, dust, and water. *M. chelonae* is an uncommon cause of meningitis; the majority of infections caused by this organism are localized cutaneous or soft tissue infections, and rarely lung infections. The organism is indistinguishable phenotypically, so we applied PCR based on the *rpo*B gene sequence followed by restriction fragment length polymorphism (RFLP) for molecular identification. The subsequent sequencing of RFLP products revealed 99.7% similarity with *M. chelonae*.


## 1. Introduction

Non-tuberculous mycobacteria (NTM) are common saprophytes in natural ecosystems, such as water, soil, food, and dust, but in certain circumstances act as opportunistic human pathogens.[1] These bacteria are characterized and classified as either slow or rapid growers. Rapidly growing mycobacteria (RGM), described by growth within 7 days and improved growth at 30 °C rather than 35 °C, are nearly indistinguishable phenotypically.[2] Despite the fact that mycobacteria belonging to the RGM group rarely cause disease, there has been an increase in the number of cases of mycobacterial infections caused by NTM species, especially by RGM, over the past two decades. They can cause localized cutaneous infections following trauma, as well as outbreaks of nosocomial infection and pseudo-outbreaks.[3] Surgical site infections with RGM are most often caused by *Mycobacterium fortuitum, Mycobacterium chelonae*, or *Mycobacterium abscessus*.[4]

Infections caused by *M. chelonae* usually involve the skin, bone, eye, and soft tissue, and rarely the lungs. Although there is a rare report of endocarditis caused by *M. chelonae*,[5] there has, to date, been no report of chronic meningitis due to *M. chelonae*. Patients with chronic meningitis have the indolent onset of symptoms compatible with chronic central nervous system infection for at least 4 weeks and have signs of chronic inflammation in the cerebrospinal fluid (CSF). We report an unusual clinical case of *M. chelonae* infection presenting as chronic meningitis.

## 2. Case report

A 21-year-old woman with clinical signs of fever and loss of consciousness was referred to the Razi Teaching Hospital emergency ward in May 2013. Her predominant symptoms included headache, which had lasted for 6 weeks and had not responded to analgesics, nausea, vomiting, vertigo, photophobia, echophonia, and seizures. Physical examinations including Babinski reflex, increase in deep tendon reflexes, and Cheyne–Stokes respiration were positive. A complete blood count (CBC) and liver function tests (LFT) were normal. Other test results included lactate dehydrogenase (LDH) of 607 IU/l, Brucella IgG 1.7 U/ml, Brucella IgM 1.5 U/ml, and an erythrocyte sedimentation rate (ESR) of 18 mm/h.

With a suspicion of bacterial meningitis, a CSF sample was taken from the patient and sent for diagnostic tests including cell count, biochemical tests, direct smear, culture, and PCR. CSF screening indicated the following results: white blood cell count (WBC) $40 \times 10^6$/ml (70% lymphocytes and 30% polymorphonuclear

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**Table 1**
Primers used for the amplification of 360-bp and 723-bp fragments of *rpo*B and *Myco* genes for the identification and confirmation of *Mycobacterium chelonae* species

| Gene | Primer sequence | Amplicon size (bp) |
|---|---|---|
| *Rpo*B | 5′ TCAAGGAGAAGCGCTACGA 3′<br>5′ GGATGTTGATCAGGGTCTGC 3′ | 360 |
| *Myco* | 5′ GGCAAGGTCACCCCGAAGGG 3′<br>5′ AGCGGCTGCTGGGTGATCATC 3′ | 723 |

leukocytes), glucose 22 mg/dl, protein 4240 mg/dl, LDH 975 IU/l, and adenosine deaminase (ADA) 97 U/l. Direct smear for bacteria and Venereal Disease Research Laboratory (VDRL) and Wright tests were all negative. Based on the CSF screening results, the patient was suspected to have tuberculous meningitis and was admitted to the infectious diseases ward and placed on treatment with ceftriaxone, vancomycin, isoniazid, rifampin, streptomycin, pyrazinamide, vitamin B6, prednisolone, and sodium valproate.

After 2 days, the results of PCR for *Mycobacterium tuberculosis* were negative, but blood and CSF cultures on Lowenstein–Jensen (LJ) medium were positive after 5 days. Thus, a PCR–restriction fragment length polymorphism (RFLP) analysis based on a 360-bp fragment of the *rpo*B gene was used to test for the probable presence of NTM species; the set of primers used is presented in Table 1.[6] Results of the PCR amplification for the *rpo*B gene were positive. The PCR product was digested with *Msp*I restriction enzyme and the digested product was analyzed by electrophoresis on a 3.5% agarose gel. The RFLP pattern on gel electrophoresis was 40, 50, 80, 95, and 105 bp, exactly matching the known restriction fragment pattern of the reference strain of *M. chelonae* (Figure 1).[6] Confirmation of *M. chelonae* was done by DNA sequencing analysis of a 723-bp fragment of the *Myco* gene, using the set of primers listed in Table 1. DNA sequencing revealed 99.7% similarity with *M. chelonae* for the *rpo*B gene (GenBank accession number **35752**).

Finally, with the diagnosis of chronic meningitis caused by *M. chelonae*, the patient's treatment was switched to doxycycline and clarithromycin. Seventy-two hours after treatment with these drugs, the patient's fever decreased, her orientation was improved, and the nausea, vomiting, vertigo, and headache slowly improved. After 3 weeks of treatment, the patient's physical condition went into remission and she was discharged from the hospital, with treatment to continue for 18–24 months.

## 3. Discussion

The identification of NTM species in general and RGM species specifically in clinical samples is of importance, because the therapeutic procedures required for these mycobacteria differ significantly depending on the species present. There are several reports on the isolation of *M. chelonae* from patients with clinical complications. In the immunocompromised patient, disseminated *M. chelonae* infection can occur.[7,8] However, Halpern et al. reported a case of disseminated cutaneous *M. chelonae* infection in an immunocompetent patient, showing the potential of the organism to cause infection in a wide range of hosts.[9]

Clinical laboratories have commonly used biochemical tests as phenotypic tests to differentiate RGM species. However, these methods are time-consuming and identification of the organism to the species level is not always possible.[3] In many studies, molecular techniques including analyses of the 32-kDa protein-encoding gene, the 16S rRNA gene, *dna*J, *rec*A, *sod*, and the internal transcribed spacer 16S–23S rRNA (ITS), have been proposed for the molecular identification of clinical isolates of RGM.[10]

While soft tissue disease is the most important clinical manifestation of this organism,[3] to date there has been no report of chronic meningitis due to *M. chelonae* in the world. Symptoms of chronic meningitis can wax and wane over weeks and months. Early symptoms of chronic meningitis include headache, nausea, and decreased memory and comprehension. When hydrocephalus complicates indolent meningitis, dementia can be a prominent finding. Later symptoms of chronic meningitis include double vision, decreased vision, or other cranial nerve palsies, unsteady gait, emesis, and confusion.[10]

We have reported a case of infection caused by *M. chelonae* in a patient with a diagnosis of mycobacterial meningitis who received primary treatment with anti-tuberculosis drugs. The later application of PCR-RFLP revealed *M. chelonae* to be the unusual cause of this case of meningitis. To our knowledge, this is the first report of mycobacterial meningitis due to *M. chelonae*, and our study provides further evidence of the unusual role of this microorganism in clinical cases. *M. chelonae* is resistant to anti-tuberculosis agents, but clarithromycin and the combination of doxycycline and amikacin have been shown to be effective against *M. chelonae* infections.

In conclusion, *M. chelonae* should be considered as a possible etiological pathogen that can be the cause of meningitis. Rapid molecular tests should be considered for the detection of the organism so that an appropriate treatment strategy can be applied.

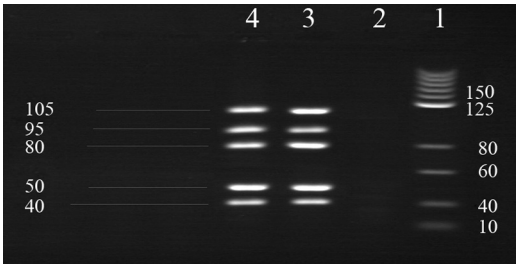


**Figure 1.** Agarose gel electrophoresis of PCR-RFLP analysis products based on the *rpo*B gene, digested with *Msp*I for the identification of *Mycobacterium chelonae*. Lane 1, PBR322 digestion with *Msp*I as DNA size marker; lane 2, negative control; lane 3, *Mycobacterium chelonae subsp. chelonae* ATCC reference strain; lane 4, patient sample.

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*Conflict of interest:* There are no conflicts of interest to declare.

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