

Case Report

Brain abscess caused by *Nocardia asiatica*

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Abstract

Background: *Nocardia* infection of the central nervous system leading to brain abscess is a rare condition but has a high mortality rate. Among the species of *Nocardia*, only three cases of brain abscess due to *Nocardia asiatica* infection have been reported.

Case Description: A 65-year-old man with a history of autoimmune hemolytic anemia treated with prednisolone presented to our hospital because of occipital headache. Brain magnetic resonance imaging showed bilateral occipital lesions. The patient underwent craniotomy and resection of the left occipital lobe lesion. *N. asiatica* was identified by 16S rRNA sequencing of the resected specimen. Treatment with trimethoprim/sulfamethoxazole led to a complete resolution of the brain lesion.

Conclusion: Because of the different antimicrobial sensitivity patterns among *Nocardia* species, both appropriate subtyping and susceptibility testing of uncommon species such as *N. asiatica* are required for the successful treatment of nocardial infections.

Key Words: Brain abscess, *Nocardia asiatica*, 16S rRNA

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Quick Response Code:**INTRODUCTION**

Nocardia infection of the central nervous system (CNS) leading to brain abscess is rare but has a high mortality rate.^[1] The recent development of 16S ribosomal RNA (rRNA) sequencing allowed the identification of *Nocardia asiatica* in 2004.^[7] Since then, several cases of *N. asiatica* infections have been reported; however, only three cases of brain abscess have been reported.^[5,15,18] Here, we describe a case of brain abscess due to *N. asiatica* infection in a patient on steroid therapy for autoimmune hemolytic anemia. In addition, we provide a review of the literature on similar cases.

CASE REPORT

A 65-year-old man with a history of autoimmune hemolytic anemia treated with prednisolone (10 mg/day for years) presented to our hospital because of occipital

headache of 1-week duration. There was no fever and his neurological examination findings were normal. The results of the laboratory tests performed on admission were normal. Brain magnetic resonance imaging (MRI) showed bilateral occipital lesions. The central part of the mass was hypointense on T1-weighted imaging (T1WI) and hyperintense on T2-weighted imaging (T2WI) [Figure 1a and b]. The peripheral rim was isointense on T1WI and hypointense on T2WI [Figure 1a and b].

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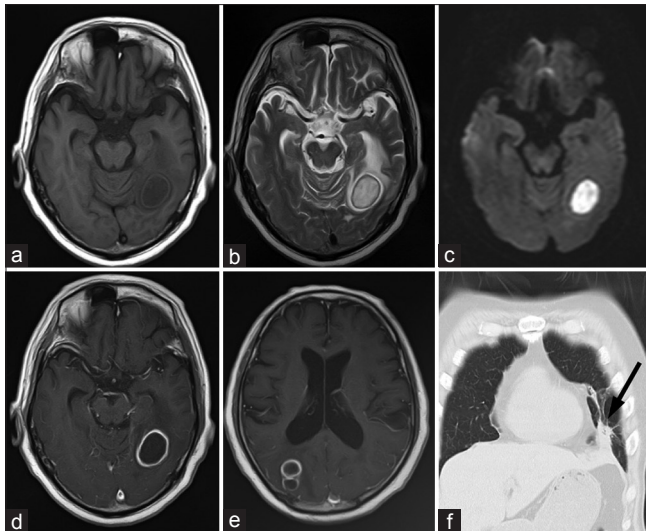


Figure 1: Preoperative images. (a) Hypointensity of the lesion and the isointensity of its peripheral rim are seen on axial T1-weighted imaging (T1WI). **(b)** Hyperintensity of the lesion and the hypointensity of its peripheral rim are seen on axial T2-weighted imaging (T2WI). **(c)** Hyperintense signals obtained using diffusion-weighted imaging. **(d and e)** Bilateral ring-enhanced lesions are seen on axial T1WI following the administration of Gd-DTPA as contrast agent. **(f)** A small nodule in the lingular segment of the left lung (arrow) is revealed by coronal thoracic computed tomography

Diffusion-weighted imaging demonstrated a hyperintense region in the abscess cavity [Figure 1c]. The lesion was ring-enhanced after the administration of the contrast agent gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) [Figure 1d and e]. Whole-body computed tomography (CT) revealed small nodules in the lingular segment of the left lung [Figure 1f]. The patient underwent left occipital craniotomy and resection of the left occipital lobe lesion. Under the guidance of intraoperative ultrasound, a pseudoencapsulated, firm mass was identified and yellowish-white pus was aspirated. The capsule, which was tightly adhered to the cerebellar tentorium, was also resected completely. The patient's postoperative course was uneventful and he was further treated with the broad-spectrum antibiotic ceftriaxone (2 g/day). Postoperative MRI confirmed total resection of the left occipital lobe lesion. Hematoxylin and eosin staining of the resected specimen showed numerous inflammatory cells around the abscess cavity, with a surrounding rim of fibrosis. The diagnosis was, therefore, brain abscess [Figure 2a]. Culture of the capsule yielded colony growth on blood agar and Ogawa media. Smears from the capsule culture revealed gram-positive branching filaments, raising suspicion that the infecting bacterium was a *Nocardia* species [Figure 2b]. Antibiotic susceptibility testing showed the sensitivity of the cultured bacterium to trimethoprim/sulfamethoxazole and minocycline. The patient was accordingly shifted to oral trimethoprim/sulfamethoxazole (640 mg/3200 mg) on postoperative day 16. Sequencing of the 16S rRNA isolated from the

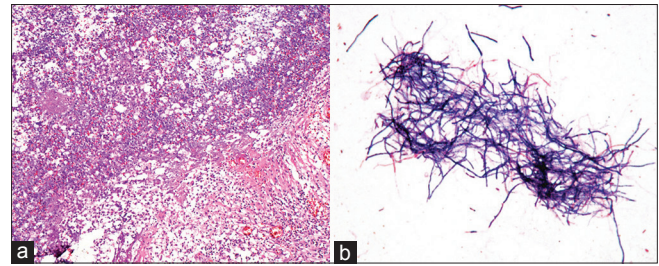


Figure 2: (a) Photomicrograph of the hematoxylin and eosin stained resected specimen shows numerous inflammatory cells around the abscess cavity, with a surrounding rim of fibrosis. ($\times 100$). **(b)** Smears from the capsule culture yielded gram-positive branching filaments, raising suspicion of a *Nocardia* species as the infectious agent

resected specimen led to the identification of *N. asiatica*. A brain MRI and thoracic CT performed 5 months after the operation revealed complete resolution of both the brain abscess and the lung lesion.

DISCUSSION

Nocardia species are gram-positive, partially acid-fast, and strictly aerobic branching filamentous bacteria.^[4] *Nocardia* infections occur more frequently in immunocompromised individuals, including those with acquired immune deficiency syndrome, lymphoma, bone marrow transplant, low CD4 T-lymphocytes, and immunosuppressive drug therapy, such as with tumor necrosis factor inhibitors or glucocorticoid steroids.^[1,2,9,10] Because of their branching filamentous forms resembling fungal hyphae, *Nocardia* were previously misclassified as fungi.^[9] Because growth on specific media for mycobacteria, acid-fast bacilli, and colony morphology sometimes may result in the confusion of *Nocardia* and *Mycobacterium*,^[13] 16S rRNA sequencing has been used to differentiate these bacteria.^[3] Antimicrobial sensitivity patterns and disease phenotypes also differ among the various *Nocardia* species.^[4] For example, *N. farcinica* is more resistant to antimicrobial agents and has a higher risk of dissemination and CNS nocardiosis.^[1,19] For these reasons, 16S rRNA sequencing combined with antimicrobial susceptibility testing has been used to identify *Nocardia* subtypes, which is necessary for effective treatment.

CNS nocardiosis most frequently manifests as brain abscesses, however, in rare cases as meningitis or spinal cord infections.^[2] *Nocardia* brain abscess accounts for only 2% of all brain abscesses.^[2,11] Their clinical course is typically gradual and insidious over months, or even years, making early diagnosis and identification difficult.^[9] The lesions are usually supratentorial (57%) rather than infratentorial.^[11] Multiple abscesses are reported in 38% of the patients with CNS nocardiosis.^[11] The coalescence of multiple daughter abscesses results in the formation of multiloculated abscesses.^[14] *Nocardia* brain abscess carries mortality rates of 55% and 20% in immunocompromised

Table 1: Reported cases of brain abscess due to *Nocardia asiatica*

Case no.	Author (year)	Patient age, years	Sex	Brain abscess	Other site	Underlying disease	Surgery for brain abscess	Antibiotics administered	Outcome
1	Wakui <i>et al.</i> (2008) ^[18]	73	M	Single	No	No	Aspiration→Recurrence after 2 days→Excision	MINO + TMP/SMX	Alive
2	Ryu <i>et al.</i> (2009) ^[15]	44	F	NR	No	Guillain-Barré syndrome	Excision	IPM/CS + TMP/SMX→Changed to MINO because of DIP	Alive
3	El-Herte <i>et al.</i> (2012) ^[5]	49	M	Multiple	Anterior mediastinum	Myasthenia gravis, Malignant thymoma	No	TMP/SMX, AMK, IMP	Alive
4	Present case	65	M	Multiple	Lung	Autoimmune hemolytic anemia	Excision	CTRX→TMP/SMX	Alive

M: male, F: female, TMP/SMX: trimethoprim/sulfamethoxazole, IMP: imipenem, IPM/CS: imipenem/cilastatin, AMK: amikacin, MINO: minocycline, CTRX: ceftriaxone, DIP: drug-induced pneumonia, NR: not reported

and immunocompetent patients, respectively. These rates are higher than those associated with other bacterial brain abscesses (10%).^[11] In case of multiple abscesses, the mortality rate rises to 66%.^[11]

The standard medical treatment for *Nocardia* brain abscesses is trimethoprim/sulfamethoxazole.^[11] Aspiration or surgical excision may be indicated for abscesses >2.5 cm. Craniotomy and excision of the entire abscess and capsule are more effective than aspiration and drainage, particularly when the abscess is resistant to antimicrobial agents.^[11]

Diagnosis is mainly based on bacteriological cultures; 82% of patients are diagnosed with cultures of aspirates from the site of infection, 31% based on the biopsy specimen, and 8.3% following cerebrospinal fluid (CSF) culture.^[1] However, the slow growth of *Nocardia* species and contamination of the cultures by other, faster-growing bacteria frequently lead to a delayed diagnosis.^[2,10] Moreover, the demonstration of *Nocardia* in a CSF culture is usually difficult because empirical therapy is typically initiated before the CSF is collected. Lumbar puncture is contraindicated in patients with brain abscess because of the risk of brain herniation. These features of *Nocardia* infection support the utility of 16S rRNA sequencing for the rapid identification of *Nocardia* species.

Sequencing of the 16S rRNA gene of *Nocardia* has become a valuable tool for accurate species-level identification. In fact, application of this method has resulted in the identification of new species of *Nocardia*.^[4] Of these, *N. asiatica* was first described in 2004, following its isolation from patients in Japan and Thailand.^[7] Since then, *N. asiatica* has been identified in patients with pulmonary infections, skin infections, and brain abscess; these cases have been documented both inside and outside of Asia.^[5,6,8,12,15-18] However, to date, only four cases of *N. asiatica* brain abscess, including the present case, have been reported in the literature

[Table 1].^[5,15,18] In three of these patients, including our patient, the capsule was excised. The long-term survival of all patients was achieved by antibiotic treatment, mainly trimethoprim/sulfamethoxazole.

In summary, the appropriate subtyping and susceptibility determination of uncommon species of *Nocardia*, such as *N. asiatica*, are necessary for the treatment of nocardial infections.

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Conflicts of interest

There are no conflicts of interest.

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