

Multiple Intracranial *Nocardia brevicatena* Abscesses in a Patient with a Previous History of Tuberculosis: A Case Report

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Background: *Nocardia brevicatena* (*N. brevicatena*) is an uncommon cause of brain infections, frequently mistaken for intracranial tuberculosis, especially in patients with a tuberculosis (TB) history, leading to improper treatment. This case report outlines the symptoms, diagnosis, and treatment of a patient with multiple brain abscesses from *N. brevicatena* after laryngeal TB, highlighting the importance of next-generation sequencing (NGS) for accurate diagnosis.

Case Presentation: This report details a 55-year-old man with a history of TB. Symptoms included dizziness, headache, and unsteady gait, with MRI revealing brain nodules and edema. He initially received anti-TB treatment, but it was ineffective. NGS identified *N. brevicatena*, and TB tests were negative. He was treated with anti-Nocardia drugs (compound sulfamethoxazole tablets (0.96 g, orally twice daily), amikacin sulfate injection (0.6 g, once daily), and imipenem-cilastatin sodium (0.5 g, every 6 hours)), leading to symptom improvement and MRI changes. Symptoms worsened when treatment was paused but resolved within a week of resuming therapy, following 45 days of treatment, the patient fulfilled the discharge criteria. After seven months, the patient fully recovered with normal MRI results.

Conclusion: Intracranial *N. brevicatena* infections are frequently misdiagnosed as TB in patients with a TB history. NGS of blood or cerebrospinal fluid accurately detects pathogens, and TB Xpert helps rule out TB. Both are crucial for targeted treatment and better patient outcomes.

Keywords: case report, Nocardia, intracranial infection

Introduction

Nocardia is a gram-positive opportunistic actinomycete. Nocardial infections of the central nervous system are clinically rare, and the multifocal intracranial subtype is even less frequently encountered, with cases predominantly reported in immunocompromised individuals.¹ Insidious onset and atypical clinical manifestations are observed in this disease, and imaging findings are easily misdiagnosed as tuberculosis, fungal abscesses or intracranial tumors, leading to a low early diagnostic rate.² Rapid disease progression, high mortality, prolonged treatment duration and frequent recurrence are documented, which bring considerable challenges to clinical diagnosis and management. In the present case report, one patient with multifocal intracranial nocardiosis is described. The clinical features, diagnostic procedures and therapeutic regimens are analyzed, so as to provide a reference for the clinical management of similar cases.

Case Presentation

A 55-year-old male patient with a history of pulmonary tuberculosis (TB) presented with persistent dizziness, paroxysmal severe throbbing headaches primarily localized to the vertex, and an unsteady gait. On admission, the patient's axillary body temperature was 36.5 °C, and the temperature remained below 37 °C throughout the entire initial hospital stay. A chest computed tomography (CT) scan revealed interstitial changes in both lungs, as well as multiple infections and partial consolidation of lung tissue. Pathological examination confirmed laryngeal TB. An enhanced magnetic resonance imaging (MRI) scan of the head showed multiple nodules in the bilateral parieto-occipital lobes, basal ganglia, left temporal lobe, and pons (Figure 1). These nodules were accompanied by significant cerebral edema. Small, spherical, peripheral, enhancing nodules were observed with extensive perilesional edema (Figure 1A–C). No thin meningeal enhancement was detected. No *Cryptococcus* was detected in the cerebrospinal fluid (CSF) using three staining methods. Aerobic bacterial culture of CSF performed for 10 consecutive days yielded negative results, with no bacterial or fungal growth observed.

Initially, the presence of positive laryngeal TB pathology suggested the possibility of multiple intracranial TB infections. However, TB treatment was ineffective. Subsequent tests were conducted for parasites and fungi. Next-generation sequencing (NGS) of blood and cerebrospinal fluid samples identified *Nocardia brevicatena* (*N. brevicatena*) (Figure 2A and B), and the TB Xpert results were negative. This confirmed the presence of multiple intracranial *N. brevicatena* infections. Meanwhile, we implemented a multidisciplinary team (MDT) consultation approach involving departments including Neurology, Respiratory Medicine, and Clinical Pharmacy. Through this MDT collaboration, we administered symptomatic and supportive treatments

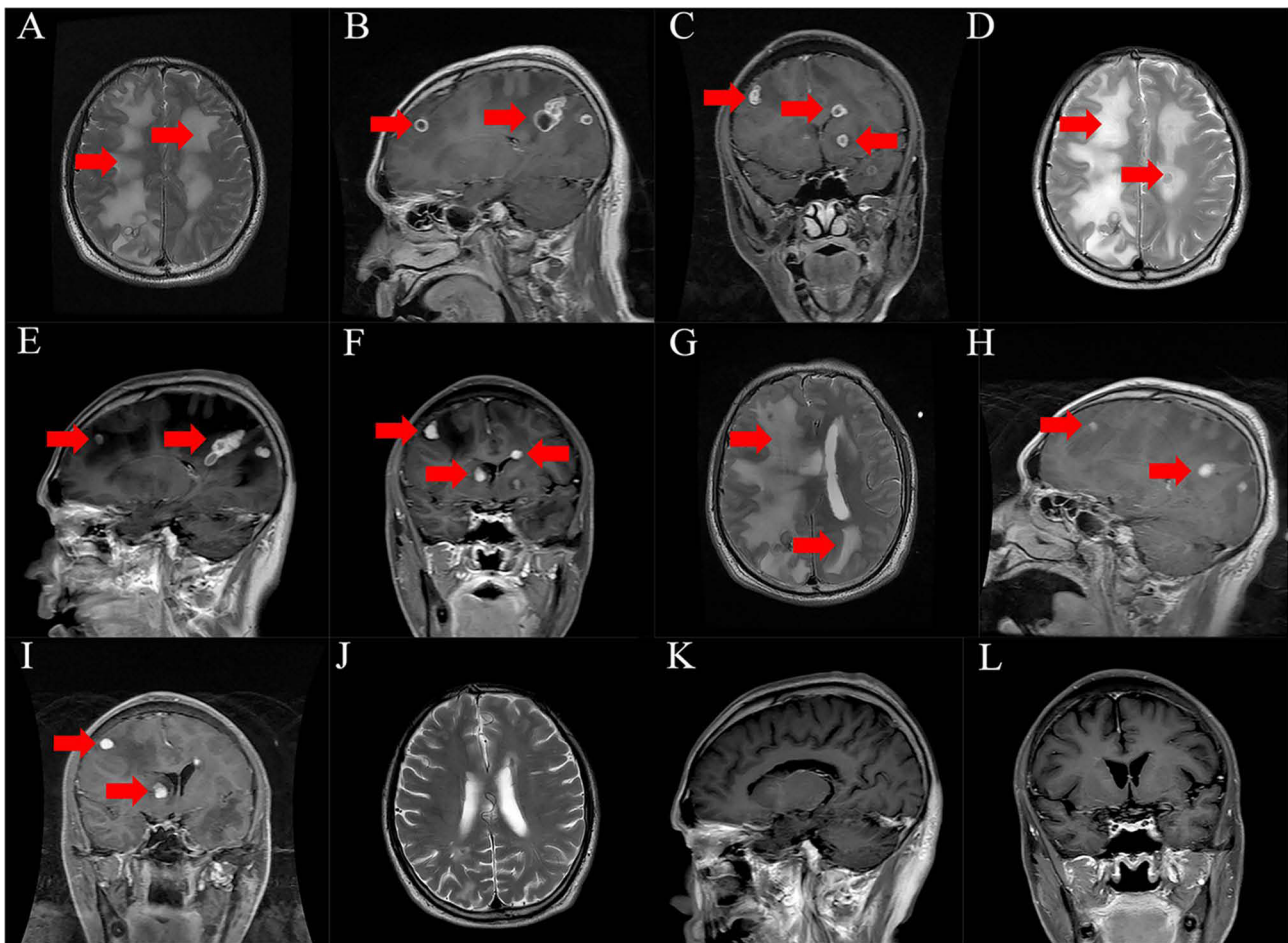


Figure 1 T1 FLAIR sequence shows a large edematous lesion (A). Images (B and C) (both T1 FLAIR) show multiple abscess lesions. Imaging findings of recurrence after the patient discontinued medication on his own (Images (D–F)). Following the reinstitution of anti-*Nocardia* therapy, the patient's symptoms improved significantly, (G–I). On T2 FLAIR sequence (J), the edema is significantly reduced compared to the previous image (A–I). On T1 FLAIR sequences (K and L), the multiple intracranial abscess lesions have disappeared.

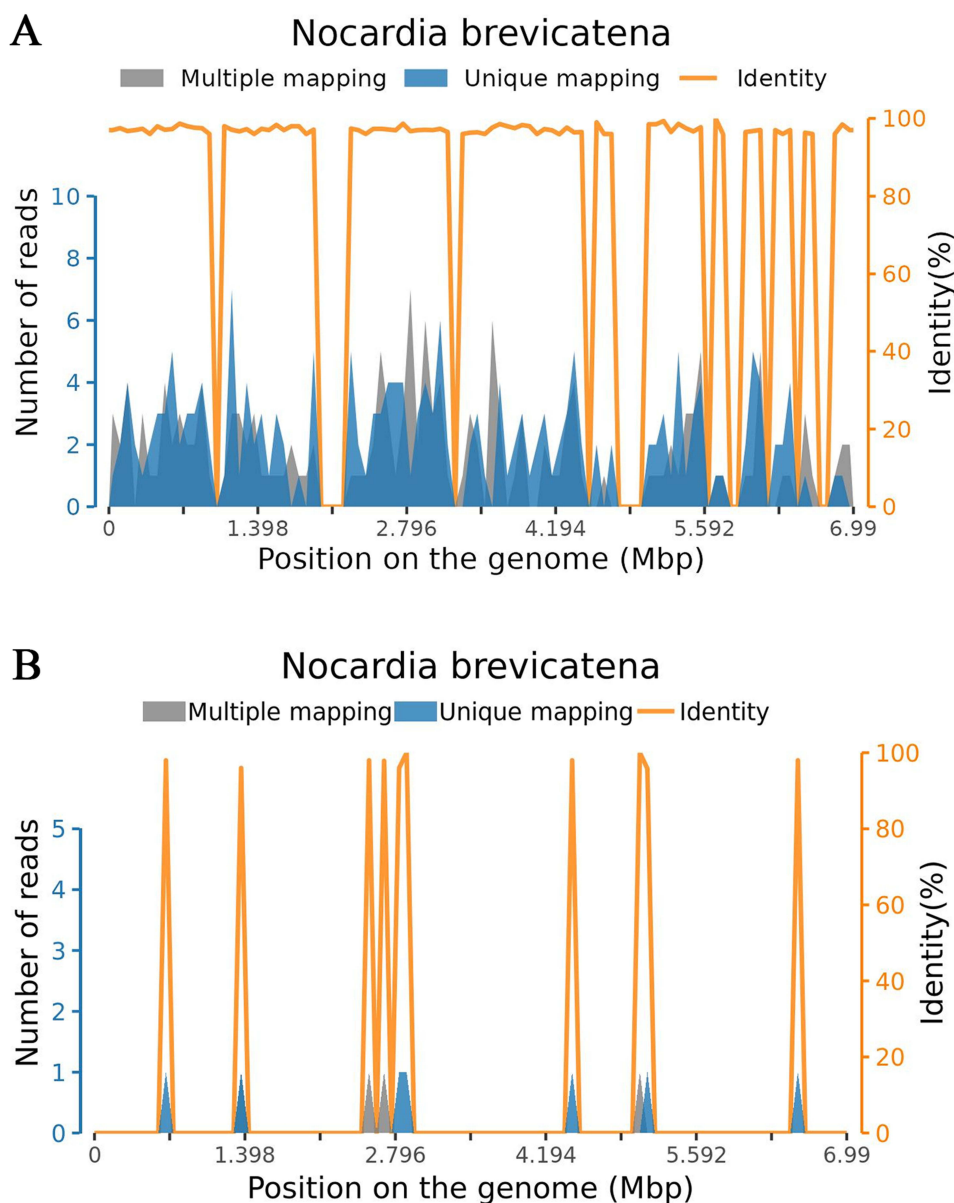


Figure 2 Sequence alignment and identity profile of *Nocardia brevicatena* detected by NGS. Multiple Mapping: reads aligning to ≥ 2 microbial species, representing conserved genomic regions (not counted as species-specific sequences); Unique Mapping: reads uniquely aligned to *N. brevicatena*, the core indicator of pathogen presence; Identity: percentage of base-pair matches to the reference genome, approaching 100% in mapped regions, confirming alignment accuracy. **(A)** Cerebrospinal fluid (CSF) sample. **(B)** Peripheral blood sample. The markedly higher number of species-specific sequences in CSF suggests a greater likelihood of primary intracranial nocardiosis.

to the patient, encompassing dehydration therapy for intracranial hypertension reduction, neuroprotective therapy, nutritional support, targeted analgesia, and maintenance of electrolyte balance. Concurrently, the triple antimicrobial therapy regimen was ultimately determined, consisting of compound sulfamethoxazole tablets (0.96 g, orally twice daily), amikacin sulfate injection (0.6 g, once daily), and imipenem-cilastatin sodium (0.5 g, every 6 hours). Following one week of treatment, the patient's condition was significantly improved. Upon discharge, the patient independently discontinued the prescribed medication and opted to resume anti-TB treatment. Two months later, the patient's condition critically deteriorated, characterized by drowsiness, necessitating readmission. On readmission, the patient's body temperature was 37.2 °C. During the second hospital stay, body temperature exhibited a slightly elevated trend compared with the first admission, with a peak temperature of 38.9 °C documented on the night of September 3, 2024. Concurrently, the patient's mean heart rate was significantly higher than that recorded at the initial admission, manifesting as a clinical pattern of overall elevated heart

rate with relatively low body temperature—defined as temperature–heart rate dissociation, which suggests the possibility of occult shock. An enhanced MRI of the brain revealed multiple nodules located in the bilateral parieto-occipital lobes, basal ganglia, left temporal lobe, and brainstem, accompanied by significant cerebral edema. Compared to the previous imaging, the walls of certain ring-enhanced lesions were thicker, and some lesions had grown larger with an expanded area of surrounding edema (Figure 1D–F). After re-initiating anti-*Nocardia* therapy—, these symptoms began to subside approximately one week later (Figure 1G–I), and after 45 days of treatment, the patient had achieved sufficient clinical recovery to meet the discharge criteria. Over the subsequent seven-month follow-up, the patient’s clinical symptoms resolved completely, and MRI scans of the brain returned to normal (Figure 1J–L).

Discussion and Conclusions

Nocardia spp. are opportunistic pathogens mainly causing lung infections,³ but they can also affect the skin, soft tissues, and CNS, with CNS nocardiosis having a 22.8% mortality rate.^{4–6} *Nocardia farcinica* is the most common species, while *Nocardia brevicatena* is rare,^{3,5,7} with few cases reported.⁸ *Nocardia brevicatena*, part of the *N. brevicatena*/*N. paucivorans* complex (including type II drug susceptibility pattern), as one of the six major pathogenic complexes within the genus *Nocardia*, cannot break down casein, xanthine, tyrosine, or hypoxanthine and only uses trehalose as a carbon source. It is distinguished from *N. paucivorans* by its ability to utilize isoamyl alcohol and 1,2-propanediol, as confirmed by DNA–DNA hybridization.^{9–12} The susceptibility pattern R(resistance)S(susceptibility)SR to gentamicin, tobramycin, amikacin, and erythromycin further differentiates *N. brevicatena* from other *Nocardia* species.¹¹

This document presents the first case of multiple intracranial *N. brevicatena* infection alongside *Mycobacterium tuberculosis* coinfection, offering potential insights for improving diagnosis and treatment of *N. brevicatena* infections.

A definitive diagnosis was crucial for this case. Considering the patient’s history of laryngeal and pulmonary tuberculosis, cerebral tuberculoma was a key differential diagnosis. Active tuberculosis was ruled out due to negative acid-fast bacilli results in CSF and sputum cultures. Brain abscess was excluded through bacterial cultures of CSF and blood. Cranial MRI and parasitic antibody tests helped rule out parasitic intracranial infections. Intracranial tumors were preliminarily excluded using tumor marker detection.

The presence of interstitial pneumonia and pulmonary infection, shown as patchy and honeycomb-like opacities in both lungs, required linking to the patient’s long-term dust exposure and pulmonary alveolar proteinosis. Given the patient’s history of tuberculosis, a multifactorial cause is possible. No immunodeficiency disorders or immunosuppressive treatments were found, suggesting that impaired immunity from previous lung injury might be a mechanism for the co-infection.

As an emerging sequencing modality, NGS presents irreplaceable value in the diagnosis of infectious diseases, particularly for the identification of rare, novel, or non-culturable pathogens, thereby providing a more comprehensive and innovative perspective on microbial communities than conventional culture methods.¹³ Compared with conventional culture approaches, NGS exhibits distinct advantages for the diagnosis of nocardiosis in terms of turnaround time, diagnostic accuracy, and the detection of mixed infections.^{14–18} Despite its rapid, broad, efficient, and robust detection capabilities,^{19–23} the limitations of NGS warrant considerable attention. These limitations include, but are not limited to, potential nucleic acid contamination, sophisticated data interpretation workflows, and challenges in the identification of antimicrobial resistance genes; furthermore, the longstanding conundrum of distinguishing colonizing agents from pathogenic pathogens remains unresolved.^{13,24,25}

N. brevicatena is an uncommon pathogen that causes brain infections. Early diagnosis is challenging in patients with a history of TB and *N. brevicatena* brain infection because detecting the pathogen in brain infections is difficult. This can potentially lead to a misdiagnosis of brain TB. NGS of blood and cerebrospinal fluid testing can identify the pathogen, and TB Xpert can help rule out TB infection, aiding in the diagnosis and treatment of *N. brevicatena* infections.²⁶

Data Sharing Statement

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Ethics Approval and Consent to Participate

The participants provided their written informed consent to participate in this study. Meanwhile, this study has been reviewed and approved by the Medical Ethics Committee of the Second Affiliated Hospital of Army Medical University,

PLA. The patient provided consent for the publication of the case details. This case report was conducted in accordance with the institutional policy of Xinqiao Hospital, Army Medical University, regarding the publication of anonymized case reports. Formal ethics committee approval was not required as per this policy, given that the report involves no experimental intervention, and all patient data have been fully anonymized.

Consent for Publication

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author Contributions

Zhaoyang Li, Yuheng Zhang, Xiaoming Zhang, Hongchun Li, Xue Gong, Qian Zhang, Jing Xu, Xiaofeng Cheng, and Jinghuan Wang are co-first authors. Tao Wang and Qiuxin Zhang are co-second authors. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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