

Infection

Solitary *Nocardia farcinica* brain abscess in an immunocompetent adult mimicking metastatic brain tumor: rapid diagnosis by pyrosequencing and successful treatment

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Abstract

Background: *Nocardia* brain abscess carries a higher morbidity and mortality rate than other bacterial cerebral abscesses, with reported mortality rates of 55% and 20% in immunocompromised and immunocompetent patients, respectively. To prevent a delay in diagnosis and treatment, an aggressive therapeutic approach is required. In the present study, a rapid and accurate molecular diagnostic approach using pyrosequencing (PS), a semiautomated molecular genotyping method of nucleotide sequencing-by-synthesis, was performed.

Case description: A 53-year-old man developed word-finding difficulties, followed by confusion and disorientation. On examination, the patient had a mixed aphasia; the receptive component was greater than the expressive component. The remainder of his neurologic examination findings was normal. Gadolinium-enhanced magnetic resonance imaging of the brain revealed a 2.0-cm multilobular, partially cystic, peripheral-enhancing mass in the posterior left temporal-parietal region with significant vasogenic edema and localized mass effect. A detailed laboratory investigation revealed that this patient was immunocompetent. An awake left posterior temporal-parietal craniotomy with cortical motor and speech mapping, using frameless stereotactic image guidance and intraoperative real-time ultrasound, was performed. Frozen section was consistent with cerebral abscess and methenamine silver staining revealed many beaded, thin-branching gram-positive bacilli. Colonies suspicious for *Nocardia* sp were seen within 2 days, and PCR followed by pyrosequencing (PS) identified *Nocardia farcinica*.

Conclusions: We report a nocardial cerebral abscess mimicking a metastatic brain tumor, and we demonstrate that PS technology can be used for the accurate and rapid identification of *N. farcinica* isolated from a brain abscess—facilitating a rapid diagnosis and successful, durable treatment.

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Keywords:

Cerebral abscess; Awake craniotomy; *Nocardia farcinica*; Polymerase chain reaction (PCR); Pyrosequencing (PS); Brain tumor

Abbreviations: AFB, acid-fast bacilli; VATS, video-assisted thoracoscopic surgery

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1. Introduction

Nocardia sp are branching, beaded, filamentous, gram-positive bacteria that characteristically exhibit weak acid-fast staining [2]. In the United States, there is an estimated incidence of nocardial cerebral abscess of approximately 0.4 cases per 100 000 population, with an estimated 500 to 1000 symptomatic cases per year [3]. *Nocardia asteroides*

complex is the most frequent cause of nocardial disease in man, accounting for greater than 80% of invasive infections resulting in systemic and central nervous system disease [2]. There are currently greater than 30 species of *Nocardia* of clinical significance; the most common isolates are *N nova* complex, *N abscessus*, *N transvalensis*, *N farcinica*, *N cyriaci-georgica*, and *N brasiliensis* [4]. Despite improvements in imaging techniques and surgical therapy, nocardial brain abscesses remain difficult to cure: the mortality rate of patients with nocardial infection is more than 3 times higher than that of patients with other bacterial brain abscesses [13]. In large part, this is due to difficulties in making a diagnosis in a timely fashion so as to institute appropriate antimicrobial therapy [13].

Microbial identification strategies have traditionally used biochemical differentiation after standard Gram stain and culture techniques. In the past decade, molecular genotyping methods such as polymerase chain reaction (PCR)–restriction fragment length polymorphism analysis and Sanger dideoxy nucleotide sequencing have come into common use, although these can be time-consuming and resource-intensive [1]. Pyrosequencing (PS) is a new semiautomated molecular genotyping method of nucleic acid sequencing-by-synthesis [20,21]. Pyrosequencing detects pyrophosphate released during DNA synthesis using PCR primers specific to the 16S rDNA of a given microorganism [5,9,21–23]. A sequencing primer is hybridized to a single-stranded, PCR-amplified DNA template, and incubated with the enzymes DNA polymerase, adenosine triphosphate sulfurylase, luciferase, and apyrase, and the substrates adenosine 5'-phosphosulfate and luciferin [21]. By sequencing well-characterized, specific, hypervariable regions of genes such as 16S rRNA, PS provides clinically useful and unambiguous data for microbial identification [9,23]. Pyrosequencing is a simple, rapid, reliable, and efficient means for discriminating microbial species, types, and strains and detecting genetic mutations that confer resistance to antibiotics. In the present study, we report a nocardial cerebral abscess mimicking a metastatic brain tumor and demonstrate that PS can be used for the rapid identification of *Nocardia* sp cerebral abscess, which facilitated rapid, successful, and durable treatment.

2. Case report

2.1. History and examination

A 53-year-old man presented with a several-month history of generalized fatigue, a mild nonproductive cough, and pleuritic chest pain. There was no fever, weight loss, chills, night sweats, or shortness of breath, and he denied any weakness, numbness, gait or balance difficulty, or visual changes. The medical history was significant for hypertension, benign prostatic hypertrophy, gastroesophageal reflux, and hematuria. His social history

included a 70-pack per year tobacco history; he quit smoking 5 years earlier. He has been employed as a foreman in a silicone factory for several years. Initial workup was performed by the pulmonary medicine team. A chest x-ray revealed a lung nodule in the right lower lobe. A chest CT revealed a 2.5 × 1.0-cm calcified nodule in the right lower lobe, and CT-guided biopsy of the lung mass demonstrated reactive cellular changes and granulomatous inflammation; there were no malignant cells. Microbiological analysis (including gram stain and culture) and neuroimaging (brain CT and/or magnetic resonance imaging [MRI]) were not performed by the pulmonary team. A staging positron emission tomography scan (which revealed only hypermetabolism of the lung nodule) was done shortly after the lung biopsy, and the patient was scheduled for a VATS-assisted nodulectomy. However, in the interim, the patient began to experience word-finding difficulties, which were followed soon after by confusion and disorientation. This prompted admission and further evaluation. On examination, the patient had a mixed aphasia; the receptive component was greater than the expressive component. The remainder of his neurologic examination findings was normal.

2.2. Laboratory studies

Routine laboratory investigations obtained on admission were normal except for a white blood cell count of 11 000 cells/ μ L. The erythrocyte sedimentation rate was 10 mm/h

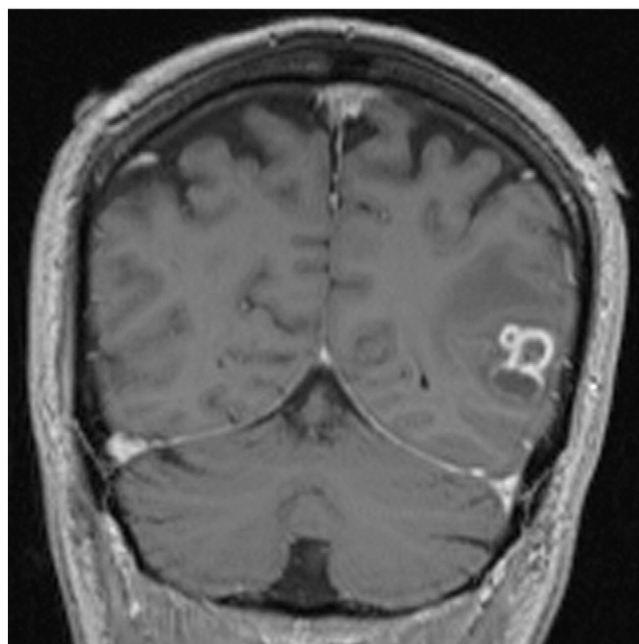


Fig. 1. Preoperative volumetric magnetic resonance image. Coronal gadolinium-enhanced T1-weighted magnetic resonance image from the preoperative volumetric MRI study demonstrating a ring-enhancing, partially cystic lesion within the left temporal-parietal region, with perilesional vasogenic edema.

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