Primary Brain Abscess Due to Nocardia Otitidiscaviarum: A Case Report

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Abstract

Nocardia can cause serious opportunistic infections in immunocompromised patients. Nocardial brain abscess in these patients has a high mortality. We describe a patient with Nocardia otitidiscaviarum brain abscess. After the abscess was evacuated at craniotomy, the patient was treated successfully with trimethoprim-sulfamethoxazole, meropenem, and amikacin. (J Intern Med Taiwan 2005; 16: 279-282)

Key Words: Nocardia otitidiscaviarum, Brain abscess, Triple therapy

Introduction

Nocardia are gram-positive, aerobic actinomycetes which may enter the body by inhalation of contaminated dust particles or via wounds contaminated with dust or soil. It is mainly an opportunistic pathogen in patients with impaired immunological function due to systemic disease or immunosuppressive therapy. Despite the relative rarity of nocardia spp. as a cause of cerebral infection, the brain is the most frequent non-pulmonary site involved in disseminated nocardiosis. We report a case of a primary cerebral abscess due to Nocardia otitidiscaviarum.

Case Report

A 68-year-old man had a several-years history of diabetes mellitus. He had a head injury which led to redness and swelling around his right orbit with a small abrasion wound. Brain computed tomography (CT) revealed right peri-orbital soft tissue swelling. He was discharged but had a persistent headache. Two months later, he developed gait difficulties, deviating to the left while walking. Two days after that, he was brought to our emergency department after an episode of loss of consciousness associated with urinary in-
continence and a fever. His blood pressure was 156/85 mmHg, heart rate 82/min, respiratory rate 20/min, and temperature 37.8 °C. His hemoglobin level was 12.4 g/dl, leukocyte count 8500/μl, blood urea nitrogen 24 mg/dl, creatinine 0.9 mg/dl, sodium 140 meq/l, and potassium 3.6 meq/l. A chest radiograph was normal. Brain CT revealed a ring-enhancing lesion in the right frontal lobe with marked perifocal edema causing compression of the right lateral ventricle and subfalcine herniation to the left (fig. 1). Meropenem, vancomycin and metronidazole were used as empiric therapy. A right craniotomy was performed to evacuate the brain abscess. Blood cultures were negative, but culture of material from the abscess grew *Nocardia* species. The organism was subsequently identified as *N. otitidiscaviarum* by analysis of the 16S rRNA sequence. The 1.5-kb 16S rRNA was amplified using primers Bac rRNA-1 (5’-GAG TTT GAT CCT GGC TCA-3’) and 16S (5’-TAC CTT GTT ACG ACT TCA CCC CA-3’). The PCR reaction mixture contained heat-lysed bacteria, 10 pmole of each primer, 0.2 mM dNTPs each, and 2.5 U BioTag DNA polymerase (Bioman, Taipei, Taiwan) in a volume of 50 μl 1X PCR buffer from the manufac-

turer. The PCR reactions were subjected to 35 cycles in a DNA thermal cycler (Perkin-Elmer) with denaturation for 45 sec at 94 °C, annealing for 45 sec at 50 °C, and extension for 1 min at 72 °C. A sequence of 740 nucleotides at the 5’ end of 16S rRNA from the PCR product was determined using primer Bac rRNA-1 in an ABI PRISM 377 sequencer analyzer (Applied Biosystems, Foster City, CA, USA). This sequence has 100% homology with *N. otitidiscaviarum* strains S639 and DSM 43242, GeneBank Accession No. AF430068 and AF430067, respectively, as demonstrated by BLAST (National Center for Biotechnology Information, National Institutes of Health, Bethesda, Md).

After the pathogen was identified, the patient was given trimethoprim-sulfamethoxazole (TMP/SMX), but the fever persisted for another 5 days, so meropenem and amikacin were added. A repeat brain CT showed a residual abscess, so it was again debrided. The fever subsided on the 22nd hospital day, and the patient’s condition improved. Antibiotics were continued and he was discharged after a total hospital stay of 75 days. A brain CT 2 weeks after discharge
showed marked regression of the lesion (fig. 2). At the time of writing, 9 months after the incident, there is no residual abscess on CT. The patient is being maintained on oral TMP/SMX and plan for total duration of treatment 12 months and regular follow up at OPD.

Discussion

*Nocardia* spp. are gram-positive, aerobic actinomycetes with rudimentary to extensively branched vegetative hypae which fragment into rod-shaped or coccoid bacteroids. Patients with immunosuppression, due to either systemic disease or immunosuppressive therapy may develop infections caused by this opportunistic pathogen. About 90% of isolates causing infection are *N. asteroides*, with *N. brasiliensis* and *N. otitidiscaviarum* involved less frequently. *N. otitidiscaviarum* (previously called *N. caviae*) was first described in 1924. It was considered to be simply a soil saprophyte until 1974 when the first human cases of infection were reported. Infection usually results from inhalation or traumatic inoculation of the organisms into the skin. Brain abscess usually results from hematogenous spread from a primary, often subacute or chronic, lung infection. The disease tends to be more acute in immunosuppressed patients. Remissions and exacerbations lasting for days or weeks are characteristic. Primary cerebral involvement by *N. otitidiscaviarum* is rare. Our patient had a normal chest x-ray without evidence of previous lung infection. It appears that he may have had direct inoculation of the skin when he had his earlier head injury with a small abrasion wound. He also had no obvious immune dysfunction other than what might be attributed to diabetes.

We were unable to isolate the organism in 3 sets of blood cultures. In fact, nocardia are rarely isolated from blood cultures unless biphasic blood culture systems are inoculated and incubated aerobically for up to 30 days with frequent and terminal subculturing. Because of slow bacterial growth, nocardiosis is difficult to diagnose, often leading to delayed treatment. A gram stain can be helpful. When the organism is successfully cultured, colonies with abundant aerial filamentous growth have a chalky white or cotton-ball appearance on blood agar. The laboratory must be alerted when nocardial infection is suspected. Colonies in pure cultures may grow after only 48 hours' incubation, but in mixed cultures of clinical material (e.g., respiratory secretions), other rapidly growing bacteria easily obscure small nocardial colonies. Furthermore, colony characteristics sufficient to arouse suspicion can take several weeks to develop.

Identification of nocardia to species level is important for both diagnosis and treatment, but this is difficult using conventional biochemical techniques (serotyping, biotyping, and typing with a yeast killer system). However, PCR, restriction enzyme analysis, and nucleic acid sequencing of the 16S rRNA gene can distinguish among species. The average time to identify nocardia isolates in culture has dropped from 2 to 3 weeks to 1 to 3 days when the expanded Micro seq 500 system for evaluation of partial 16S ribosomal RNA sequencing is employed.

Sulfonamides alone or TMP/SMX is standard therapy for disseminated nocardiosis. However, managing nocardial infection is often complicated by drug intolerance, such as allergic reactions to sulfonamides; primary drug-resistance; or the development of resistance during therapy. Surgical intervention may influence the ultimate outcome, particularly for patients requiring drainage or excision of abscesses or an empyema. The optimal duration of therapy is uncertain, but long-term treatment is the rule because nocardial infections tend to relapse. Immunocompetent patients with pulmonary or systemic nocardiosis (excluding central nervous system involvement) should be treated for a minimum of 6 to 12 months. Central nervous system infection should be treated for 12 months. All immunosuppressed patients should receive a minimum of 12 months' therapy. Our patient had a poor clinical response to TMP/SMX alone, with improvement achieved after...
adding meropenem and amikacin, plus repeat drainage of the abscess. In one published series, imipenem was more active against the *N. asteroides* group than meropenem but meropenem was more active than imipenem against both *N. brasiliensis* and *N. otitidiscaviarum*. This may be due to a subtle difference in its stability against β-lactamase 12.

In conclusion, increased awareness of nocardial brain abscess may help in treating patients with prompt specific therapy. The combination of TMP/SMX with meropenem and amikacin for patients with disseminated nocardiosis merits further investigation.

References

**Nocardia otitidiscaviarum**

所引起的原發性腦部膿瘍：個案報告

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摘 要

*Nocardia* 常可在免疫功能不全的病人身上造成機緣性感染，而其中由*Nocardia* 所造成的腦部膿瘍常常造成極高的致死率。我們在此提出一個因感染*Nocardia otitidiscaviarum* 造成腦部膿瘍的個案，在經過顱骨切開術併發症清除的手術之後，施予Trimethoprim-sulfamethoxazole，Meropenem 及 Amikacin 的抗生素治療，因而治療成功的例子。