

CASE REPORT

Brain Abscess Caused by *Nocardia asteroides* in a Diabetic Patient: A Rare Case Report

Hossein Ali Rahdar^a, Hamid Heidari^b, Morteza Karami-Zarandi^c, Tahereh Soori^d, Parisa Asadollahi^e, and Hossein Kazemian^{e,*}

^aDepartment of Microbiology, School of Medicine, Iranshahr University of Medical Sciences, Iranshahr, Iran; ^bDepartment of Microbiology, Faculty of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; ^cDepartment of Microbiology, Faculty of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran; ^dAutoimmune Bullous Diseases Research Center, Department of Dermatology, Tehran University of Medical Sciences, Tehran, Iran; ^eClinical Microbiology Research Center, Ilam University of Medical Sciences, Ilam, Iran

Nocardia brain abscess is usually associated with immunodeficiency, but can sometimes emerge in healthy individuals. This infection can be acquired through inhalation or direct inoculation of the bacteria, followed by dissemination to various organs, including the brain, through blood circulation. Mortality rate due to nocardial cerebral abscess is three times higher than that associated with cerebral abscess caused by other types of bacteria. Moreover, patients with *Nocardia asteroides*-associated brain abscess show poorer prognosis compared to patients with brain abscess caused by other *Nocardia* species, which is probably due to the high tendency of *N. asteroides* to become resistant to numerous antibiotics. It is, therefore, of paramount importance to diagnose and treat *N. asteroides* cerebral abscess in patients as soon as possible. The current paper is a rare report of a brain abscess caused by *N. asteroides* in a diabetic patient who failed to respond to multiple antibiotics (trimethoprim/sulfamethoxazole and amikacin), but improved by receiving imipenem and linezolid, and was finally successfully treated by surgical operation and long-term antibiotic therapy (imipenem and linezolid).

INTRODUCTION

Nocardia species are Gram-positive, filamentous, branching, strict aerobe, and relatively slow-growing bacteria which belong to the order Actinomycetales [1,2]. These organisms have maintained a saprophytic existence in soil (the main reservoir of the bacteria), sludge, contaminated water, plants, and spoiled material

throughout the world. Aerosols can transmit *Nocardia* species directly into the lung, leading to the development of lung lesions called pulmonary nocardiosis. The other type of infection caused by these bacteria is cutaneous lesions which are acquired through the traumatic percutaneous inoculation of the bacteria. These lesions are often presented as localized nodular processes, with the central nervous system involvement, which are often developed

*To whom all correspondence should be addressed: Hossein Kazemian, PhD, Clinical Microbiology Research Center, Ilam University of Medical Sciences, Ilam, Iran; Email: h.kazemian@outlook.com; ORCID: 0000-0003-4590-396X.

Abbreviations: ESR, erythrocyte sedimentation rate; CRP, C reactive protein; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CSF, cerebrospinal fluid; CT, computed tomography; MR, magnetic resonance; PCR, polymerase chain reaction; SLE, systemic lupus erythematosus; IV, intravenous.

Keywords: Brain abscess, *Nocardia asteroides*, Diabetes

Author Contributions: HAR, HH, MK: Contributed to the design and investigation of study; TS, PA: Writing the manuscript; HK: Supervision.

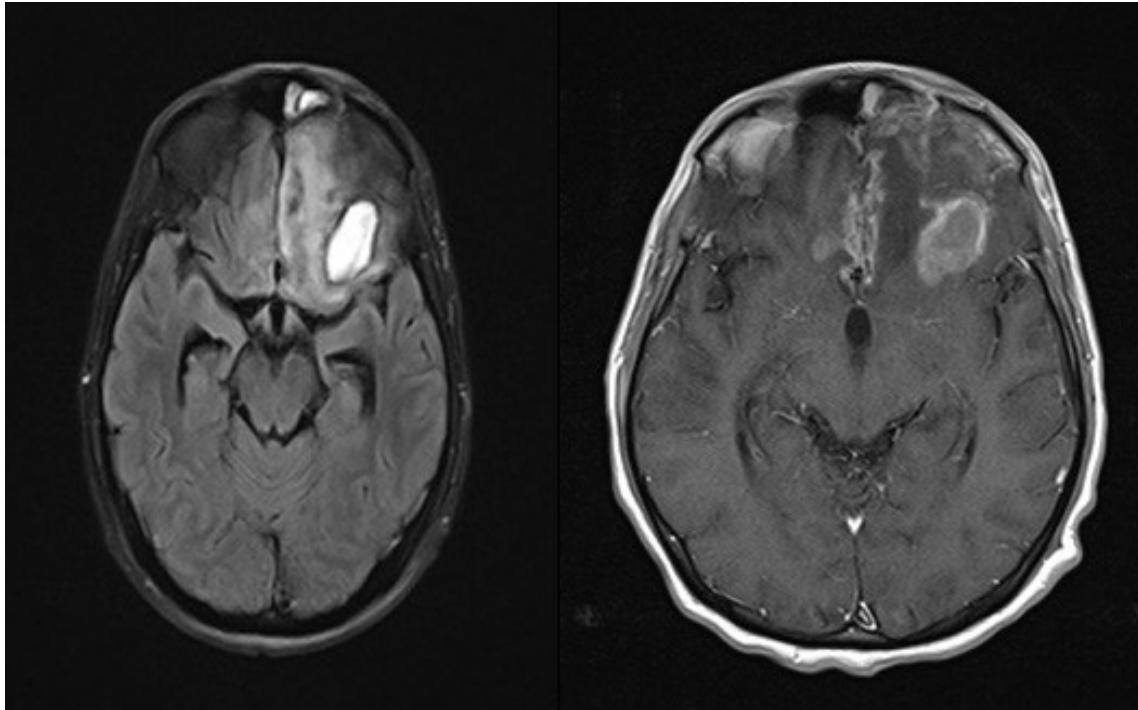


Figure 1. Coronal MR views of case showing a right temporal-parietal brain abscess.

through the hematogenous dissemination of the bacteria [3].

Cerebral abscess is a rare but serious type of nocardial infection, the mortality rate of which is three times higher than that associated with abscesses caused by other types of bacteria [4]. Moreover, the cerebral abscess due to *N. asteroides* has a higher mortality rate compared to that caused by other *Nocardia* species which is probably due to the high tendency of *N. asteroides* to become resistant to numerous antibiotics [5]. This is a rare report of a brain abscess caused by *N. asteroides* in a diabetic patient in Iran.

CASE PRESENTATION

A 71-year-old man with type 2 diabetes mellitus was presented to the Ali-Ibn-Abi Taleb Hospital in the city of Zabol, Sistan and Baluchestan province, Iran, with slow speech, persistent headache, dyspnea, and fever for 4 weeks before referral, and recent neurological symptoms such as dizziness without vomiting, seizure, or paralysis. The patient was a farmer living in a small village in Zabol who had fallen off a tree, which had led to shoulder injury and scratching. His examination revealed that the patient was suffering from a 2-month history of subcutaneous abscess of the right shoulder by an unknown agent. Because of the mixed bacterial flora in the lesion, the microbiological analysis of the abscess was not conclusive.

The body temperature, heart rate, and blood pres-

sure of the patient were 39°C, 98/min, and 140/100 mmHg, respectively at the time of primary hospital admission. Laboratory evaluations demonstrated that the blood cell count and glucose levels were normal and the blood hemoglobin level was 15g/dL with an elevated erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) levels up to 9 mm/hr and mg/L. Other laboratory findings such as alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatinine levels were 221 U/liter, 49 U/liter, 86 U/liter, and 121 μ mol/L, respectively. In addition, analysis of the peripheral blood lymphocyte subsets showed CD3+CD4+ of 420 cells/ μ L (47%), CD3+CD8+ of 241 cells/ μ L (27%), and a CD4+/CD8+ ratio of 1.70. Blood, cerebrospinal fluid (CSF), and urine samples were negative for bacterial growth. The PPD skin and anti-HIV 1, 2 tests were also negative. Chest and paranasal sinus X-ray and urine analysis were normal. CSF analysis revealed 19 WBC (39% lymphocytes, 5% monocytes, 56% PMNs)/mm³, protein and glucose levels of 89 mg/dL and 78 mg/dL, respectively.

A contrast-enhanced computed tomography scan (CT scan) of the brain revealed an enhanced lesion with marked peripheral edema in the frontal lobe. Magnetic resonance (MR) images with gadolinium revealed a heterogeneous lesion with a significant amount of perilesional edema (Figure 1). Finally, surgical operation was undertaken and the abscess was drained.

Gram staining revealed branching Gram-positive



Figure 2. Small white colonies of *N. asteroides*.

filamentous rods. These rods appeared acid fast in a modified Ziehl-Neelsen staining procedure. Cultures on chocolate agar and blood agar plates revealed a pure growth of small white colonies appearing after 2 days incubation at 37°C. The grown colonies are shown in Figure 2. Results of the phenotypic (resistance to lysozyme, growth at 37°C, catalase, lack of decomposition of casein, tyrosine, and xanthine) and molecular tests led to the identification of *N. asteroides* [6-8]. Polymerase chain reaction (PCR) products of 16S rRNA gene were sequenced and analyzed (Accession number: KX951411) by NCBI GenBank and Ribosomal Database for data analysis. The results showed 100% similarity to the reference strain of *N. asteroides* (ATCC 19247).

Antimicrobial susceptibility testing was carried out by E-test for amikacin, tobramycin, cefotaxime, amoxicillin-clavulanic, imipenem, ciprofloxacin, and trimethoprim-sulfamethoxazole antibiotics and the bacterium was resistant to all the tested antibiotics except imipenem and ciprofloxacin. Empirical treatment using multiple antibiotics (trimethoprim/sulfamethoxazole 20 mg/kg/day IV and amikacin 15 mg/kg/day) had been unsuccessful. However, the patient was improved by replacing the antibiotics with imipenem (500 mg IV every 6 hours) and linezolid (600 mg orally, every 12 hours) and finally treated by surgical operation and long-term antibiotic therapy using imipenem and linezolid.

DISCUSSION

Nocardia asteroides complex consists of different species with heterogeneous antimicrobial susceptibility patterns including *N. abscessus*, *N. asteroides*, *N. brevicatena*, *N. cyriacigeorgica*, *N. farcinica*, *N. nova* complex, and *N. transvalensis* complex. *N. asteroides* is the main species responsible for nocardial pneumonia among immunocompromised and immunocompetent individuals. Immunosuppression due to malignancy, long-term corticosteroid therapy, diabetes mellitus, lymphopenia, and autoimmune diseases are associated with increased incidence of *Nocardia* infections. The patient in this report had type 2 diabetes as a chronic immunosuppressive disease.

Nocardiosis in humans often occurs through either pulmonary inhalation or direct skin contact with the bacteria, followed by dissemination through the vascular tissue (13.5%). Nocardial brain abscesses, which mostly occur as early lesions with no evidence of extra-cranial lesions, are responsible for about 1% to 2% of all brain abscesses. The most common clinical manifestations observed in patients with nocardial brain abscess are seizures and focal neurological deficits [9,10]. Essien and colleagues [11] reported a rare case of brain abscess in a woman with systemic lupus erythematosus (SLE). One month after the initiation of immune suppression treatment, complications such as homonymous hemianopia, nausea and headache started, and an abscess in the oc-

cipital region was detected by MRI. In the CSF culture, *N. asteroides* was identified and therapy was started with intravenous (IV) meropenem and oral linezolid for 3 months, following which the patient was cured completely. Similar to our study, antibiotic therapy by a carbapenem and linezolid was effective against microorganism.

Moreover, Effendi et al. [12] reported a brain abscess caused by *N. thailandica* in a lymphocytic leukemia patient. Abscess culture and DNA sequencing were used for the detection of the infectious agent. Similar to the current case, trimethoprim/sulfamethoxazole treatment was unsuccessful. The patient was treated with IV ceftriaxone (2 grams daily for 5 months) while, in our study the isolate was completely resistant to a third-generation cephalosporin antibiotic, cefotaxime. In another study conducted by Stuebe et al., a metastasis mimicking brain abscess was described in an immunocompromised patient [13]. *Nocardia* was detected by culture from the biopsy sample and combination therapy using trimethoprim/sulfamethoxazole and ceftriaxone, followed by amoxicillin/clavulanic acid and minocycline was performed for 12 months. In our study, no susceptibility was observed to amoxicillin-clavulanic and trimethoprim-sulfamethoxazole and administration of the latter was also not efficient.

In another report by Browne et al. [14], a case of nocardial brain abscess was described in a patient with diabetes mellitus and similar to the present case, the patient was suffering from lung abscesses. *N. cyriacigeorgica* was defined as the underlying infectious agent and empirical therapy was started for the patient using IV ceftriaxone and oral trimethoprim-sulfamethoxazole. In contrast to our study, this regimen was successful and the patient's neurological complications improved rapidly. Another case of brain abscess by *N. cyriacigeorgica* was reported by Gabay et al. [15]. This case was an immunocompromised patient (due to steroid therapy) who was completely cured with a trimethoprim/sulfamethoxazole and meropenem regimen.

Unlike the mentioned studies, treatment of nocardial brain abscess is not always successful – leading to patient's death. Several records of death have been reported in the literature; for instance, despite antibiotic treatment with cefoperazone sodium and sulbactam sodium, a patient died because of a brain abscess in the frontal lobe by *N. farcinica* [16]. In addition, in a case series reported by Campioli et al. [17], 14 patients out of 24, were completely cured and 8 patients died following antibiotic therapy alone or combined with surgery. Most of the cured patients in this study were treated by combination therapy using trimethoprim-sulfamethoxazole and linezolid/ceftriaxone/moxifloxacin. In the above studies, trimethoprim-sulfamethoxazole was an effective part of combination therapies, but we found that its prescription in combined regimen was unsuccessful.

As discussed in the above brief literature review, brain abscess can be caused by different *Nocardia* species. Although in most studies, trimethoprim-sulfamethoxazole, linezolid, ceftriaxone, and moxifloxacin have been used for empirical therapy, these antibiotic regimens are not always successful and, therefore, precise identification of *Nocardia* species and determination of antibiotic susceptibility pattern are needed for proper treatment.

Diagnosis of *Nocardia* species via common culture-based methods could be difficult due to the overgrowth of the faster growing competitors. Moreover, some species are biochemically inactive and show inert activity in different biochemical tests. Molecular methods, such as PCR-sequencing of the *16S rRNA* gene, are reliable and fast methods for identification of *Nocardia* species [18].

It occasionally happens that nocardial brain abscesses mimic necrotic metastasis of brain tumors in imaging methods such as CT scan; therefore, immediate diagnosis and treatment or early surgical intervention are required [19]. Surgical management is often followed by antibiotic therapy. In this report, the patient received the first line anti-nocardial therapy after the surgery, which failed to treat the patient. The therapy was then switched to long-term use of imipenem and linezolid, after which the patient completely recovered from the infection. Immunosuppressed patients and those with CNS diseases should receive at least 12 months of antimicrobial therapy because of the high relapse rate of this infection [20].

CONCLUSION

This is a rare report of a brain abscess caused by *N. asteroides* in a type 2 diabetic patient in Iran. The majority of patients with nocardial infections are immunocompromised, and diabetes mellitus, as a chronic immunosuppressive disease, was the major risk factor for the nocardial brain abscess reported in the patient in this study. The etiological agent in this case report was confirmed by culture of the brain biopsy and molecular detection of the cultured microorganism. Although the investigated isolate was resistant to different classes of antibiotics including trimethoprim-sulfamethoxazole, cefotaxime, amoxicillin-clavulanic, amikacin, and tobramycin, successful treatment was achieved through early diagnosis and surgical removal of the mass lesion, followed by long-term antibiotic therapy (imipenem and linezolid).

Funding: The study received no funding.

REFERENCES

1. Brown-Elliott BA, Brown JM, Conville PS, Wallace RJ Jr. Clinical and laboratory features of the *Nocardia* spp. based

- on current molecular taxonomy. *Clin Microbiol Rev.* 2006 Apr;19(2):259–82.
2. Rahdar HA, Bahador A, Shahraki-Zahedani S, Karami-Zarandi M, Soori T, Jafari S, et al. Pulmonary Nocardiosis in Pemphigus Vulgaris Patients from Tehran, Iran. *Infect Disord Drug Targets.* 2021;21(1):78–83.
 3. Lerner PI. Nocardiosis. *Clin Infect Dis.* 1996 Jun;22(6):891–903.
 4. Yorke RF, Rouah E. Nocardiosis with brain abscess due to an unusual species, *Nocardia transvalensis*. *Arch Pathol Lab Med.* 2003 Feb;127(2):224–6.
 5. Izawa D, Sakano K, Okumura H, Kuwata T, Tsuji N. [Two cases of *Nocardia farcinica* brain abscess]. *No Shinkei Geka.* 2011 Dec;39(12):1167–72.
 6. Yeates C, Gillings MR, Davison AD, Altavilla N, Veal DA. Methods for microbial DNA extraction from soil for PCR amplification. *Biol Proced Online.* 1998 May;1(1):40–7.
 7. Javadi A, Pourmand MR, Hamed J, Gharebaghi F, Baseri Z, Rahdar HA, et al. Production and Characterization of Biosurfactant by *Nocardia* Species Isolated From Soil Samples in Tehran. *Tenside Surfactants Deterg.* 2021;58(1):74–80.
 8. Baio PV, Ramos JN, dos Santos LS, Soriano MF, Ladeira EM, Souza MC, et al. Molecular identification of nocardia isolates from clinical samples and an overview of human nocardiosis in Brazil. *PLoS Negl Trop Dis.* 2013 Dec;7(12):e2573.
 9. Mamelak AN, Obana WG, Flaherty JF, Rosenblum ML. Nocardial brain abscess: treatment strategies and factors influencing outcome. *Neurosurgery.* 1994 Oct;35(4):622–31.
 10. Malincarne L, Marroni M, Farina C, Camanni G, Valente M, Belfiori B, et al. Primary brain abscess with *Nocardia farcinica* in an immunocompetent patient. *Clin Neurol Neurosurg.* 2002 May;104(2):132–5.
 11. Essien F, Wolfley G, Tate J, Latack W, Carroll M. *Nocardia asteroides* occipital abscess as a cause of lupus nephritis? *Clin Case Rep.* 2022 Feb;10(2):e05265.
 12. Effendi M, Tirmizi S, McManus D, Huttner AJ, Peaper DR, Topal JE. *Nocardia thailandica* Brain Abscess in an Immunocompromised Patient. *Case Rep Infect Dis.* 2021 Jun;2021:6620049.
 13. Stuebe C, Dayawansa S, Huang JH, Harris FS. *Nocardia* Brain Abscess Mimicking Metastases in an Immunocompromised Patient. *Cureus.* 2021 Dec;13(12):e20248.
 14. Browne WD, Lieberson RE, Kabbesh MJ. *Nocardia cyriacigeorgica* Brain and Lung Abscesses in 77-Year-Old Man With Diabetes. *Cureus.* 2021 Nov;13(11):e19373.
 15. Gabay S, Yakubovsky M, Ben-Ami R, Grossman R. *Nocardia cyriacigeorgica* brain abscess in a patient on low dose steroids: a case report and review of the literature. *BMC Infect Dis.* 2022 Jul;22(1):635.
 16. Song J, Dong L, Ding Y, Zhou J. A case report of brain abscess caused by *Nocardia farcinica*. *Eur J Med Res.* 2021 Aug;26(1):83.
 17. Corsini Campioli C, Castillo Almeida NE, O'Horo JC, Challener D, Go JR, DeSimone DC, et al. Clinical Presentation, Management, and Outcomes of Patients With Brain Abscess due to *Nocardia* Species. *Open Forum Infect Dis.* 2021 Apr;8(4):ofab067. <https://doi.org/10.1093/ofid/ofab067>.
 18. Tatti KM, Shieh WJ, Phillips S, Augendrahn M, Rao C, Zaki SR. Molecular diagnosis of *Nocardia farcinica* from a cerebral abscess. *Hum Pathol.* 2006 Aug;37(8):1117–21.
 19. Menkü A, Kurtsoy A, Tucer B, Yildiz O, Akdemir H. *Nocardia* brain abscess mimicking brain tumour in immunocompetent patients: report of two cases and review of the literature. *Acta Neurochir (Wien).* 2004 Apr;146(4):411–4.
 20. Wilson JW. Nocardiosis: updates and clinical overview. *Mayo Clin Proc.* 2012 Apr;87(4):403–7.