


CASE REPORT

Brain abscess due to *Nocardia asiatica* in a 63-year-old patient with adult-onset still disease: A case report

Fernando Raul Salazar Reinoso¹  | Gioconda Stefania Romero-Santana²  |
Andrea Emilia Mawyin Juez¹ | Jorge Andrés Calderon Navas¹ |
Andrés Santiago Ronquillo Piloso¹

¹Unidad de Cuidados Intensivos, Hospital de Especialidades “Teodoro Maldonado Carbo”, Guayaquil, Ecuador

²Servicio de Hospitalización, Hospital Clínica Kennedy, Guayaquil, Ecuador

Correspondence

Fernando Raul Salazar Reinoso, Intensive Care Services, Hospital de Especialidades “Teodoro Maldonado Carbo”, Av. 25 de Julio, Guayaquil 090203, Ecuador.
Email: mdsalazarr@hotmail.com

Abstract

Cerebral nocardiosis is a rare and opportunistic cerebral infection caused by *Nocardia* spp., a gram-positive, aerobic bacteria of the Actinomycetes order. Patients with cell-mediated immunodeficiencies are often targeted by this microorganism, for which early diagnosis and therapeutic approach are essential.

KEYWORDS

basal ganglia, case report, cerebral nocardiosis, immunodeficiency, *Nocardia asiatica*

1 | INTRODUCTION

Nocardiosis is an infectious disease caused by a gram-positive, aerobic bacterium of the order of Actinomycetes; they behave as opportunistic microorganisms and are commonly found in soil, water, and organic matter, with more than 90 species identified and 54 associated with human diseases.^{1,2}

Infection by *Nocardia* often occurs in immunocompromised hosts, in particular those with a history of organ transplant, including BMT (Bone Marrow Transplant) and solid organ recipients, in which there is a high risk of mortality in the first year after transplantation.^{1,3}

The prevalence of nocardiosis is considered rare worldwide, and in Ecuador, it still remains unknown.

Here, we present a case of a patient with medical history of adult-onset Still's disease (AOSD) who developed neurological symptoms; further imaging testing revealed signs of infection in the brain that lead us to consider *Nocardia* as the etiological agent responsible for his condition.

2 | CASE REPORT

A 63-year-old Ecuadorian male patient with a history of type 2 diabetes mellitus (T2DM) and adult-onset Still's disease (AOSD) was admitted to a local hospital for presenting chronic fever and fatigue. AOSD was diagnosed approximately 3 years ago and treated with 2 cycles of Etanercept, oral corticosteroids, and methotrexate. His symptoms were attributed to the usage of monoclonal antibodies. However, after completing the treatment, his condition continues to decline with persistent daily fevers.

On clinical examination, the patient presented Cushing's like fascia (“moon face”) and subdermal nodules in the left hypochondrium and left forearm. A chest computed tomography (CT) scan revealed consolidation in the right lung vertex (Figure 1).

Based on the patient's immunosuppression history, tuberculosis was initially suspected, but all test results were negative, including the sputum culture.

Subsequently, a fiber bronchoscopy was performed with negative results, and the patient was started on a course of Piperacillin/tazobactam and quinolone.

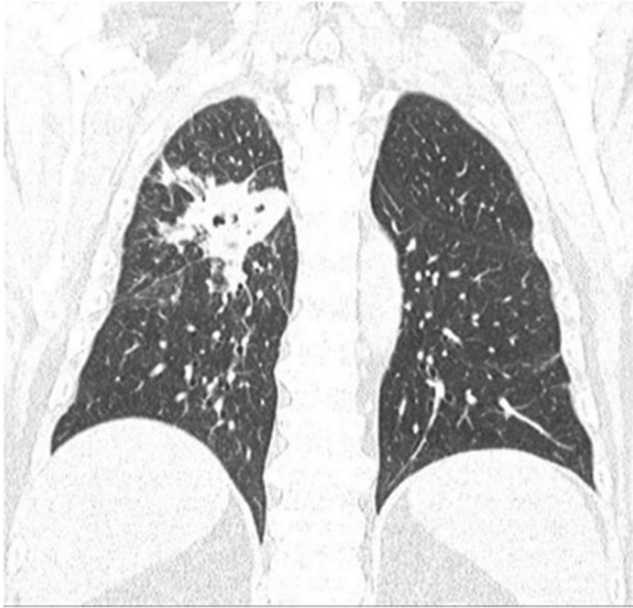


FIGURE 1 Chest CT. Coronal CT image shows a consolidation with cavitation in the center located at the right upper lobe of the lung.

During hospitalization, the patient became lethargic and within less than 24 h he presented left-sided hemiparesis. The neurology department was consulted to assess for a cerebrovascular accident (CVA). The brain CT scan showed hypodense lesions at the level of the anterior limb of the internal capsule and right lenticular nucleus. A magnetic resonance imaging (MRI) of the brain revealed rounded lesions at basal ganglia and bilateral subcortical cortical lesions in the frontal, parietal, and temporal lobes with bilateral cerebellar lesions of different sizes on T2-weighted imaging (T2-WI) and Fluid-attenuated inversion recovery-weighted imaging (FLAIR-WI) (Figure 2). Based on the imaging findings, the diagnostic was leaning toward infection of the central nervous system or brain metastasis.

His condition continued to decline to a state of stupor and was admitted to ICU. The patient was sedated and put on ventilatory support. Cerebrospinal fluid (CSF) reported adenosine deaminase (ADA): 11 UI/L, proteins: 110 g/dl, glucose: 82 mg/dL, Lactate Dehydrogenase (LDH): 35 U/L, negative liquid cultures, no growth in Chinese ink culture, C-reactive protein (CRP): negative for TB.

In collaboration with the infectious diseases department, the patient received antituberculous drugs plus a course of broad-spectrum antibiotics. A control brain CT scan revealed an increase in size and number of the

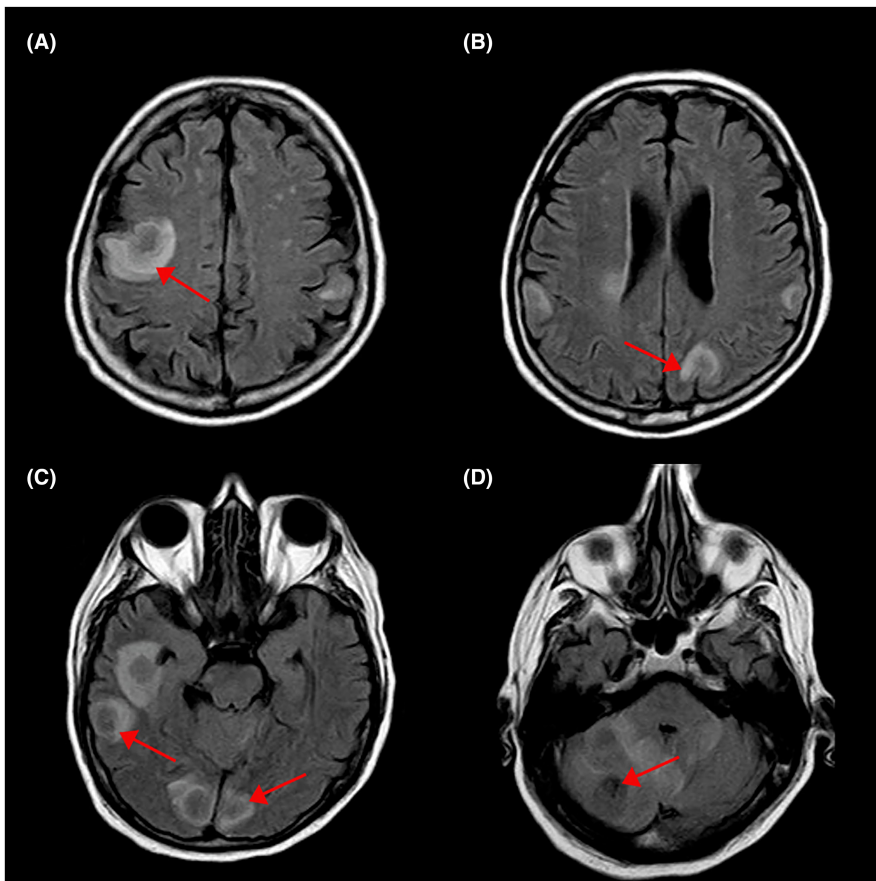


FIGURE 2 Brain MRI. FLAIR sequence axial sections (A, B), cortical and subcortical rounded heterogeneous lesions in different sizes with perilesional edema. (C) Heterogeneous cortical and subcortical lesions at the right temporal lobe, bilateral occipital paramedian with surrounding edema. (D) At the posterior fossa: bilateral confluent lesions in the right cerebellum and cerebellar peduncle. Note the arrows represent lesions.

FIGURE 3 Contrast MRI and spectroscopy. (A, B) Contrast-enhanced Brain MRI T1 sequence, axial section: rounded lesions with ring enhancement near the basal ganglia, posterior commissure, and temporal lobe, right side (C) coronal section, rounded lesions at the supra and infratentorial level in enhancement contrast ring. (D) Spectroscopy study shows (arrow) low levels of the choline metabolite with a choline and creatine ratio of 0.12, suggestive of lesions of infectious origin.

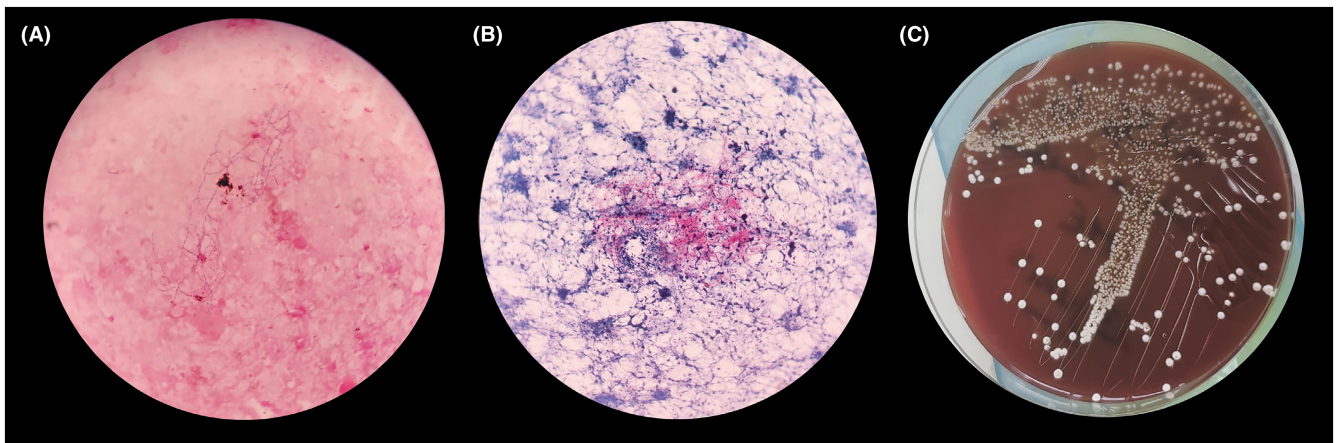
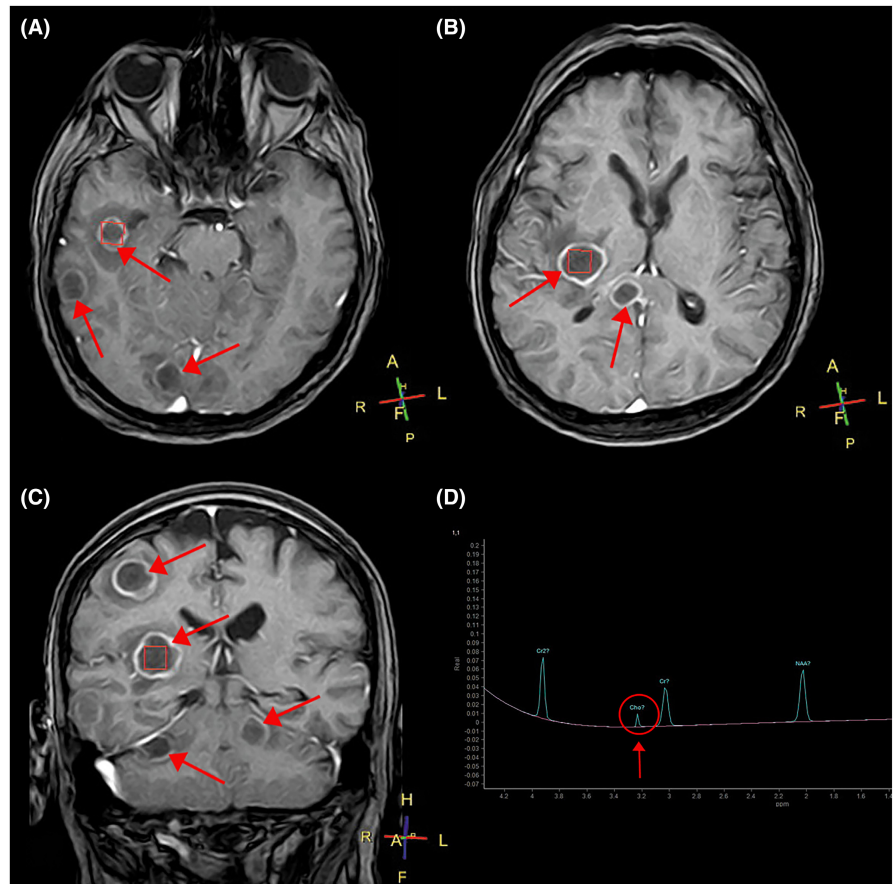


FIGURE 4 Microbiology studies. (A) Gram stain: Branched Gram-positive Bacillus. (B) Kinyoun stain: resistant acid alcohol branched bacteria. (C) Culture in Sabouraud: plaster-like folded yellowish-white colonies (popcorn) identification. *Nocardia* species.

aforementioned lesions. Brain MRI with spectroscopy showed a peak of choline that confirmed neuro infection (Figure 3). Despite the treatment, fever persisted, and symptoms were not improving. After consulting the neurosurgery department, a CT-assisted stereotactic brain biopsy of the lesions was obtained with no apparent complications, and samples were analyzed with Kinyoun stain confirming the presence of filamentous gram-positive

bacillus compatible with *Nocardia* (Figure 4). Molecular Biology study: Sanger method Sequencing of the 16S rRNA gene confirmed 99.83% of *Nocardia asiatica*. Based on these results, a change in antibiotic treatment with trimethoprim/sulfamethoxazole (TMP-SMX) was decided upon. The patient presented partial improvement; however, further complications consequent to paralytic ileus led to multi-organ failure, and death.

3 | DISCUSSION

Nocardiosis is a neglected tropical disease in which microorganisms can be introduced through inhalation, ingestion, or inoculation.^{2,4} Most frequently present in pulmonary diseases, followed by extrapulmonary diseases, in which the central nervous system (CNS) is the most common dissemination site due to local effects of granulomas or abscess formation in the brain, spinal cord, or meninges. Intracranial abscesses account for 2% of the cases, with a mortality rate of 31%, greater than other types of infection.^{4,5} *Nocardia* spp. is known for its tropism to brain tissue, leading to neurological symptoms such as headache, nausea, aphasia, and hemiparesis.⁶

To the best of our knowledge, there is a strong association between chronic glucocorticoid therapy and nocardiosis, attributed to the inherent effects in the host's immune mechanisms, mainly decreasing cellular immunity, making patients vulnerable to these infections.¹ This was evidenced in this patient with a 3-year history of AOSD chronically treated with oral corticosteroids (prednisone) and methotrexate, in addition to 2 cycles of etanercept.

In an immunocompromised patient, the infection starts in the lungs before spreading hematogenously to the central nervous system and other organs. According to the case study, the first CT scan of the chest performed on the patient showed consolidative injury on the right pulmonary vertex, corroborating the pulmonary compromise, although the patient never presented respiratory symptoms.

On MRI studies, brain abscesses produced by *Nocardia* are described as areas of purulent necrosis, observed as ring lesions consistent with abscess formation followed by necrosis, and edema caused by vascular exudation and infiltration.⁷ In the reported case, MRI images revealed similar results: rounded lesions at the basal ganglia, as well as bilateral cortical lesions in the frontal, parietal, temporal lobes, and cerebellum with different sizes on T2-weighted imaging (T2-WI) and FLAIR-WI. Interestingly, as above-stated the lesions increased in number and size further complicating the patient's state.

MRS (magnetic resonance spectrum) is optimal for differentiating between brain abscesses, gliomas, and cystic or necrotic foci.⁵

The core of brain abscesses lacks of the metabolites present in normal brain tissue; therefore, NAA, creatine, and choline levels are low, yet lactic acid is elevated. In addition, valine, leucine, and isoleucine are essential markers to reach this diagnosis; however, their absence does not rule out an intracranial abscess.⁵

The diagnosis is confirmed with direct observation through microscopy of samples prepared with a special stain such as Kinyoun, where resistant acid alcohol branched filamentous bacteria are identified, but this

method is less sensitive than gram staining,⁸ in which *Nocardia* is spotted as thin and long microorganism branching with tiny noncontiguous gram-positive beads of varying sizes. Culture sensitivity is 85%–95% and is carried out in a Sabouraud glucose syrup media that generates folded yellowish-white or plaster-like colonies similar to popcorn.^{4,8}

The gold standard for the identification of *Nocardia* species is molecular biology with amplification and sequencing of one or two gene(s) among RRs (i.e., the gene coding for 16S rRNA), hsp65, secA1, and sodA.⁸ *Nocardia* PCR testing is recommended only for patients with high suspicion of nocardiosis and no other obvious diagnosis.⁹

Proteomic profile analysis using MALDI-TOF MS (Matrix Assisted Laser Desorption/Ionization Mass Spectrometry) allows a rapid identification serving as an aid for an early diagnosis and prompt empiric treatment.⁴

Due to its pharmacokinetics and good penetration into the CNS, Trimethoprim/Sulfamethoxazole remains as the preferred drug for treating Nocardiosis.⁷ The recommended dose is 25–50 mg/kg per day of oral trimethoprim to the patient for 3 months. However, cost and toxicity with prolonged therapy up to 6–12 months limit its widespread use.^{4,10}

For less severe cases, swiss guidelines recommend routine usage of this antibiotic, but if there is no positive response or signs of toxicity are evident, switching to imipenem is recommended.

Through-out his hospitalization, our patient received levofloxacin, amikacin, linezolid, and TMP-SMX in standardized doses, that seemed to some degree helped his condition, but his severe immunosuppression was the key factor for his incomplete improvement.

During the Grand Round presented by Derung and colleagues, the usage of interferon-gamma in refractory cases of severe *Nocardia* infection was suggested, stating that this cytokine at the center of the immunity triggers various antimicrobial effector functions, regulating proteins in support of oxidative, nitrosative, protonated, and membranolytic defense. It also inhibits the intracellular growth of pathogens, improving the course of nocardiosis. Its success depends on the underlying molecular pathophysiology and should only be considered an adjuvant compound.¹¹

Surgical treatment is necessary when there is a significant brain abscess(es) not responding to antimicrobial therapy or if a co-infection is suspected.⁸ Craniotomy for excision of the entire abscess and capsule is more effective than aspiration. An essential factor in recurrence is the retention of the capsule, so performing a craniotomy to clear both abscess and capsule altogether will avoid it.¹⁰ It is important to mention that surgical excision is indicated only when the lesion is located in the non-eloquent brain

area. If the lesion is found in the eloquent area, aspiration and drainage are recommended.

4 | CONCLUSION

Nocardiosis is a rare bacterial infection and is widely unknown in our country; it requires applied microbiology laboratory techniques to establish its diagnosis in order to provide a specific treatment. The differential diagnosis approach is challenging as this pathology is often confused with other infectious processes that affect the central nervous system.

It has a high incidence among immunocompromised patients in endemic regions and is prone to be misdiagnosed, similar to Tuberculosis.

Unfortunately, compared to the patients in the few previously published studies, this patient had a poor response to antibiotics, resulting in a fatal outcome.

AUTHOR CONTRIBUTIONS

Andrea Emilia Mawyin Juez: Investigation. **Jorge Andrés Calderon Navas:** Resources. **Andrés Santiago Ronquillo Piloso:** Conceptualization. **Fernando Raul Salazar Reinoso:** Supervision; writing – original draft. **Gioconda Stefania Romero-Santana:** Writing – review and editing.

ACKNOWLEDGMENT

The authors thank Dr. Raul Romero, Dra. Jessica Navas, and Dra Karla Wellington for their valuable contributions to the editing of this paper. Responsibility for any errors remains with the authors. This case and its outcomes are published with the written consent of the patient for educational purposes.

FUNDING INFORMATION

The author(s) received no financial support for the research, authorship, and/or publication of this article.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

DATA AVAILABILITY STATEMENT

All the findings are present within the manuscript.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy. A copy of the written consent is available for review by the editor in chief of this journal on request.

ORCID

Fernando Raul Salazar Reinoso  <https://orcid.org/0000-0001-5820-7600>

Gioconda Stefania Romero-Santana  <https://orcid.org/0000-0002-3915-1442>

REFERENCES

1. Abdul M, Momin B, Saroj B, et al. Disseminated Nocardiosis in an immunocompetent adult: diagnostic challenges. *J Microbiol Infect Dis.* 2019;9(1):46-50. doi:10.5799/jmid.537170
2. Yagishita M, Tsuboi H, Tabuchi D, et al. Clinical features and prognosis of nocardiosis in patients with connective tissue diseases. *Mod Rheumatol.* 2021;31(3):636-642. doi:10.1080/14397595.2020.1823070
3. Leite IM, Trigueiros F, Martins AM, Fonseca M, Marques T. Disseminated Nocardiosis: a case report. *Cureus.* 2019;11:8. doi:10.7759/CUREUS.5294
4. Dewan Duggal S, das Chugh T. Nocardiosis: a neglected disease highlights of the study. *Med Princ Pract.* 2020;29:514-523. doi:10.1159/000508717
5. Zhu JW, Zhou H, Jia WQ, You J, Xu RX. A clinical case report of brain abscess caused by *Nocardia brasiliensis* in a non-immunocompromised patient and a relevant literature review. *BMC Infect Dis.* 2020;20:328. doi:10.1186/s12879-020-05052-0
6. Lau YL, Bustamante J, Martínez-Barricarte R. Isolated Nocardiosis, an unrecognized primary immunodeficiency? *Front Immunol.* 2020;11:590239. doi:10.3389/fimmu.2020.590239
7. Wang T, Jia Y, Chu B, Liu H, Dong X, Zhang Y. Nocardiosis in kidney disease patients under immunosuppressive therapy: case report and literature review. *Int J Med Sci.* 2019;16(6):838-844. doi:10.7150/IJMS.32440
8. Margalit I, Lebeaux D, Tishler O, et al. How do I manage nocardiosis? *Clin Microbiol Infect.* 2021;27(4):550-558. doi:10.1016/J.CMI.2020.12.019/ATTACHMENT/34D02DD4-69AF-436F-9867-07CA9C23DAD9/MMC1.DOCX
9. Rouzaud C, Rodriguez-Nava V, Catherinot E, et al. Clinical assessment of a *Nocardia* PCR-based assay for diagnosis of Nocardiosis. *J Clin Microbiol.* 2018;56(6):8. doi:10.1128/JCM.00002-18
10. Karam C, Siadati A. Diagnosis and neurosurgical management of cerebral Nocardiosis. *J Neurol Surg Rep.* 2021;82(2):e21-e24. doi:10.1055/s-0040-1722345
11. Derungs T, Leo F, Loddenkemper C, Schneider T. Treatment of disseminated nocardiosis: a host-pathogen approach with adjuvant interferon gamma. *Lancet Infect Dis.* 2021;21(10):e334-e340. doi:10.1016/S1473-3099(20)30920-8

How to cite this article: Salazar Reinoso FR, Romero-Santana GS, Mawyin Juez AE, Calderon Navas JA, Ronquillo Piloso AS. Brain abscess due to *Nocardia asiatica* in a 63-year-old patient with adult-onset still disease: A case report. *Clin Case Rep.* 2023;11:e06816. doi:10.1002/ccr3.6816