Immunocompetent patient with *Nocardi a abscessus* brain abscess: Case report and review of the literature

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**ABSTRACT**

Nocardia cerebral abscess is uncommon. It accounts for 1%-2% of all cerebral abscesses. It typically occurs in immunocompromised patients but cases in immunocompetent hosts been reported. Diagnosis of Nocardia brain abscess can be difficult and misleading. In this report we report a case of *Nocardia abscessus* brain abscess that was misdiagnosed initially as brain tumor. The patient has been successfully managed medically along with surgical evacuation twice.

**Key Words:** Nocardia, Nocardiosis, *Nocardia abscessus*, Brain abscess, Brain abscess in immunocompetent patient, Cerebral infection

1. **INTRODUCTION**

Nocardiosis is a localized or disseminated infection caused by the soil-borne aerobic actinomycete Nocardia.1-5 There are more than 50 species of Nocardia with around 33 species causing diseases in humans.1,4,6 *N. asteroides* complex is considered the common source of nocardiosis. Nocardia *asteroides* complex includes: *Nocardia asteroides, brasiliensis, otitidiscaviarum, transvalensis, farcinica* and *Nocardia nova.*7 Nocardiosis presents most commonly as pulmonary disease, as inhalation is the most common method of infection, which may be followed by dissemination to multiple sites by hematologic spread.8 Nocardia cerebral abscess accounts for only 1%-2% of all cerebral abscesses and is mostly via hematogenous spread, but cases of primary central nervous system infections have been reported.9-11 Nocardia brain abscess typically occurs in immunocompromised patients and less commonly in immunocompetent hosts.12

We describe a case of an immunocompetent 34-year-old male with a *Nocardia abscessus* brain abscess and review similar reported cases in the literature.

2. **CASE PRESENTATION**

A 34-year-old Moroccan gentleman presented to a local hospital complaining of headache for one month. The headache was mainly located at the right temporal region, constant and progressive in severity. It was associated with asthenia and disorientation in space and time. The patient denied history of fever. He complains of intermittent hands and abdomen pruritus 3 weeks prior to presentation. No pul-
Pulmonary complaints and denied any neurological symptoms. Past medical/surgical history is significant for two surgical interventions of left foot, one for osteoma of the second toe and the other for hallux valgus with postoperative complication in the form of algoneurodystrophy. He traveled to Morocco twice two years prior to presentation. The patient is a sportive person who enjoys boxing, walking and hunting in the forests. There is a positive history of contact with stagnant water during a hunting trip in the forest.

The patient underwent CT scan and Magnetic Resonance Imaging (MRI), which showed right temporal mass surrounded by enormous cerebral edema associated with midline shift. A tumorous lesion was suspected and the patient started on Methylprednisolone 120 mg once daily. He was then transferred to Amiens University Health Center (CHU-Amiens).

On arrival to CHU-Amiens, the patient was vitally stable, afebrile, and alert but disoriented to time and place. He had a normal pulmonary and cardiac examination. The abdomen was soft with neither tenderness nor rigidity. There was no motor, sensory or cranial nerve deficits. Laboratory investigations revealed a C-reactive protein 12 mg/dl, ESR of 10 mm/h, WBC count 15,200/microliter, HgB 14.4 g/dl, BUN 17 mg/dl and Creatinine 0.9 mg/dl. Neutrophil function test, lymphocyte count, lymphocytes immunophenotyping, levels of immunoglobulin, C3 and C4 were normal. Human immunodeficiency, hepatitis B and hepatitis C viruses testing were negative. Formal ophthalmic examination revealed left homonymous hemianopsia. MRI done at the local hospital has been re-read by a neuroradiologist and revealed an intraxial lesion in the right temporal lobe measuring $43 \text{ mm} \times 40 \text{ mm} \times 30 \text{ mm}$ associated with significant mass effect on the right lateral ventricle and about 12 mm of midline shift. The lesion shows restricted diffusion. It has multiple microcystic appearance as evident on CT scan (see Figure 1) and T2-weighted MR imaging. It is surrounded by a peripheral hypointense rim on T2-weighted images with multi-loculated contrast enhancement (see Figure 2) which is suggestive of Nocardial brain abscess rather than a brain tumor.[13] Based on these findings, Methylprednisolone was stopped immediately and the patient taken to the operating room urgently.

Initially the patient underwent abscess puncture and drainage under Neuronavigation guidance. Aspiration using a Sedan biopsy needle was unfortunately unsuccessful as the content was very viscous. Therefore, we were not able to evacuate the collection enough. We withdrew a scant amount of the abscess that enabled identification of the Nocardia by DNA sequencing method. It was susceptible to Imipenem/Cilastatin (Tienam), Amikacin and Trimethoprin/Sulfamethoxazole (Bactrim), Ceftriaxone and Minocycline.

Postoperatively, the patient was started on intravenous Cefotaxime and Metronidazole empirically for three days until the culture and mass spectrophotometry showed $N. \text{ abscessus}$. It was sensitive to all tested antibiotics except Erythromycin, Moxifloxacin, Levofloxacin, and Pristinamycine. The antibiotics then adjusted to intravenous Imipenem/Cilastatin (Tienam), Amikacin and Trimeprorin/Sulfamethoxazole (Bactrim). A week later, the patient was found very somnolent and confused. CT scan was done and showed lack of regression in the size of the abscess. Therefore, we decided to do good evacuation of the abscess through a small craniotomy. On day 10 of antibiotics initiation, Amikacin was changed to Minocycline and on Day 21, Bactrim had to be discontinued due to the development of neutropenia. Finally, after six weeks, Tienam was changed to Ceftrixone. As part of the research for an etiology, Thoracoabdominopelvic CT scan was done that was negative except for an opacity and mediastinal adenopathy. Bronchial fibroscopy did not show anomalies and test of the bronchoalveolar lavage aspirate was totally negative including for Nocardia or evidence of alveolar proteinosis.

The patient had an uneventful hospital stay. The left homonymous hemianopsia improved. He was discharged after six weeks to continue on intravenous Ceftriaxone for an additional three months and oral Minocycline for at least one year. At one-year follow up, the patient was doing well, no recurrence manifested and cerebral MRI was negative apart from post-operative changes.
Figure 2. a. T2 MR sequence showing hyperintense mass with hypointense rim; b. T1 MRI with gadolinium showing rim enhancement; c. Diffusion MR sequence showing restricted diffusion; d. ADC map showing hypointensity confirming restricted diffusion

3. DISCUSSION

Nocardia is an aerobic actinomycete gram-positive bacterium. It is typically an opportunistic organism that can cause local or systemic diseases in infected hosts. However, it can less commonly infect immunocompetent individuals. Nocardia include more than 80 species of which around 33 cause diseases in humans. It can be found in soil, decayed vegetable matters, dust particles, and aquatic environment. Variable mode of entries were reported including; ingestion of contaminated food material, cutaneous inoculation and inhalation. The exact incidence of nocardiosis is not well established, as it is not a reportable organism and difficulty in diagnosis. The risk factors for the majority of nocardiosis cases are the causes of immunocomprised state including; glucocorticoid use, malignancy, HIV infection and organ and hematopoietic stem cell transplantation. Other conditions reported to be associated with nocardiosis are alveolar proteinosis, diabetes mellitus, alcoholism, inflammatory bowel disease and tuberculosis.

Cerebral abscess is a focal inflammation and collection of infected materials within the brain parenchyma. Pathogen invasion can occur either by direct spread or hematogenous
seeding. Direct spread such as from infected paranasal sinuses or otitis media. Hematogenous seeding can occur following bacteremia originating from different sources, for example, chronic pulmonary infection, skin infection or endocarditis. Nevertheless, in 20%–40% of cases no primary source can be found. Microbiologically, brain abscess can be caused by various pathogens depending mostly upon the source of the primary infection, age of the patient and his/her immunological status. By far, the most common pathogens causing cerebral abscess are Staphylococcus and Streptococcus species. However, various organisms can cause brain abscess. In one systemic review of 123 studies including 9,699 cases of brain abscess, only about 0.6% of abscesses were caused by Nocardia. However, the incidence of Nocardia brain abscess varies in the literature that mostly lies between 1%-2% of cases and it is predominantly seen in immunocompromised patients. Nevertheless, up to one third of nocardiosis cases can be seen in immunocompetent individuals. Based on animal studies, there are arguments that immunocompetent patients with Nocardia brain abscess might have inherent immune defect particularly of cell-mediated immunity. This theory needs to be formally investigated in human subjects. Different species of Nocardia can infect the central nervous system. The majority of the infecting species are N. asteroides, N. farcinica, N. cyriacigeorgica. Less common species include N. transvalensis, N. brasiliensis and N. otitidiscaviarum. There are case reports of infections by N. carnea, N. exalbida, N. nova, N. asiatica. Mortality rate from Nocardia brain abscess depends upon the therapeutic modality: 7% with combined targeted antimicrobial therapy and neurosurgery; 22% with targeted antimicrobial therapy alone and 36% for patients treated with neurosurgery alone.

N. abscessus has been defined in the year 2000 after redefinition of the Nocardia taxonomy based upon molecular speciation rather than biochemical speciation. Nocardiosis caused by N. abscessus is uncommon in comparison to that caused by other Nocardia species. It is reported to cause 15%-18% of nocardiosis cases. Few cases have been documented in humans including pericarditis, pulmonary infection, cutaneous and soft tissue lesions and brain abscess in immunocompromised patients. To our knowledge, N. abscessus brain abscess in an immunocompetent host has been reported five times in the literature. In this report we present a sixth case of cerebral abscess by N. abscessus in an immunocompetent patient.

Mortality from N. abscessus is reported to be as high as 31%-34.6% but this reported mortality was in infected immunocompromised patients. There is no reported mortality in the five reported cases of brain abscess caused by N. abscessus pathogen in the immunocompetent patients. Two of the cases were treated solely by antibiotic. The other three cases were treated by combinations of antibiotics and surgical evacuation. As all Nocardia species, laboratory identification might be challenging using routine culture methods. Four out of the five reported cases detailed the methods of microbiological detection of the organism and treatment specifications. All were partially acid-fast positive. Routine cultures were negative and the diagnosis of the N. abscessus was done by molecular methods except in one case where the culture yielded Nocardia. Duration of antibiotics treatment was variable ranging from 6 weeks to one year.

In our case, the diagnosis was made using DNA sequencing followed by culture and spectrophotometry. The patient was treated by neurosurgical intervention along with targeted antibiotic therapy for one year. The source of the infection was not evident indicating a possible primary infection. The history of contact with stagnant water and soil triggers possible dermatoic inoculation of the organism, nevertheless, no skin manifestations of nocardiosis found on history or clinical examination. It is noteworthy that the abscess capsule was very hard to pierce, a finding that was also noted in another reported case of N. abscessus brain abscess. As the abscess content was very viscous, a sufficient evacuation was not possible necessitating open surgical evacuation. Therefore, we recommend an open neurosurgical evacuation in cases of suspected N. abscessus or failure to sufficiently aspirate the content material due to viscosity.

4. CONCLUSIONS
This is the sixth reported case of cerebral abscess in an immunocompetent patient caused by N. abscessus. Due to rarity of the condition, no specific guidelines are available in the literature. Therefore, delay in diagnosis can occur unless a high index of suspicion is maintained. Prompt diagnosis is important, as the outcome seems better with prompt surgical evacuation and targeted antibiotic therapy. On the basis of increased incidence and reports of Nocardia brain abscess in both immunocompromised and immunocompetent patients, we recommend searching actively for Nocardia in brain abscess cases specially in situations - although not specific - of multiloculated abscess on imaging, hard abscess capsule, negative routine cultures or viscous abscess content.

AUTHORS’ CONTRIBUTION
The first two authors contributed equally to the paper.

CONFLICTS OF INTEREST DISCLOSURE
The authors declare they have no conflicts of interest.
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