

Multiple Nocardial Brain Abscesses in an Immunocompetent Patient

Davinder Singh Rana^{*}, P. K. Sethi, Anuradha Batra, Ish Anand, Pooja Gupta, Samir Patel

Department of Neurology, Sir Ganga Ram Hospital, New Delhi, India

Abstract

Nocardial brain abscess is a rare central nervous system (CNS) infection with high morbidity and mortality. Nocardial brain abscess is usually associated with immunocompromised patients, but sometimes may appear in healthy individuals. Clinical presentation: We report a case of nocardial brain abscess treated at our department in an immunocompetent patient who was initially treated for CNS tuberculosis but was later found to have Nocardiosis. The patient was treated with surgical evacuation and long-term antibiotics. The patient recovered well at discharge. Conclusion: Nocardial brain abscess is a rare CNS infection that needs to be differentiated from other brain lesions. It could occur in immunocompromised patients or healthy individuals. Treatment includes surgical intervention and long-term antibiotics therapy. Early identification, appropriate and prolonged treatment are crucial for a favorable outcome.

Keywords

Nocardiosis, Immunocompetent, CNS Infection, Tuberculosis, Surgical Intervention, Long-Term Antibiotics

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1. Introduction

Nocardiosis is an uncommon gram-positive bacterial infection caused by aerobic actinomycetes. *Nocardia* have ability to cause localized or systemic suppurative disease in humans and animals. Typically regarded as an opportunistic infection, but approximately 1/3rd patients are immunocompetent. *Nocardia* are ubiquitous in the environment: soil, organic matter, and water. Human infection usually occurs from minor trauma and direct inoculation of the skin or soft tissues or by inhalation.

Nocardiosis is usually acquired by inhalation, and therefore the pulmonary form is the most common clinical feature [1]. However, Nocardiosis in the central nervous system (CNS) may occur as an isolated intracranial lesion or as a part of disseminated infection [2, 3]. *Nocardia* intracranial abscesses are rare and generally occur in immunocompromised patients but they are extremely rare in

immunocompetent hosts [4, 5]. *Nocardia* cerebral abscesses account for only 1% to 2% of all cerebral abscesses, but carry considerably higher mortality rates of 55% and 20% in immunocompromised and immunocompetent patients, respectively [6, 7]. Here, we describe an immunocompetent patient in whom *Nocardia* had caused multiple cerebral abscesses. This case highlights the importance of including nocardia on the differential diagnosis especially in patients who present with abnormal MRI scan findings that mimic tuberculoma or neoplastic disease. Clinical awareness of this condition could expedite the diagnostic process and help improve morbidity and mortality.

2. History

52 year old female known case of hypertension, hypothyroidism was referred to our hospital with numbness in left upper limb, followed by weakness in left upper limb

* Corresponding author

E-mail address: davinder1966@gmail.com (D. S. Rana)

for 15 days and numbness, followed by weakness in left lower limb for 1 week. She also had headache for 5 days. There was no history of vomiting, fever, weight loss or anorexia.

3. Examination

The examination revealed pulse rate of 80 beats/min, Blood Pressure of 130/80mmHg and a body temperature of 37 degree Celsius. There was no pallor/cyanosis/icterus, absence of digital clubbing, pedal edema and palpable lymph nodes. The patient was conscious, was following verbal commands, cranial nerve examination was normal, Pupils – NSNR, Left hemiplegia (LL- 2/5, UL- 1/5), Plantars- Right flexor, Left extensor and sensations were intact.

4. Investigations

Her hemoglobin was 10.8 gm%, Total Leukocyte Count was 9900/ cumm, platelet count was 1.11 lakh/cumm, ESR was 22 mm at 1st Hour, serum creatinine of 0.83 mg/dl, BUN of 13.4 mg/dl, Na 142Meq/L, K 3.8Meq/L, serum Ca 9.1 mg/dl, PO_4^{3-} 3.2 mg/dl, serum bilirubin 0.6 mg/dl, SGPT 24 IU, SGOT 24 IU, ALP 86 IU, serum protein of 6.8gm% and serum albumin of 3.6gm%. Her HIV status was negative, ANA was negative, ACE levels were 14.2(normal), c-ANCA was negative and p-ANCA was also negative. Her immunological profile revealed IgA of 264.80 mg/dL (35-350), IgG 657.10 mg/dL (650-1600), IgM 300.30 mg/dL (50-300) and IgE 6.13 (<35). The tumor markers CA 19-9 of 8.2 (<35), CEA of 0.36 (0-3) and CA 125 of 7.2 (<35) were negative.

Patient was already put on anti-tubercular drugs and steroids since past 10 days as possibility of tuberculoma was kept, and we initially continued it. Contrast enhanced MRI (CEMRI) of Brain revealed right frontal ring enhancing lesion as shown in Fig. 1.

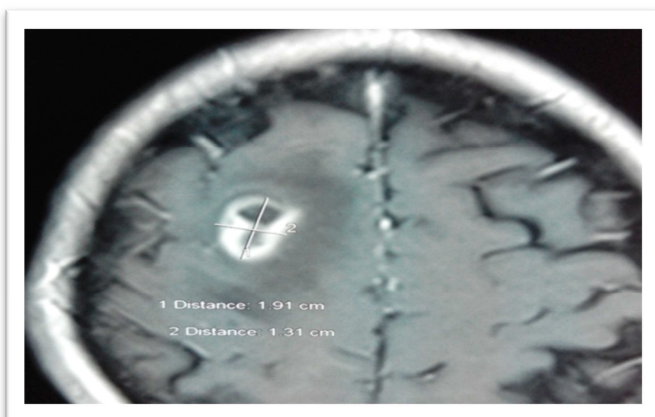


Fig. 1. CEMRI Brain showing right frontal ring enhancing lesion.

The CT Thorax of the patient revealed right upper lobe cavitory lesion shown in Fig. 2.

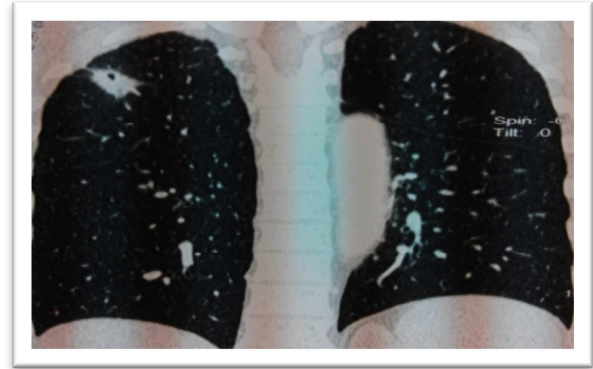


Fig. 2. CT Thorax showing cavitory lesion in right upper lobe.

Bronchoscopy, EBUS and Bronchoalveolar lavage were done but bronchial aspirate didn't show any Acid Fast Bacilli (AFB) or tumor cells and routine culture, AFB culture, fungal cultures were negative. After 3 days of hospitalization she had an episode of seizure and left sided weakness also worsened (dense hemiplegia), so repeat CEMRI Brain was done which revealed increase in number of lesions with increase in perilesional edema as depicted in Fig. 3.

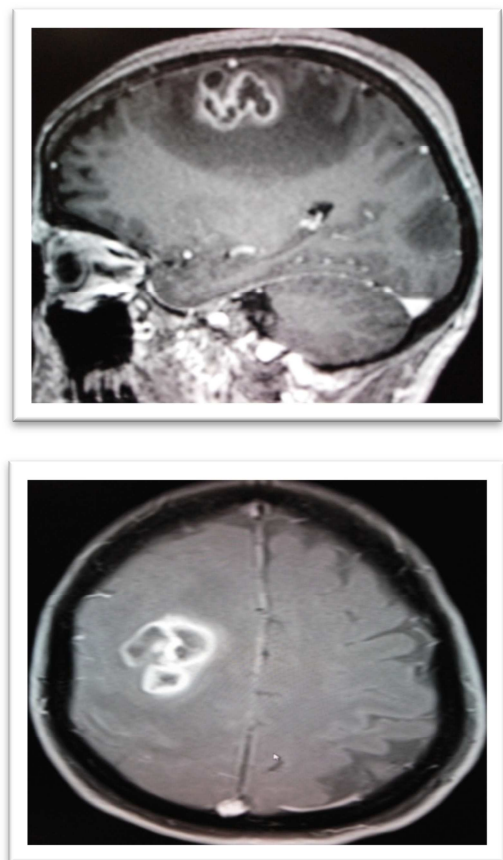


Fig. 3. (a), (b). CEMRI Brain images showing increased number of lesions with surrounding edema.

PET-CT revealed large lobulated FDG avid iso to hyperdense mass lesion with multiple enhancing septae within right frontal region with significant perilesional edema with few ring enhancing lesions in left frontal and right occipital lobes with perilesional edema as shown in Fig. 4.

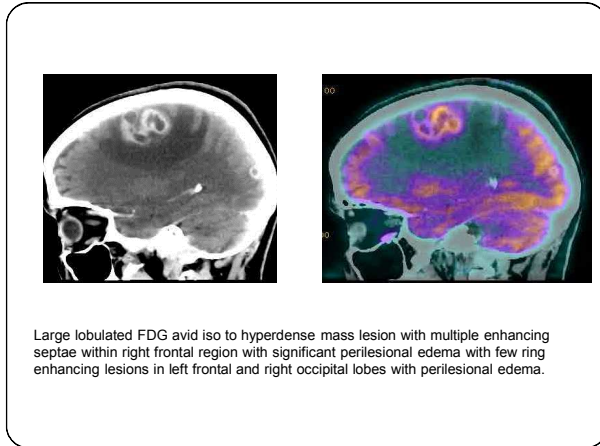


Fig. 4. PET-CT showing iso to hyperdense mass lesion with multiple enhancing septae within right frontal region with surrounding edema.

Right frontoparietal craniotomy with abscess removal was done. Gram stain revealed few gram positive branching filamentous bacteria. Kinyoun Stain revealed few acid fast organism resembling nocardia as shown in Fig. 5.

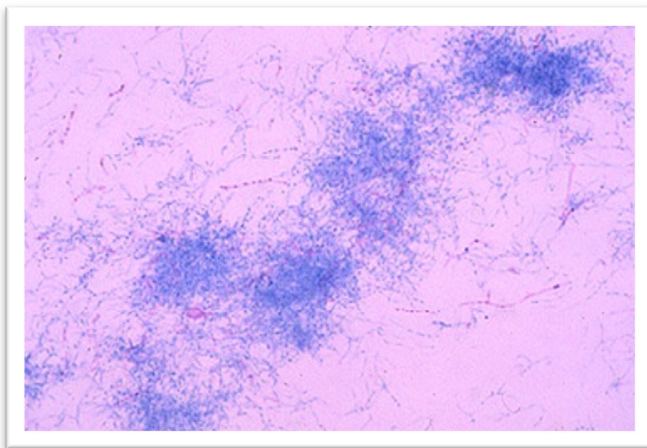


Fig. 5. Kinyounstain showing acid fast Nocardia.

Routine culture and sensitivity (Pus) revealed growth of *Nocardia* sp. Biopsy of right frontal lesion revealed necrotizing suppurative inflammation consistent with brain abscess. ATT was stopped. She was managed with IV antibiotics (amikacin, imipenem and cotrimoxazole) and 2 weeks later her limb power starting improving (grade 3/5). She later developed pancytopenia, so cotrimoxazole was stopped. Bone marrow examination revealed normoblastic erythroid hyperplasia with reduced iron stores. Bone marrow biopsy revealed all normal marrow components. She was put

on Vit B12 and folic acid supplementation and her blood counts normalized. She was given IV Imipenem and Amikacin for 6 weeks. She was discharged in stable condition with normal limb power on oral antibiotics as per culture sensitivity reports (Augmentin, Minocycline).

5. Risk Factors

The risk of nocardial infection is increased in immunocompromised patients, particularly those with defects in cell-mediated immunity e.g solid organ or hematopoietic stem cell transplantation, long term steroid therapy, HIV infection (especially if the CD4 count is <100 cells/mm³), malignancy (most often after recent chemotherapy or glucocorticoid therapy), diabetes mellitus [8, 9]. Chronic lung disease and alcoholism are additional risk factors for pulmonary nocardiosis.

6. Sites of Infection

Most common disease sites are the lung, central nervous system (CNS), and skin. Systemic (≥ 2 sites involved) – seen in approx. 32 percent; among patients with systemic disease, 44 percent have central nervous system (CNS) involvement. Pulmonary (only) – 39 percent. CNS (only) – 9 percent. Cutaneous or lymphocutaneous – 8 percent. Single site extrapulmonary (eg, eyes, bone) – 12 percent [10].

7. CNS Nocardiosis

Isolated CNS disease has been reported, but this probably represents dissemination from a resolved or transient pulmonary or cutaneous infection. The hallmark of CNS nocardiosis is formation of a parenchymal abscess that can occur in any region of the brain. Signs and symptoms of nocardial brain abscess are diverse and nonspecific. Patients may present with fever, headache, meningismus, seizures, and/or focal neurologic deficits. In some patients, typically those with intact immune systems, CNS nocardiosis remains clinically silent, at times persisting for years before a diagnosis is made. CNS nocardiosis can present with symptoms suggesting a mass lesion without any symptoms typically associated with infection. In such patients, nocardial brain abscess may be erroneously diagnosed as a primary or metastatic neoplasm prior to biopsy [11, 12]. Nocardial meningitis is an infrequent manifestation of CNS nocardiosis and can occur with or without an associated brain abscess. The CSF typically demonstrates a neutrophilic pleocytosis, reduced glucose, and elevated protein concentration, findings that are characteristic of bacterial meningitis.

Disseminated nocardiosis defined as two non-contiguous

sites of involvement that may or may not include a pulmonary focus. *Nocardia* can disseminate from a pulmonary or cutaneous focus to virtually any organ. Although dissemination is presumed to result from hematogenous spread, identifying *Nocardia* in blood cultures is uncommon due in part to their fastidious nature.

8. When to Suspect

It should be suspected in any patient who presents with brain, soft tissue, or cutaneous lesions, and a concurrent or recent pulmonary process. It is important to have a high index of suspicion in the appropriate clinical settings, especially in patients not responding to antituberculous treatment. When patient presents with concomitant brain and lung lesions, the differential diagnosis to be kept in mind include tuberculosis, neoplastic disease, and nocardiosis.

9. Diagnosis

A definitive diagnosis requires the isolation and identification of the organism from a clinical specimen. Establishing a diagnosis of nocardiosis is problematic since an invasive procedure is often required to obtain an adequate specimen and recovery of *Nocardia* in the laboratory is difficult because of its slow growth. In the proper clinical setting, a presumptive diagnosis of nocardiosis can be made if partially acid-fast filamentous branching rods are visualized in clinical specimens.

Gram stain-*Nocardia*spp appear as delicate, filamentous, sometimes beaded, branching gram-positive rods. Modified acid-fast staining - partially acid-fast filamentous branching rods are visualized in clinical specimens. The acid-fast nature of *Nocardia* is most reliably demonstrated when organisms are stained by a modified Kinyoun procedure. This method substitutes 1 percent sulfuric acid for acid alcohol as a decolorizer, which allows the less tenaciously acid-fast *Nocardia* to retain fuchsin. Polymerase chain reaction- for identification of *Nocardia*spp provides more accurate and rapid results than the conventional methods using biochemical and susceptibility testing, however, PCR is not available in most clinical laboratories. In routine aerobic cultures, *Nocardia*spp have variable colonial morphology, from chalky white to pigment-producing orange, yellow, or brown colonies, and usually require 5 to 21 days for growth.

10. Treatment

No prospective randomized trials have determined the most effective therapy for nocardiosis. Thus, the choice of antimicrobials is based upon cumulative retrospective

experience, investigations in animal models, and in vitro antimicrobial activity profiles. Most authorities recommend trimethoprim-sulfamethoxazole as part of first-line therapy for nocardiosis.

Other agents: Amikacin, imipenem, meropenem, third-generation cephalosporins (ceftriaxone and cefotaxime), minocycline, extended spectrum fluoroquinolones (eg, moxifloxacin), linezolid, tigecycline, and dapsone [13, 14].

Initial treatment (ie, induction therapy) is recommended intravenously for at least three to six weeks and/or until clinical improvement is documented.

Isolated CNS disease

TMP-SMX 15 mg/kg IV of the trimethoprim component per day in two to four divided doses PLUS
Imipenem 500 mg IV every 6 hours

CNS disease with multiorgan involvement (ie, at least one other site)

TMP-SMX 15 mg/kg IV of the trimethoprim component per day in two to four divided doses PLUS

Imipenem 500 mg IV every 6 hours PLUS

Amikacin 7.5 mg/kg IV every 12 hours

Switching to combination oral therapy (with two drugs based upon susceptibility studies) is recommended after a minimum of six weeks of intravenous therapy and clear evidence of clinical improvement [13].

Recommended antibiotics :

A sulfonamide (eg, TMP-SMX 10 mg/kg of the trimethoprim component per day in two or three divided doses) AND/OR Minocycline (100 mg twice daily) AND/OR Amoxicillin-clavulanate (875 mg twice daily)

The total duration of therapy (IV followed by oral) is based upon the severity and extent of disease and the clinical and radiographic response to treatment. Patients with CNS involvement should be treated for at least one year, and some suggest indefinite suppressive therapy in immunocompromised patients. Clinical improvement is usually seen within two weeks after initiation of appropriate therapy. Patients who continue to be symptomatic and/or have progression of their primary lesions after two weeks of therapy should be carefully reevaluated. Poor response may represent primary drug resistance, poor penetration of drug into the infected tissue compartment, or the presence of an abscess requiring surgical drainage.

11. Conclusion

Nocardiosis is often misdiagnosed because of its rarity and

nonspecific clinical picture. Symptomatology could be insidious, variable and without fever or other clear infective symptoms, delaying diagnosis and treatment. It is important to emphasize that an increased awareness of the various presentations of nocardiosis in combination with a high index of clinical suspicion can precipitate a rapid diagnosis and improve survival in an otherwise fatal disease. CNS nocardiosis occurs in both immunocompromised and immunocompetent individuals. *Nocardia* should be included in the differential diagnosis when evaluating any patient with risk factors for immunosuppression and a possible opportunistic infection. Obtaining an accurate diagnosis and the initiation of early treatment are essential but can be very challenging. However, if a tissue biopsy can be obtained then nocardia can be quickly diagnosed by examination of pathological material with gram stain or a modified acid fast. This case highlights the importance of obtaining a tissue biopsy for microbiological and culture identification for organisms such as nocardia on the initial presentation when an infectious process is considered in the differential diagnosis and early treatment can be initiated.

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