Brain Abscesses Caused by *Nocardia farcinica* in a 44-Year Old Woman with Multiple Myeloma: A Rare Case and Review of the Literature

**Patient:** Female, 44-year-old

**Final Diagnosis:** Brain abscess • *Nocardia* infection

**Symptoms:** Seizures • status epilepticus • weakness in all 4 limbs • weakness of upper and lower limb

**Medication:** Amikacin • Meropenem • Trimethoprim-sulfamethoxazole

**Clinical Procedure:** Left frontal craniotomy with gross-total resection of the left frontal space-occupying lesion

**Specialty:** Infectious Diseases • Microbiology and Virology • Neurosurgery

**Objective:** Rare disease

**Background:** Central nervous system infection by the *Nocardia* species is associated with high morbidity and mortality. Its occurrence in patients with multiple myeloma is rare and acquisition of the infection in such patients was associated with the use of novel therapeutic agents (eg, bortezomib and lenalidomide) or bone marrow transplantation. Here, we report the first case of *Nocardia* brain abscesses in a patient with multiple myeloma, without the above risk factors.

**Case Report:** A 44-year-old woman with IgG-kappa type multiple myeloma presented with generalized tonic-clonic seizures. Magnetic resonance imaging of the brain revealed 3 space-occupying lesions in left frontal, left parietal, and right parietal regions. Craniotomy and enucleation of the left frontal lesion revealed an abscess. The culture result was *Nocardia farcinica*. The patient was treated with meropenem, amikacin, and trimethoprim-sulfamethoxazole for 6 weeks, followed by trimethoprim-sulfamethoxazole for 12 months, with good outcome.

**Conclusions:** Cerebral nocardiosis is a rare entity and its occurrence in our case may hint toward myeloma-associated humoral immune dysfunction as a pathogenesis and the importance of humoral immunity in the defense against this infection. However, chemotherapy-induced cell-mediated dysfunction cannot be ruled out as a risk factor for the infection. Despite its rarity, this case aims to raise awareness of the condition and reiterate the importance of considering the rare but life-threatening conditions in the differential diagnosis of brain lesions, especially when there is a misdiagnosis of the radiological findings, as occurred in this and previous cases; this avoids delays in appropriate surgical and medical treatment, which can affect outcomes.

**Keywords:** Brain Abscess • Central Nervous System Bacterial Infections • Central Nervous System Infections • Multiple Myeloma • *Nocardia* • *Nocardia farcinica*

**Full-text PDF:** https://www.amjcaserep.com/abstract/index/idArt/937952
Background

A Nocardia brain abscess is a rare central nervous system (CNS) infection caused by the Nocardia species and is associated with high morbidity and mortality [1]. It occurs mostly in immunocompromised patients as opportunistic infections but can appear in otherwise healthy individuals [1]. Nocardia infection can occur via inhalation or direct inoculation, causing primary pulmonary or cutaneous disease, respectively [1]. Involvement of other sites, such as the CNS, develops mainly by hematogenous dissemination [2].

A Nocardia brain abscess in patients with multiple myeloma is extremely rare. In the few reported cases in the literature, acquisition of this infection in such patients was in association with the use of novel therapeutic agents (eg, bortezomib and lenalidomide) or bone marrow transplantation, which impairs cell-mediated immunity, an important host defense against the infection [3-8]. To the best of our knowledge, this is the first reported case of Nocardia brain abscesses in a multiple myeloma patient without any of the above reported risk factors.

Case Report

A 44-year-old woman was transferred to our Neurosurgical Unit from the Intensive Care Unit of Kuwait Cancer Control Center. Her past medical history was significant for diabetes, hypertension, and hysterectomy 6 years earlier, which was due to dysfunctional uterine bleeding. A year prior to her current presentation, she reported having persistent back pain, and further assessment revealed a stable L3 fracture. On further investigation, multiple myeloma (IgG kappa type; International Staging System-IIa) was diagnosed 8 months prior to her current presentation. The patient was started on cyclophosphamide, thalidomide, and dexamethasone and zoledronic acid.

The patient was paraplegic (Medical Research Council [MRC] power scale 0/5 in both lower limbs) and had severe weakness of her eyes spontaneously and obeying commands (Glasgow Coma Scale score was E4, V 11, M6). On further examination, the patient was paraplegic (Medical Research Council [MRC] power scale 0/5 in both lower limbs) and had severe weakness of the upper limbs (MRC power scale 2/5 and 1/5 in the right upper limb and left upper limb, respectively). No sensory level was noted. Deep tendon reflexes were sluggish throughout.

The patient underwent left frontal craniotomy with total excision of the left frontal space-occupying lesions. Intraoperative findings were conclusive for the diagnosis of an abscess, and samples were sent for microbiology and histopathological assessment. Microscopy and staining revealed slender, branching, gram-positive bacilli, which were weakly acid-fast and morphologically resembling Nocardia. The organism were cultured on blood and chocolate agar under aerobic conditions at 37°C. Colonies were visible at 48 h, but were left to grow for a total of 10 days. Identification of Nocardia farcinica took less than 1 h and was done via matrix-assisted laser desorption ionization time-of-flight mass spectrometry technology using a VITEK MS machine. This was followed by antibiotic sensitivity testing (Table 1).

The left and right posterior fronto-parietal lesions were not dealt with because they were small and in eloquent areas. The patient was extubated the next day, and the postoperative non-contrast CT scan of the brain showed the left frontal lesions appearing to be no longer visible (Figure 2). She remained at our neurosurgical institute for around 3 weeks before being transferred to the referring hospital to continue medical treatment. Prior to being transferred, the Glasgow Coma Scale score was 15/15 and power in all limbs showed discrete improvement.

The antibiotic regimen was changed to intravenous meropenem, amikacin, and trimethoprim-sulfamethoxazole for 6 weeks, followed by trimethoprim-sulfamethoxazole for 12 months, with very good neurological status and recovery. To the best of our knowledge, no additional abscess formation occurred.
Figure 1. T1-weighted magnetic resonance imaging of brain after gadolinium administration revealed multiple ring-enhancing lesions. (A) Axial view showing multi-compartment left frontal lesions (arrows) measuring 4.6×3.8×3.2 cm with mass effect. (B) Axial view showing left and right fronto-parietal lesions measuring 1.2×2.2×3 cm and 1.6×1.3×1.5 cm, respectively, (arrows) in close proximity to an eloquent area (primary motor cortex is located within the yellow highlighted box). (C) Sagittal view demonstrating the lesions surrounded by extensive vasogenic edema (asteriks). (D) Diffusion-weighted imaging showing diffusion restriction as indicated by the hyperintensity (arrows). (E) Non-contrast computed tomography of brain showing several hypodense round lesions in the left frontal region (arrows) with well-defined hyperdense ring, surrounded by edema (asteriks), causing mass effect and effacement of the anterior horn of left lateral ventricle.
**Table 1.** Susceptibility of *Nocardia farcinica* isolate to different antimicrobials.

| Antimicrobials            | Susceptibility result |
|---------------------------|-----------------------|
| Ampicillin                | R                     |
| Amikacin                  | S                     |
| Trimethoprim-sulfamethoxazole | S                  |
| Meropenem                 | S                     |
| Ciprofloxacin             | S                     |
| Clarithromycin            | R                     |
| Gentamicin                | S                     |
| Ceftriaxone               | R                     |
| Linezolid                 | S                     |
| Minocycline               | S                     |
| Vancomycin                | S                     |
| Piperacillin-tazobactam   | R                     |

S – sensitive; R – resistant.

**Discussion**

*Nocardia* (order *Actinomycetales*) is a complex genus of weakly staining gram-positive and catalase-positive bacteria. It is a rod-shaped, partially acid- and alcohol-fast bacteria forming irregular branching colonies on agar [2-9]. Numerous species are defined, with some being nonpathogenic, and others responsible for nocardiosis [10]. The pathogenic species have low virulence, and disease most frequently occurs as an opportunistic infection in immunocompromised individuals with defects in cell-mediated immunity (eg, organ transplant recipients and HIV-positive patients) [1,2,11-13]. However, infection of individuals who are immunocompetent is not uncommon, with up to 60% of *Nocardia* infections occurring in immunocompetent hosts, and up to two-thirds of patients with CNS infection not having predisposing risk factors [14-19]. Clinical manifestations vary from pulmonary, lympho-cutaneous, and disseminated nocardiosis with deep abscess formation at any site and CNS involvement [2,10,20].

To date, this is the seventh reported case of *Nocardia* brain abscesses in a patient with multiple myeloma (Table 2) [3,4,6-8]. Multiple myeloma has been reported to affect the humoral immunity more than the cell-mediated, while the medications used to treat it impair cellular immunity [5,6,21,22]. Previously reported cases have stated that the use of novel therapeutic agents (eg, bortezomib, lenalidomide) results in changes in cellular immunity, thereby increasing the risk of a spectrum of infectious agents, including *Nocardia*. In a different cohort of patients with CNS nocardiosis, an association with bone marrow transplantation was reported [5]. In our case, neither bone marrow transplantation nor novel therapeutic agents for multiple myeloma were implicated in the development of the *Nocardia* brain abscesses. However, cell-mediated dysfunction due to cyclophosphamide, thalidomide, and dexamethasone therapy for multiple myeloma can also occur and hence may have been a risk factor for the development of *Nocardia* infection in this patient. Even though cellular immunity has been shown to be important in the host defense of patients with *Nocardia* infection, the humoral immunity also appears to play a major significant role in the host defense against the infection [23]. Our patient had IgG kappa multiple myeloma, which is known to have increased risk of defective antibody response and hence infection [24]. Therefore, we postulate that the pathogenesis of cerebral nocardiosis in our patient may also be directly related to the myeloma-associated humoral immunity dysfunction, and therefore this should not be ruled out as a risk factor. Nevertheless, despite the severe immunodeficiency and higher risk of infections in patients with multiple myeloma, the development of brain abscesses is reported to be extremely rare [4].

*Nocardia* brain abscesses are an uncommon entity, whereby 25% to 40% of patients with systemic nocardiosis develop cerebral infection [9]. CNS infection can also be isolated without evidence of systemic disease, occurring in up to 40% of cases [25]. CNS involvement most frequently manifests as cerebral abscesses, although meningitis and diffuse cerebral infiltration have been reported [25,26]. These brain abscesses originate mainly from a primary focus, such as the lungs or skin,
and represent only 2% of all brain abscesses [15,27]. Patients with CNS nocardiosis most commonly present with focal neurological deficits, non-focal findings, and seizures, as was seen in our case [28]. In addition, fever and signs of septicemia are generally absent [1]. CT and MRI findings can reveal single or multiple contrast-enhancing lesions.

It is estimated that about 86% of all Nocardia infections in humans are caused by Nocardia asteroides [2,12,16,17,20,29]. Infection of the CNS can rarely be caused by N. cyriacigeorgica, brasiliensis, farcinica [12,17,18]. In previously reported cases of Nocardia brain abscesses in patients with multiple myeloma, the involved species were N. cyriacigeorgica, N. paucivorans, and N. farcinica, with N. farcinica being the most commonly reported [3,4,6-8]. N. farcinica infections are occurring more frequently than previously recognized [9]. It may also be more virulent than the other species and appears to possess a high degree of antibiotic resistance; making treatment difficult [9,30]. This rare condition is often diagnosed late in the course of the disease due to the slow progression of symptoms and the lack of specific laboratory findings [31]. Furthermore, it is mostly misdiagnosed as neoplasm on imaging, which can

Table 2. Summary of previously published case reports of cerebral nocardiosis in patients with multiple myeloma.

| Author, year of study | Age/Sex | Chemotherapy regimen | Clinical presentation | Nocardia species | Treatment | Outcome |
|-----------------------|---------|-----------------------|-----------------------|------------------|-----------|---------|
| Monticelli J et al, 2015 [3] | 70/M | Melphalan/ Prednisone/ Bortezomib, followed by Lenalidomide/ Dexamethasone | Seizures | Nocardia paucivorans | TMP-SMX plus meropenem; followed by ciprofloxacin | Survived |
| Pamukçuoğlu M et al, 2014 [4] | 61/F | Cyclophosphamide, Bortezomib and Dexamethasone | Seizures | Nocardia cyriacigeorgica | Surgical excision; meropenem followed by amoxicillin-clavulanic acid | Survived |
| Pamukçuoğlu M et al, 2014 [4] | 60/F | Cyclophosphamide, Bortezomib and Dexamethasone | Dysarthria and gait disturbances | Nocardia cyriacigeorgica | Surgical excision; imipenem/ cilastatin followed by TMP-SMX | Survived |
| AlSamman S et al, 2014 [6] | 64/M | Lenalidomide | Seizures | Nocardia farcinica | Ceftriaxone plus TMP-SMX | Survived |
| Matin A t al, 2017 [8] | 68/F | Melphalan, Bortezomib, Thalidomide, Adriamycin, Cyclophosphamide, Cisplatin and Etoposide | Right sided facial palsy with right sided hemiplegia | Nocardia farcinica | Surgical debridement; TMP-SMX, Linezolid and Imipenem followed by TMP-SMX plus Tedizolid | Survived |
| Xu N et al, 2021 [7] | 69/F | Bortezomib, Ixazomib, Dexamethasone and Cyclophosphamide | Convulsion of the limbs with left-sided hemiplegia | Nocardia farcinica | TMP-SMX plus Ceftriaxone followed by TMP-SMX plus Moxifloxacin | Survived |
| Our Case | 44/F | Cyclophosphamide, thalidomide and Dexamethasone | Seizures | Nocardia farcinica | Surgical excision; Meropenem, Amikacin and TMP-SMX followed by TMP-SMX | Survived |

M – male; F – female; TMP-SMX – Trimethoprim-Sulfamethoxazole. Novel therapeutic multiple myeloma agents are highlighted in **bold**.
result in delays in initiating appropriate antimicrobial therapy and surgical treatment [27,20,18]. This occurred in our case, whereby the radiological findings were interpreted as multiple brain metastasis; this dilemma at presentation has been reported in other cases in the literature [16]. Difficulties in culturing Nocardia is another factor that results in a delay in reaching a diagnosis [28].

The optimal management approach for cerebral nocardiosis has not yet been established. However, craniotomy and enucleation of the abscess followed by prolonged antimicrobial therapy based on sensitivity results has been the preferred treatment option and is associated with a lower relapse of infection and reduced mortality of 24% [17,20,27,28,32,33]. In contrast, mortality rates with antimicrobial therapy alone and aspiration alone were 30% and 50%, respectively [28].

The prognosis of cerebral nocardiosis carries a high mortality and morbidity among all brain abscesses [17,27,34]. A significantly higher mortality rate of 66% has been found in multiple Nocardia brain abscesses compared to those with single lesions (33%) and other bacterial brain abscesses (10%) [16,28,32]. With the advent of newer generation antibiotics, the mortality has decreased from nearly 90% to 33% in single brain abscesses [16,35]. However, in the presence of multiple brain abscesses, the mortality still remains high, at 66% [16,35]. It has also been reported that the mortality rates differ between immunocompetent and immunocompromised patients and are 20% and 55%, respectively [18].

**Conclusions**

Nocardia brain abscesses are a rare encounter especially in patients with multiple myeloma. Published literature on the topic is scarce, consisting mainly of case reports. Its occurrence in our case may hint toward myeloma-associated humoral immunity dysfunction, indicating the importance of the humoral immunity in the host defense against the infection. However, chemotherapy-induced cell-mediated dysfunction cannot be ruled out as a risk factor for the development of the infection in our patient. This report aims to raise awareness of the condition and add pivotal data to the literature. In addition, it reiterates the importance of considering the rare but life-threatening conditions as part of the differential diagnosis of brain lesions, especially when there is a misdiagnosis of the radiological findings, as occurred in this and previous cases in the literature.

Recognition of cerebral nocardiosis requires a high index of suspicion and early aggressive treatment with surgical enucleation of the abscess wall, prolonged antibiotics, and long-term surveillance, which are essential to prevent infection relapse, morbidity, and mortality.

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**Declaration of Figures’ Authenticity**

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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