Open Forum Infectious Diseases

MAJOR ARTICLE

Clinical Presentation, Management, and Outcomes of Patients With Brain Abscess due to *Nocardia* Species

Cristina Corsini Campioli,[1] Natalia E. Castillo Almeida,[1] John C. O'Horo,[1,2] Douglas Challener,[1] John Raymond Go,[1] Daniel C. DeSimone,[1,3] and M. Rizwan Sohail[4]

[1]Division of Infectious Diseases, Department of Medicine, Mayo Clinic, Rochester, Minnesota, USA, [2]Division of Pulmonary and Critical Care, Mayo Clinic, Rochester, Minnesota, USA, [3]Department of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota, USA, and [4]Section of Infectious Diseases, Baylor College of Medicine, Houston, Texas, USA

Background. Nocardial brain abscesses are rare, and published literature describing brain abscesses due to *Nocardia* species is limited to individual case reports or small series. We report one of the largest contemporary retrospective studies describing risk factors, diagnostic evaluation, management, and outcomes of nocardial brain abscess.

Methods. Retrospective review of all adults with brain abscess due to culture-confirmed *Nocardia* species at our institution between January 1, 2009, and June 30, 2020.

Results. Overall, 24 patients had nocardial brain abscesses during the study period. The median age at presentation was 64 years, and 62.5% were immunocompromised. Pulmonary and cutaneous infections were the most common primary sites of nocardial infection. All 24 patients had magnetic resonance imaging performed, and the frontal lobe was the most commonly involved. The most common organism isolated was *Nocardia farcinica*, followed by *Nocardia wallacei* and *Nocardia cyriacigeorgica*. Thirteen patients were managed with antimicrobial therapy alone, while 11 had both medical and surgical management. In all patients, dual therapy was recommended for the initial 6 weeks of treatment, and 22 patients received at least 1 oral agent as part of their final antibiotic regimen, predominantly trimethoprim-sulfamethoxazole and linezolid. Fourteen patients achieved complete clinical and radiographic resolution of infection.

Conclusions. *Nocardia* is an important cause of brain abscess in the immunocompromised host. Early diagnostic and therapeutic aspiration may help health care providers confirm the diagnosis, choose an appropriate antimicrobial regimen, and achieve source control.

Keywords. brain abscess; management; *Nocardia*; risk factors.

Brain abscesses are rare, with a worldwide estimated incidence ranging from 0.3 to 1.3 per 100 000 persons per year [1]. However, they tend to occur with considerably higher frequency in immunocompromised patients. Nocardial brain abscesses are exceedingly uncommon and comprise only 2% of all intracranial abscesses [2]. *Nocardia* has a unique tropism for the brain [3]. Infection is usually acquired through inhalation. Central nervous system (CNS) involvement may occur via hematogenous spread or direct extension from a contiguous cranial infection site following head trauma [4, 5]. The spectrum of CNS infection ranges from diffuse cerebral infiltration, meningitis, spinal cord infection, to brain abscess.

Over the last 30 years, the introduction of new antibiotics and diagnostic procedures has considerably changed the management of brain abscesses. However, even with the advancement of imaging technologies and antimicrobial therapy, mortality rates for nocardial brain abscesses remain high, up to 30%, compared with 10% for other bacterial causes [6].

Published data on the *Nocardia* spp. causing brain abscesses are dated or limited to case reports or small case series that often lack details about diagnostic and management interventions and clinical outcomes data. Understanding the interplay between patient factors and laboratory and and radiologic findings of nocardial brain abscesses may improve the identification of individuals at risk. Therefore, we aimed to describe the clinical presentation, treatment, and outcomes of patients with *Nocardia* brain abscess in a contemporary cohort at a large referral center.

METHODS

We retrospectively reviewed all adult patients (≥18 years old) with an *International Classification of Disesases,* Ninth Revision and Tenth Revision, Clinical Modification diagnosis of brain abscess at our institution from January 1, 2009, through June 30, 2020. A brain abscess was defined as a localized intracerebral collection of necrotic material surrounded by a well-vascularized capsule associated with at least 1 of the following 3 characteristics: (a) positive blood cultures for *Nocardia* spp., (b) positive cultures for *Nocardia* spp. in brain abscess

Received 18 November 2020; editorial decision 28 January 2021; accepted 1 February 2021.
Correspondence: Cristina Corsini Campioli, MD, Division of Infectious Diseases, 200 First Street SW, Rochester, MN 55905 (corsinicampioli.cristina@mayo.edu).

Open Forum Infectious Diseases®2021

DOI: 10.1093/ofid/ofab067

aspirate, (c) presence of *Nocardia* organisms on histopathology of the excised brain material.

Clinical specimens from blood and brain aspirate were cultured on-site in BD Bactec mycobacteria growth indicator tube (MGIT) 960 broth in mycobacterial growth indicator tubes (Becton, Dickinson and Company, Franklin Lakes, NJ, USA) and on Middlebrook 7H11/7H11S agar biplates incubated at 35°C to 37°C for up to 6 weeks. Positive MGIT broth was subcultured to a Middlebrook 7H11 agar plate, and isolated colony growth was identified using Sanger sequencing of a 500-bp region of the 16S rRNA gene. A 100% match to the database entry was required for identification. From August 2014, matrix-assisted laser desorption ionization time-of-flight mass spectrophotometry (MALDI-TOF MS) was added to supplement species identification using Sanger sequencing [7, 8].

Brain abscess cases were further categorized as health care–associated infections (HAIs) if brain abscess developed ≥48 hours after admission, was not present at the time of admission, and the patient was admitted for a cause other than *Nocardia* [9]. Immunocompromised patients were defined as solid organ or bone marrow transplant recipients, patients with hematologic or solid malignancy, and those currently on antineoplastic chemotherapy, immunomodulators, or other immunosuppressive drugs, including corticosteroids (≥5 mg/d for >14 days). Final antibiotic therapy was defined as an antibiotic regimen used for >50% of the total duration of therapy. Species were labeled susceptible if >80% of isolates tested were susceptible. Relapsed was defined as the association of clinical and radiological signs of nocardiosis with the isolation of the same *Nocardia* species after the cessation of antimicrobial treatment for nocardiosis. Clinical, laboratory, and radiographic data were extracted from the electronic health record. The study was approved by the Mayo Clinic Institutional Review Board (IRB# 20-000488).

Categorical variables were reported as frequencies and proportions. Continuous variables were reported as median (interquartile range [IQR]). Five-year mortality was reported with a Kaplan-Meier curve. Statistical analysis was performed using JMP, version 14.1.0 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Demographic Characteristics

A total of 247 adult patients with brain abscess were screened, and 24 (9.7%) patients met the study criteria. The median age at presentation (IQR) was 64 (58.5–71.2) years, and 75% were males. The most common underlying medical conditions were chronic kidney disease (45.8%), hypertension (33.3%), and diabetes mellitus (29.1%). Fifteen (62.5%) patients were immunocompromised, including 3 patients (20%) with head and neck malignancy. Other malignancies included prostate cancer (20%), lung adenocarcinoma (13.3%), and lymphoma (13.3%). Two patients (8.3%) had head and neck surgery. Nine patients (37.5%) were on prednisone, with a median dose (IQR) of 10 (8.7–23) mg for >2 weeks. Seven (29.2%) patients were on other immunomodulatory therapies as summarized in Table 1. The median time from solid organ transplant (SOT) to diagnosis of *Nocardia* spp. brain abscess (IQR) was 876 (261–1698) days. A total of 4 patients were on trimethoprim-sulfamethoxazole (TMP-SMX) for *Pneumocystis* pneumonia prophylaxis. The median Charlson Comorbidity Index (CCI) score (IQR) was 7 (4.25–10).

Clinical and Radiologic Presentation

Lung and cutaneous infections were the most common primary sites of nocardial infection (37.5% and 12.5%, respectively). Lung infections were more frequent in immunocompromised than immunocompetent hosts (71% vs 29%). The immunocompetent host was more likely to have nocardiosis due to presumed direct inoculation secondary to trauma than the immunocompromised patients (62% vs 38%). Three (12.5%) cases were HAIs, and the infectious diseases (ID) team was consulted on all patients during their hospitalization.

All 24 patients had magnetic resonance imaging (MRI) performed, and 19 (79.1%) patients had a head computed tomography (CT). Of the patients who had a head CT, 13 (68.4%) had similar findings, but 6 (31.6%) had fewer lesions when compared with the MRI. Eight (33.3%) patients had >1 intracranial fluid collection. The most common location was the frontal lobe (41.6%), followed by parietal (37.5%), temporal (33.3%), and occipital (12.5%). Two patients had cerebellar involvement. The fluid collections' median diameter size (IQR) was 14 (10–21) mm, and midline shift was observed in 8.4% of cases.

Microbiology

All 24 patients had a positive culture result from direct brain abscess sampling. The most common species isolated were *Nocardia farcinica* (n = 9; 37.5%), *N. wallacei* (n = 3; 12.5%), *N. cyriacigeorgica* (n = 3; 12.5%), *N. abscessus* (n = 1; 4.1%), *N. otitidiscaviarum* (n = 1; 4.1%), *N. transvalensis* (n = 1; 4.1%), and *N. argoensis* (n = 1; 4.1%). Similarly, all 24 patients had peripheral blood cultures performed, but only 3 patients had a positive blood culture for *Nocardia* spp. (Table 2).

Management and Outcomes

Thirteen (54.2%) patients were managed solely by medical management, while 11 (45.8%) had both medical and surgical management (Table 2). The median time from nocardial brain abscess diagnosis to surgical therapeutic intervention (IQR) was 3 (0.2–6) days.

Corticosteroids were used as part of the medical treatment in 10 (41.6%) patients, mostly due to midline shift and neurologic deficits. Dexamethasone was most commonly used (8; 33.3%), with a median dose (IQR) of 6 (4–12) mg per day and a median duration (IQR) of 14 (5–71.5) days.

Table 1. Clinical Characteristics of Patients With Nocardial Brain Abscess

Variables	Nocardial Brain Abscess Cases (n = 24)
Demographics, No. (%)	
Female	6 (25)
Male	18 (75)
Age, median (IQR), y	64 (58.5–71.2)
Race (%)	
White	23 (95.8)
Black or African American	1 (4.2)
Comorbidities, No. (%)	
Malignancy	13 (54.1)
Head and neck	3 (12.5)
Chronic kidney disease	11 (45.8)
Hemodialysis	4 (16.6)
Essential hypertension	8 (33.3)
Diabetes mellitus	7 (29.1)
Insulin-dependent	3 (12.5)
Congestive heart failure	6 (25)
Peripheral vascular disease	5 (20.8)
Chronic obstructive pulmonary disease	3 (12.5)
Immunocompromised, No. (%)	15 (62.5)
Solid organ transplant	7 (29.1)
Kidney	4 (16.7)
Lung	2 (8.3)
Liver	1 (4.2)
Bone marrow transplant	3 (12.5)
Prednisone (≥5 mg/d)	9 (37.5)
Calcineurin inhibitors	6 (25)
Antiproliferative agents	6 (25)
mTOR inhibitors	1 (4.2)
CCI, median (IQR)	7 (4.5–10)

Abbreviations: CCI, Charlson Comorbidity Index; IQR, interquartile range; mTOR, mammalian target of rapamycin.

The most common empiric antibiotic therapy used alone and/or in combination was TMP-SMX in 41.6% of cases, followed by vancomycin (37.5%), linezolid (33.3%), metronidazole (33.3%), and meropenem (21.1%). A total of 20 patients (83.3%) had at least 1 active antibiotic started empirically. The most common definitive antibiotic regimen based on susceptibilities is summarized in Table 2. Susceptibility testing varied among different species. All isolates were susceptible to TMP-SMX. Additional trends included *N. farcinica* susceptible to linezolid, moxifloxacin, and imipenem; *N. wallacei* was susceptible to minocycline and linezolid; *N. cyriacigeorgica* was susceptible to ceftriaxone and linezolid. In all patients, dual therapy was administered for the initial 6 weeks of treatment. A total of 8 (33.3%) patients received monotherapy, with 7 receiving TMP-SMX monotherapy as part of the final regimen after 6 weeks of induction therapy. The median duration of parenteral antibiotic therapy was 21 days. Twenty-two (91.7%) patients received at least 1 oral agent as part of their final antibiotic regimen, mainly TMP-SMX and linezolid. The final median antibiotic duration (IQR) was 322 (180.5–365) days. Thirty-six percent of patients receiving immunosuppressive therapy had reductions in immunosuppression as part of their management.

Fourteen (58.3%) patients achieved complete resolution of the clinical manifestations and radiographic resolution of brain fluid collection. Two (8.3%) had permanent neurological deficits (left hemiparesis and seizure, respectively), 3 (12.5%) patients relapsed, and 1 (4.1%) patient progressed despite medical therapy requiring surgical intervention at a later time during his hospital course. A total of 7 (29.1%) patients died, with a median time from diagnosis to death of 169 days. Four of these (16.6%) deaths were related to underlying chronic conditions including malignancy and cardiovascular disease. The average follow-up time for this cohort was 19 months. Figure 1 shows that ~60% of patients with nocardial brain abscess survived at 5 years.

DISCUSSION

The current study is one of the largest contemporary cohorts to describe the risk factors, clinical and radiographic features, management interventions, and outcomes of nocardial brain abscess. *Nocardia* brain abscess occurs mostly in the fifth to sixth decades of life [10, 11], with the peak occurrence between ages 43 and 75 years. Purported risk factors for developing nocardial brain abscess include age, gender, and immunocompromised status [12, 13]. In our cohort, patients who presented with a nocardial brain abscess were older and predominantly Caucasian males, consistent with prior reports [14–16]. Higher incidence of nocardial brain abscesses in older age may be due to immunosenescence, a physiological part of aging linked to a higher risk of infection in part due to the excessive production of pro-inflammatory cytokines by macrophages and fibroblasts that may impact the innate and adaptive immune systems, which are crucial in the development of nocardial brain abscess [17, 18].

Systemic infection with *Nocardia* spp. most often occurs in immunosuppressed patients and rarely in immunocompetent individuals [4, 19, 20]. In our cohort, the percentage of immunocompromised individuals, including 10 transplant patients and those receiving corticosteroids, was higher than in other published studies [21–26]. Cell-mediated immune deficiencies, in particular, seem to be a major predisposing factor for *Nocardia* infections [20, 27]. As seen in our series, steroids or other immunosuppressive medications such as calcineurin inhibitors, antiproliferative agents, and mTOR inhibitors can suppress cell-mediated immunity, likely contributing to the high prevalence of *Nocardia* infections [20, 27, 28]. As the overall population ages and more patients receive various immunosuppressive therapies due to expanding indications, we may see more nocardial abscesses in the future.

Chronic corticosteroid therapy, especially at higher doses and with prolonged durations, has been associated with

Table 2. Clinical Presentation and Management of Patients With Nocardial Brain Abscess

Cases	Age, Gender	Immunocompromised Host	Primary Source	Brain Abscess Location	Diameter, mm[a]	Positive Blood Cultures	*Nocardia* Spp. on Direct Brain Abscess Sampling	Final Antibiotic Therapy	Final Antibiotic Route	Duration of Therapy, d	Type of Surgical Intervention	Outcome
1	80, M	Yes	Pulmonary	Frontal	12	No	*N. wallacei*	Moxifloxacin, amikacin	Oral/IV	84	None	Died[b]
2	72, M	Yes	Skin	Frontal, parietal and midbrain	17	Yes	*N. farcinica*	TMP-SMX	IV	180	Open aspiration	Relapsed and died
3	74, M	No	Unknown	Parietal, brain stem and cerebellum	13	No	*N. farcinica*	TMP-SMX	Oral	336	Open aspiration	Permanent neurologic deficit
4	63, F	No	Pulmonary	Frontal, occipital and temporal	21	No	*N. cyriacigeorgica*	Ceftriaxone	IV	168	None	Cured
5	77, F	No	CNS trauma	Temporal	24	No	*Nocardia* spp.	TMP-SMX, doxycycline	IV/oral	168	Open aspiration	Cured
6	50, M	Yes	Unknown	Temporal	41	No	*N. farcinica*	Linezolid, amoxicillin-clavulanate	Oral	224	Open aspiration	Relapse and died
7	94, M	Yes	Pulmonary	Temporal and parietal	15	No	*N. farcinica*	Linezolid, imipenem	Oral/IV	14	Stereotactic	Died[b]
8	73, F	No	Unknown	Parietal	8	No	*N. wallacei*	Linezolid, TMP-SMX, minocycline	Oral	308	None	Relapse and died[b]
9	65, M	Yes	Pulmonary	Cerebellum and forebrain	10	No	*N. farcinica*	TMP-SMX, moxifloxacin, doxycycline	Oral	280	None	Cured
10	69, M	No	Pulmonary	Frontal	10	No	*N. cyriacigeorgica*	TMP-SMX	Oral	365	None	Required delayed surgical intervention
11	50, M	Yes	Unknown	Parietal	5	No	*N. otitidiscaviarum*	TMP-SMX, amikacin	Oral/IV	260	None	Cured
12	66, M	Yes	Skin	Brain stem	4	No	*Nocardia* spp.	TMP-SMX, amoxicillin-clavulanate	Oral	365	None	Cured
13	49, M	No	Pulmonary	Parietal	6.6	Yes	*N. farcinica*	TMP-SMX, moxifloxacin	Oral	365	None	Cured
14	61, M	Yes	Skin	Frontal	4	No	*Nocardia* spp.	TMP-SMX	Oral	365	None	Cured
15	64, M	Yes	Unknown	Midbrain	21	No	*Nocardia* spp.	TMP-SMX	Oral	365	None	Permanent neurologic deficit
16	60, F	Yes	Unknown	Temporal and parietal	10	No	*N. argoensis*	TMP-SMX, moxifloxacin	Oral	365	Open aspiration	Cured
17	34, M	Yes	Pulmonary	Temporal	26	No	*Nocardia* spp.	TMP-SMX	Oral	365	Open aspiration	Cured
18	64, M	Yes	Unknown	Occipital and temporal	17	No	*N. cyriacigeorgica*	Linezolid, TMP-SMX	Oral	504	Open aspiration	Cured
19	50, M	Yes	CNS trauma	Frontal, occipital, temporal, and parietal	13	No	*N. farcinica*	TMP-SMX, ceftriaxone	Oral/IV	196	None	Died
20	61, F	No	Unknown	Frontal	10	No	*N. farcinica*	Linezolid, ceftriaxone	Oral/IV	182	None	Cured
21	69, M	No	Unknown	Parietal	22	No	*N. farcinica*	TMP-SMX	Oral	365	Stereotactic	Cured
22	69, F	Yes	Pulmonary	Frontal	20	No	*N. transvalensis*	TMP-SMX, doxycycline	Oral	365	None	Cured
23	58, M	No	Unknown	Frontal	20	No	*N. abscessus*	TMP-SMX, amoxicillin-clavulanate	Oral	365	Open aspiration	Cured
24	63, M	Yes	Pulmonary	Frontal	25	Yes	*N. wallacei*	TMP-SMX, imipenem	Oral/IV	20	Stereotactic	Died

Abbreviations: CNS, central nervous system; F, female; IV, intravenous; M, male; TMP-SMX, trimethoprim-sulfamethoxazole.

[a]Diameter of the largest lesion in cases when more than 1 lesion was present.

[b]Death related to *Nocardia* infection.

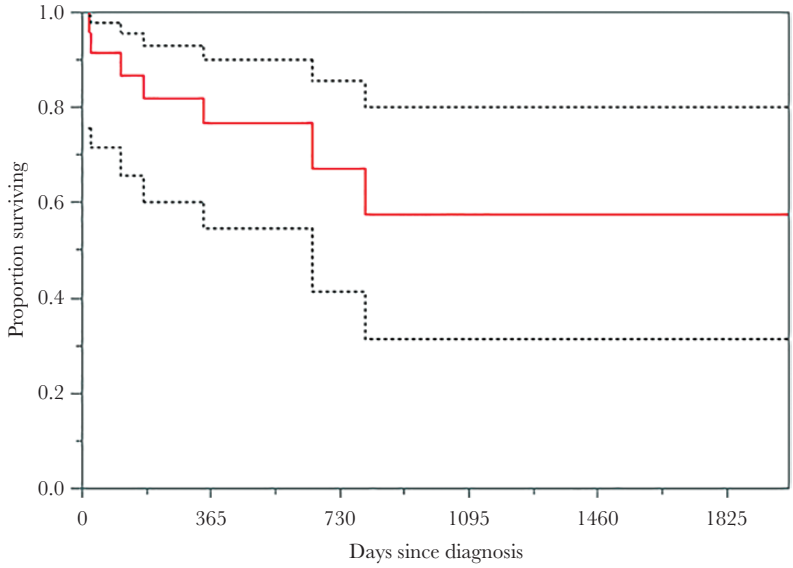

Figure 1. Survival curve is patients with *Nocardia* spp. brain abscess.

increased risk of opportunistic infections such as *Pneumocystis* pneumonia—thus the recommendation for TMP-SMX prophylaxis [5, 29]. Daily TMP-SMX prophylaxis also may prevent nocardiosis and account for the reduced prevalence of this organism in patients with AIDS and SOT recipients [30, 31]. However, breakthrough nocardial infections may occur in the context of low-dose or intermittent TMP-SMX prophylaxis [32–34]. Interestingly, in our series, 4 patients were on 1 TMP-SMX double-strength tablet daily for prophylaxis and still developed nocardial brain abscess. Therefore, if the suspicion for *Nocardia* infection is high, use of TMP-SMX prophylaxis should not dissuade clinicians from considering nocardial abscesses in differential diagnosis.

Primary lung infection, likely due to inhalation, was the most frequent mechanism of infection acquisition in our cohort, similar to earlier observations [26, 35]. Hematologic spread with a high propensity to the skin and subcutaneous tissue or CNS has also been described [5, 19, 36]. In our series, *Nocardia* spp. grew in the blood cultures of only 3 patients. Detailed skin examination and CT of the chest can be helpful to identify the primary site of infection. Interestingly, although ID was consulted in all cases in our series and a thorough evaluation was performed, the primary infection source could not be identified in 41.7% of the cases. We hypothesize that infection may have started as a direct inoculum from trauma or inhalation but infection at the primary site was subclinical and therefore no primary source was identified.

Nocardial brain abscesses may present as a hyperenhancing multiloculated ring lesions. As the infection usually occurs through inhalation and from direct spread from the sinuses [37], the frontal lobe is commonly involved. However, location, size, and appearance of nocardial brain abscesses alone cannot be used to differentiate these from other causes of bacterial abscesses. Sometimes it is difficult to differentiate nocardial abscesses from intracranial metastatic malignancy on CT or MRI [38]. Therefore, while MRI continues to be the preferred radiologic method for imaging of suspected nocardial abscesses [39], diagnostic aspiration is necessary to confirm the diagnosis and for selection of appropriate antimicrobial therapy.

The importance of isolating and culturing the *Nocardia* spp. is due to concern for resistance to specific antimicrobial agents [40]. However, *Nocardia* spp. have relatively slow growth, and they can be difficult to culture in the laboratory, making the 16S rRNA gene sequencing method a reliable alternative for identification [19]. Kiska et al. [41] concluded that no single method could accurately identify all *Nocardia* spp. associated with human infections. A combination of the antimicrobial susceptibility pattern, colony pigment, biochemical tests, and molecular techniques could potentially identify all isolates to the species level. To date, no specific brain tropism has been identified to a particular species. The present study was concordant with previous reports [3, 42–45] where *N. farcinica* and *N. abscessus* were the most commonly encountered species.

In general, the most active agents against *Nocardia* species include TMP-SMX, amikacin, minocycline, and imipenem [46, 47]. However, no randomized trials have been performed to compare the efficacy of different antibiotic regimens for nocardiosis. A study by Brown-Elliott et al. involving 522 clinical isolates reported that only 2% of the isolates demonstrated

in vitro resistance to TMP-SMX [40]. Hamdi et al. reported similar results [46]. Sulfonamides and trimethoprim are small lipophilic antibiotics. At high doses, the penetration into the cerebrospinal fluid, in both the absence and the presence of meningeal inflammation, is considered sufficient for the treatment of CNS infections with susceptible bacteria [48]. Based on these observations, TMP-SMX is considered the mainstay of therapy [26, 49]. Acknowledging the high morbidity and mortality associated with nocardial brain abscesses, TMP-SMX should be used in combination with another highly bioavailable antimicrobial with good CNS penetration for induction therapy for nocardial brain abscess. Given the small number of patients in our study and earlier publications, no definitive recommendations can be made, and larger, multicenter studies are needed to determine the optimal treatment regimen.

Despite the limited literature, surgical excision is considered necessary in most cases [2, 50]. Lee et al. reported aspiration alone in 90.9% of their patients with no reported deaths [51]. In a study by Hall et al. [52], surgical aspirations alone were considered appropriate as the initial management of brain abscess. Others have proposed that craniotomy and excision of the entire abscess and wall are more effective than aspiration and drainage [2]. In our patient population, 54.2% of the cases had no surgical management, likely due to the smaller median brain abscess diameter size in our cohort (14 mm). In general, surgical aspiration is recommended and preferred in lesions larger than 2.5 cm in diameter [2].

Patients with nocardial brain abscess may have residual motor deficits and hearing impairment even with successful treatment for underlying infection [2]. In our cohort, hemiparesis and seizure were encountered only in few cases. The majority (62.5%) of our patients had a good outcome. Poor outcomes, including death, were mainly due to patients' underlying comorbidities. This is further supported by a high median CCI score in our cohort. Due to the small size, we were unable to conclude if medical management vs a combination of medical and surgical management impacts patient outcomes. However, it stands to reason that early diagnosis and surgical management may be associated with reduced morbidity and mortality due to early and effective source control.

Limitations

The retrospective nature of the study with a case determination that was based on the claims data set is the primary limitation. Decisions regarding diagnostic testing and therapeutic interventions were left to the discretion of treating physicians and were not based on any standardized protocol. Due to the small size of our cohort, we were unable to assess the statistical significance of our observation. Finally, even though the Mayo Clinic in Minnesota receives patients from other cities and rural areas, the high prevalence of immunocompromised patients and those presenting from the Midwest limits our ability to generalize our findings.

CONCLUSIONS

Older, immunocompromised, and high-morbidity populations are at increased risk for nocardial brain abscesses. Early diagnostic and therapeutic aspiration may help health care providers confirm diagnosis, choose an appropriate antimicrobial regimen, and reduce morbidity and mortality due to early and adequate source control.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Acknowledgments

Financial support. None for all authors.

Potential conflicts of interest. M.R.S.: honoraria/consulting fee: Medtronic Inc., Philips, and Aziyo Biologics, Inc. (all <US$10K); research grant: Medtronic. J.C.O. has provided consulting services for Elsevier, Inc., and Bates College. All other authors: none. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Patient consent. The design of the work was approved by the local institutional review board (IRB# 20-000488). The study was considered minimal risk, and patient consent requirements were waived.

Author contributions. Cristina Corsini Campioli, MD: conception or design of the work, data collection, data analysis and interpretation, drafting the article, critical revision of the article, final approval of the version to be published; Natalia E. Castillo Almeida, MD: drafting the article, critical revision of the article, final approval of the version to be published; John C. O'Horo, MD: conception or design of the work, critical revision of the article, final approval of the version to be published; Douglas Challener, MD: data analysis and interpretation, critical revision of the article; John Raymond Go, MD: critical revision of the article; Daniel C. DeSimone, MD: critical revision of the article; M. Rizwan Sohail, MD: conception or design of the work, drafting the article, critical revision of the article, final approval of the version to be published.

References

1. Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess: systematic review and meta-analysis. Neurology **2014**; 82:806–13.
2. Mamelak AN, Obana WG, Flaherty JF, Rosenblum ML. Nocardial brain abscess: treatment strategies and factors influencing outcome. Neurosurgery **1994**; 35:622–31.
3. Al Tawfiq JA, Mayman T, Memish ZA. *Nocardia abscessus* brain abscess in an immunocompetent host. J Infect Public Health **2013**; 6:158–61.
4. Alijani N, Mahmoudzadeh S, Hedayat Yaghoobi M, et al. Multiple brain abscesses due to *Nocardia* in an immunocompetent patient. Arch Iran Med **2013**; 16:192–4.
5. Cattaneo C, Antoniazzi F, Caira M, et al. *Nocardia* spp. infections among hematological patients: results of a retrospective multicenter study. Int J Infect Dis **2013**; 17:e610–4.
6. Cassir N, Million M, Noudel R, et al. Sulfonamide resistance in a disseminated infection caused by *Nocardia wallacei*: a case report. J Med Case Rep **2013**; 7:103.
7. Patel R. MALDI-TOF MS for the diagnosis of infectious diseases. Clin Chem **2015**; 61:100–11.
8. Buckwalter SP, Olson SL, Connelly BJ, et al. Evaluation of matrix-assisted laser desorption ionization-time of flight mass spectrometry for identification of

Mycobacterium species, *Nocardia* species, and other aerobic *Actinomycetes*. J Clin Microbiol **2016**; 54:376–84. Available at: https://www.cdc.gov/hai/index.html.
9. Centers for Disease Control and Prevention. Healthcare-associated infections.
10. Mcclelland CJ, Craig BF, Crockard HA. Brain abscesses in Northern-Ireland - 30-year community review. J Neurol Neurosur Psychiatry **1978**; 41:1043–47.
11. Nicolosi A, Hauser WA, Musicco M, Kurland LT. Incidence and prognosis of brain abscess in a defined population: Olmsted County, Minnesota, 1935-1981. Neuroepidemiology **1991**; 10:122–31.
12. Zhang C, Hu L, Wu X, et al. A retrospective study on the aetiology, management, and outcome of brain abscess in an 11-year, single-centre study from China. BMC Infect Dis **2014**; 14:311.
13. Muzumdar D, Jhawar S, Goel A. Brain abscess: an overview. Int J Surg **2011**; 9:136–44.
14. Manzar N, Manzar B, Kumar R, Bari ME. The study of etiologic and demographic characteristics of intracranial brain abscess: a consecutive case series study from Pakistan. World Neurosurg **2011**; 76:195–200; discussion 79–83.
15. Menon S, Bharadwaj R, Chowdhary A, et al. Current epidemiology of intracranial abscesses: a prospective 5 year study. J Med Microbiol **2008**; 57:1259–68.
16. Ong CT, Tsai CF, Wong YS, Chen SC. Epidemiology of brain abscess in Taiwan: a 14-year population-based cohort study. PLoS One **2017**; 12:e0176705.
17. Aw D, Silva AB, Palmer DB. Immunosenescence: emerging challenges for an ageing population. Immunology **2007**; 120:435–46.
18. De Martinis M, Franceschi C, Monti D, Ginaldi L. Inflamm-ageing and lifelong antigenic load as major determinants of ageing rate and longevity. FEBS Lett **2005**; 579:2035–9.
19. Chung TT, Lin JC, Hsieh CT, et al. *Nocardia farcinica* brain abscess in an immunocompetent patient treated with antibiotics and two surgical techniques. J Clin Neurosci **2009**; 16:1675–7.
20. Al-Tawfiq JA, Al-Khatti AA. Disseminated systemic *Nocardia farcinica* infection complicating alefacept and infliximab therapy in a patient with severe psoriasis. Int J Infect Dis **2010**; 14:e153–7.
21. Tseng JH, Tseng MY. Brain abscess in 142 patients: factors influencing outcome and mortality. Surg Neurol **2006**; 65:557–62; discussion 562.
22. Xiao F, Tseng MY, Teng LJ, et al. Brain abscess: clinical experience and analysis of prognostic factors. Surg Neurol **2005**; 63:442–9; discussion 449–50.
23. Landriel F, Ajler P, Hem S, et al. Supratentorial and infratentorial brain abscesses: surgical treatment, complications and outcomes-a 10-year single-center study. Acta Neurochir **2012**; 154:903–11.
24. Frank M, Woschnagg H, Mölzer G, Finsterer J. Cerebellar nocardiosis and myopathy from long-term corticosteroids for idiopathic thrombocytopenia. Yonsei Med J **2010**; 51:131–7.
25. Kim YK, Sung H, Jung J, et al. Impact of immune status on the clinical characteristics and treatment outcomes of nocardiosis. Diagn Microbiol Infect Dis **2016**; 85:482–7.
26. Yang M, Xu M, Wei W, et al. Clinical findings of 40 patients with nocardiosis: a retrospective analysis in a tertiary hospital. Exp Ther Med **2014**; 8:25–30.
27. Adjamian N, Kikam A, Wessell KR, et al. *Nocardia* brain abscess and CD4(+) lymphocytopenia in a previously healthy individual. Case Reports Immunol **2015**; 2015:374956.
28. Wilson JW. Nocardiosis: updates and clinical overview. Mayo Clin Proc **2012**; 87:403–7.
29. Martínez Tomás R, Menéndez Villanueva R, Reyes Calzada S, et al. Pulmonary nocardiosis: risk factors and outcomes. Respirology **2007**; 12:394–400.
30. Peterson PK, Ferguson R, Fryd DS, et al. Infectious diseases in hospitalized renal transplant recipients: a prospective study of a complex and evolving problem. Medicine (Baltimore) **1982**; 61:360–72.
31. Goodlet KJ, Tokman S, Nasar A, Cherrier L, Walia R, Nailor MD. Nocardia prophylaxis, treatment, and outcomes of infection in lung transplant recipients: A matched case-control study. Transpl Infect Dis **2020**:e13478. doi:10.1111/tid.13478.
32. Chouciño C, Goodman SA, Greer JP, et al. Nocardial infections in bone marrow transplant recipients. Clin Infect Dis **1996**; 23:1012–9.
33. Coussement J, Lebeaux D, van Delden C, et al; European Study Group for *Nocardia* in Solid Organ Transplantation. *Nocardia* infection in solid organ transplant recipients: a multicenter European case-control study. Clin Infect Dis **2016**; 63:338–45.
34. Lebeaux D, Freund R, van Delden C, et al. Outcome and treatment of nocardiosis after solid organ transplantation: new insights from a European study. Clin Infect Dis **2017**; 64:1396–405.
35. Matulionyte R, Rohner P, Uçkay I, et al. Secular trends of *Nocardia* infection over 15 years in a tertiary care hospital. J Clin Pathol **2004**; 57:807–12.
36. McNeil MM, Brown JM. The medically important aerobic actinomycetes: epidemiology and microbiology. Clin Microbiol Rev **1994**; 7:357–417.
37. Lange N, Berndt M, Jörger AK, et al. Clinical characteristics and course of primary brain abscess. Acta Neurochir (Wien) **2018**; 160:2055–62.
38. Lin YJ, Yang KY, Ho JT, et al. Nocardial brain abscess. J Clin Neurosci **2010**; 17:250–3.
39. Sartoretti E, Sartoretti T, Gutzwiller A, et al. Advanced multimodality MR imaging of a cerebral nocardiosis abscess in an immunocompetent patient with a focus on amide proton transfer weighted imaging. BJR Case Rep **2020**; 6:20190122.
40. Brown-Elliott BA, Biehle J, Conville PS, et al. Sulfonamide resistance in isolates of *Nocardia* spp. from a US multicenter survey. J Clin Microbiol **2012**; 50:670–2.
41. Kiska DL, Hicks K, Pettit DJ. Identification of medically relevant *Nocardia* species with an abbreviated battery of tests. J Clin Microbiol **2002**; 40:1346–51.
42. Farran Y, Antony S. *Nocardia abscessus*-related intracranial aneurysm of the internal carotid artery with associated brain abscess: a case report and review of the literature. J Infect Public Health **2016**; 9:358–61.
43. Galacho-Harriero A, Delgado-López PD, Ortega-Lafont MP, et al. *Nocardia farcinica* brain abscess: report of 3 cases. World Neurosurg **2017**; 106:1053.e15–24.
44. Benek HB, Akcay E, Yilmaz H, Yis R, Yurt A. *Nocardia cyriacigeorgica* brain abscess with *Pemphigus vulgaris*: first report. Br J Neurosurg. **In press**.
45. Kumar VA, Augustine D, Panikar D, et al. *Nocardia farcinica* brain abscess: epidemiology, pathophysiology, and literature review. Surg Infect (Larchmt) **2014**; 15:640–6.
46. Hamdi AM, Fida M, Deml SM, Abu Saleh OM, Wengenack NL. Retrospective analysis of antimicrobial susceptibility profiles of *Nocardia* species from a tertiary hospital and reference laboratory, 2011 to 2017. Antimicrob Agents Chemother. **In press**.
47. Mosel D, Harris L, Fisher E, et al. Disseminated *Nocardia* infection presenting as hemorrhagic pustules and ecthyma in a woman with systemic lupus erythematosus and antiphospholipid antibody syndrome. J Dermatol Case Rep **2013**; 7:52–5.
48. Wang EE, Prober CG. Ventricular cerebrospinal fluid concentrations of trimethoprim-sulphamethoxazole. J Antimicrob Chemother **1983**; 11:385–9.
49. Rosman Y, Grossman E, Keller N, et al. Nocardiosis: a 15-year experience in a tertiary medical center in Israel. Eur J Intern Med **2013**; 24:552–7.
50. Cooper CJ, Said S, Popp M, et al. A complicated case of an immunocompetent patient with disseminated nocardiosis. Infect Dis Rep **2014**; 6:9–12.
51. Lee GY, Daniel RT, Brophy BP, Reilly PL. Surgical treatment of nocardial brain abscesses. Neurosurgery **2002**; 51:668–71; discussion 671–2.
52. Hall WA, Martinez AJ, Dummer JS, Lunsford LD. Nocardial brain abscess: diagnostic and therapeutic use of stereotactic aspiration. Surg Neurol **1987**; 28:114–8.