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Disseminated Nocardia niwae Infection With Central Nervous System Involvement: A Report of Two Cases and Review of Literature

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Abstract

We describe two new cases of *Nocardia niwae* infection in a single center, together with two previously published cases identified through a literature review, to summarize the clinical, microbiological, and outcome patterns seen so far for this rare species. Of the four cases, three patients were immunocompromised, and one was immunocompetent. All four had disseminated infection with both central nervous system (CNS) and pulmonary involvement, and three were initially misdiagnosed as malignancy before *Nocardia* was identified. Two of the four patients died, and both were immunocompromised. Antimicrobial susceptibility was similar across the isolates tested: all four were susceptible to trimethoprim-sulfamethoxazole and linezolid, and all isolates with available data were susceptible to amikacin and resistant to amoxicillin-clavulanate. Across these four cases, *N. niwae* infection was consistently associated with dissemination and CNS involvement. Its tendency to mimic malignancy on imaging underscores the need for tissue biopsy with culture sensitivities and molecular diagnostic tests for timely diagnosis and targeted therapy.

Categories: Internal Medicine, Infectious Disease
Keywords: antimicrobial susceptibility pattern, brain abscess, disseminated nocardiosis, malignancy mimicry, nocardia niwae

Introduction

Nocardia species are aerobic, filamentous, partially acid-fast actinomycetes that cause opportunistic infections in humans, most commonly involving the lungs with potential for hematogenous dissemination to extrapulmonary sites, particularly the central nervous system (CNS) [1,2]. Although nocardiosis predominantly affects immunocompromised individuals, up to one-third of cases occur in immunocompetent hosts, and clinical presentation can be highly variable [2].

Advances in molecular diagnostics, including 16S rRNA sequencing and genomic sequencing of microbial cell-free DNA, along with proteomic methods such as matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry, have led to the identification of numerous novel *Nocardia* species with distinct microbiological and clinical characteristics [3].

Nocardia niwae is a rare species first described in 2011 from isolates recovered from the respiratory tract of patients in Florida, United States [4], based on microbiological data with minimal accompanying clinical detail. Since then, only a few cases with detailed clinical characterization have been published, limiting understanding of its pathogenicity, dissemination patterns, and optimal management.

In this report, we describe two cases of *N. niwae* infection and review reported cases with available clinical data to characterize patterns of host susceptibility, disease distribution, CNS involvement, antimicrobial susceptibility, exposure risks, and geographic trends for this rare pathogen.

Case Presentation

Case 1

A 49-year-old male landscaper with a history of active tobacco use and prior multifocal influenza pneumonia nine months earlier presented with a two-week history of progressive generalized headache, followed by acute-onset altered mental status and fever.

Initial laboratory evaluation revealed hyponatremia, leukocytosis, hypoalbuminemia, and elevated total protein. Neuroimaging with computed tomography (CT) (Figure *1a*) and magnetic resonance imaging (MRI) demonstrated four heterogeneously peripherally enhancing parenchymal lesions involving the right temporal lobe (largest, measuring 2.1 cm) (Figure *1b*), left parietal (Figure *1c*), and left frontal and left thalamic (Figure *1d*) regions, with associated mass effect. CT of the chest revealed a consolidative focus in

the left upper lobe consistent with infectious pneumonia.

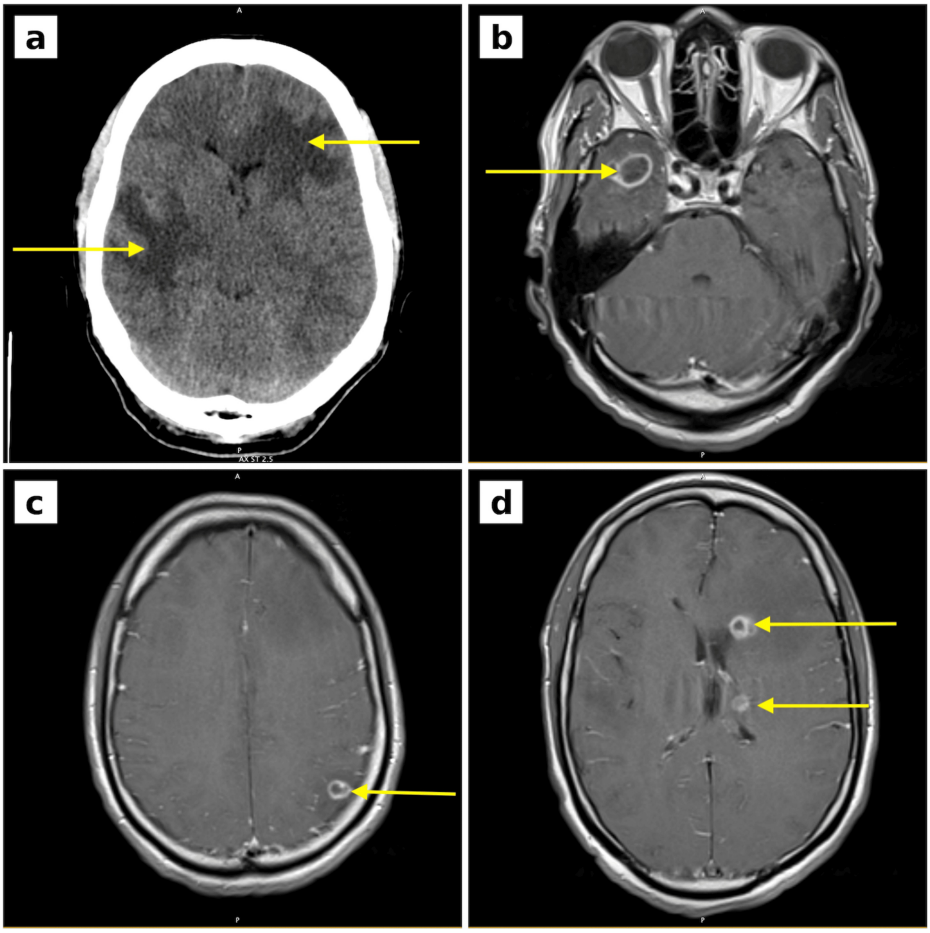


FIGURE 1: Multifocal brain lesions on CT and MRI, Case 1

(a) Axial non-contrast CT showing multifocal cerebral hypoattenuating lesions involving the right temporal (lower arrow) and left frontoparietal (upper arrow) regions with surrounding edema. (b) Axial T1-weighted post-contrast MRI showing a large ring-enhancing lesion with surrounding edema and mass effect in the right temporal lobe (arrow). (c) Axial T1-weighted post-contrast MRI showing a ring-enhancing lesion in the left parietal region (arrow). (d) Axial T1-weighted post-contrast MRI showing ring-enhancing lesions involving the left frontal (upper arrow) and left thalamic (lower arrow) regions.

CT: computed tomography; MRI: magnetic resonance imaging.

During the diagnostic evaluation, he was diagnosed with advanced HIV infection (CD4 percentage 7%, absolute CD4 count 250 cells/µL) with an HIV-1 viral load of 24,000 copies/mL and genotypic resistance to multiple antiretroviral classes.

The patient was empirically started on intravenous cefepime, vancomycin, and metronidazole. Due to significant mass effect from the dominant right temporal lesion, he underwent right temporal craniotomy with drainage of the anterior temporal lobe abscess. Postoperatively, he required intubation and remained febrile, prompting escalation of antimicrobial therapy to intravenous linezolid and meropenem.

Given concern for concomitant meningitis, lumbar puncture was performed three days after the craniotomy. Cerebrospinal fluid analysis demonstrated elevated protein (172 mg/dL), decreased glucose (23 mg/dL), and pleocytosis (188 nucleated cells/µL) with mixed neutrophilic and lymphocytic predominance (55% neutrophils, 42% lymphocytes). Routine cultures, cryptococcal antigen testing, and multiplex polymerase chain reaction were negative; however, molecular testing (MicroGenDX, Lubbock, TX) detected *N. niwae*. Plasma cell-free DNA sequencing (Karius, Redwood City, CA) also identified *N. niwae*.

Intraoperative cultures from the brain abscess demonstrated partially acid-fast, Gram-positive rods on staining, and histopathology revealed filamentous branching organisms (Figure *2*). Species identification was confirmed as *N. niwae* by MALDI-TOF mass spectrometry. Antimicrobial susceptibility testing demonstrated susceptibility to trimethoprim-sulfamethoxazole (TMP-SMX), linezolid, and ceftriaxone, with

resistance to ciprofloxacin and amoxicillin-clavulanate; full results are summarized in Table *1*.

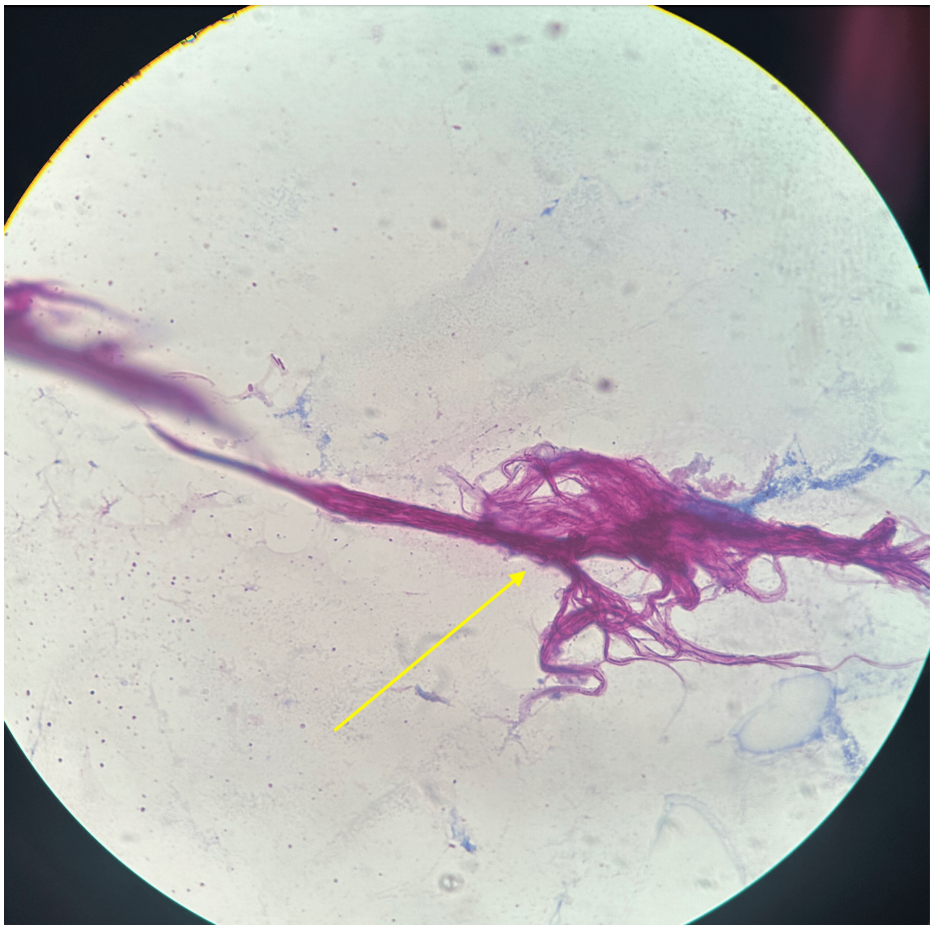


FIGURE 2: Modified Kinyoun stain of brain abscess tissue at 1000× magnification, Case 1

Branching, beaded, filamentous organisms consistent with *Nocardia* species (arrow).

Antimicrobial agent	MIC (µg/mL)	Interpretation
Trimethoprim-sulfamethoxazole	0.25/4.8	S
Linezolid	2	S
Ceftriaxone	2	S
Amikacin	≤0.5	S
Tobramycin	≤2	S
Clarithromycin	2	S
Doxycycline	4	I
Moxifloxacin	2	I
Imipenem	8	I
Minocycline	2	I
Ciprofloxacin	4	R
Amoxicillin-clavulanate	≥256	R

TABLE 1: In vitro antimicrobial susceptibility testing for Nocardia niwae, Case 1

MIC: minimum inhibitory concentration; S: susceptible; I: intermediate; R: resistant.

He was treated for disseminated nocardiosis with CNS and pulmonary involvement using combination antimicrobial therapy with TMP-SMX, linezolid, and ceftriaxone at CNS-penetrating doses. Antiretroviral therapy with bictegravir/emtricitabine/tenofovir alafenamide was initiated approximately two weeks after commencement of nocardiosis-directed treatment in view of extensive CNS disease. Unfortunately, the patient had difficulty with antibiotic adherence and required recurrent hospitalizations related to his infection.

Case 2

A 68-year-old woman with a history of hypothyroidism, anxiety, and osteoporosis presented with a three-week history of progressive cough, dyspnea, chest pain, hemoptysis, fevers, night sweats, and unintentional weight loss following a recent COVID-19 infection. She was undergoing outpatient evaluation for suspected malignancy after prior imaging had identified a 4 cm right upper lobe mass (Figure *3a*, *3b*), with bronchoscopy and image-guided biopsy pending at the time of presentation.

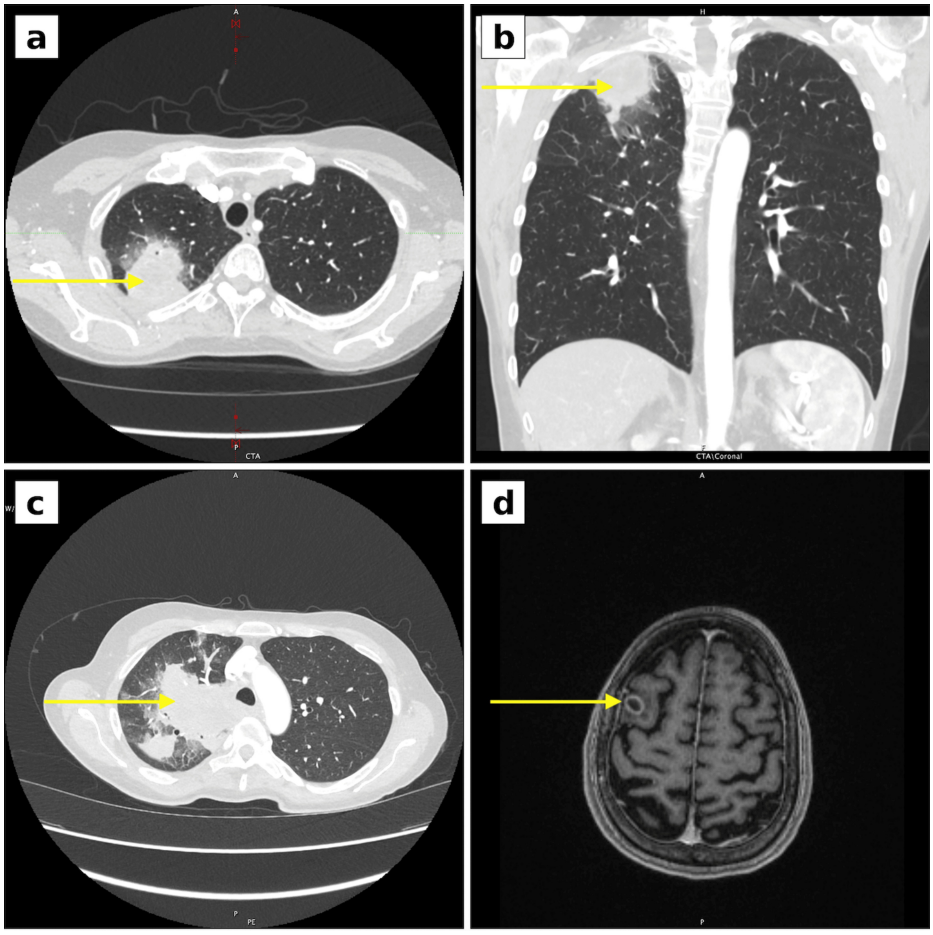


FIGURE 3: Right upper lobe mass and CNS dissemination on chest and brain imaging, Case 2

(a) Axial contrast-enhanced CT angiogram of the chest showing a right upper lobe mass with cavitation and surrounding ground-glass opacity (arrow). (b) Coronal contrast-enhanced CT angiogram showing the right upper lobe mass and adjacent parenchymal changes (arrow). (c) Axial CT pulmonary angiogram of the chest showing interval enlargement of the right upper lobe mass and cavitation, compared with (a) (arrow). (d) Axial T1-weighted post-contrast MRI of the brain showing a peripherally enhancing right frontal cortical lesion (arrow).

CNS: central nervous system; CT: computed tomography; MRI: magnetic resonance imaging.

On admission, laboratory evaluation revealed leukocytosis. Sputum cultures demonstrated mixed growth of Gram-positive rods, Gram-positive cocci, and Gram-negative rods, while blood cultures remained negative. Repeat chest imaging showed rapid enlargement of the right upper lobe mass with cavitation and surrounding ground-glass opacities (Figure *3c*), raising concern for superimposed infection. Empirical therapy with intravenous vancomycin and piperacillin-tazobactam was initiated.

Bronchoscopy with tissue sampling demonstrated suppurative necrosis, and cultures grew aerobic, partially acid-fast organisms concerning for *Rhodococcus* versus *Nocardia* species. Cytology was negative for malignant cells, and prior image-guided lung biopsy similarly showed no evidence of malignancy or organisms on special stains. Empirical antibiotics were discontinued, and targeted therapy with oral TMP-SMX and intravenous imipenem was initiated.

Neuroimaging performed during hospitalization revealed a 1.2 cm peripherally enhancing cortical lesion in the right frontal lobe (Figure *3d*), concerning for hematogenous dissemination. The patient denied headache or visual symptoms, and cerebrospinal fluid analysis demonstrated no pleocytosis (2 nucleated cells/µL) or evidence of meningitis (protein 34 mg/dL, glucose 65 mg/dL).

Definitive microbiological identification of bronchoscopic tissue culture using MALDI-TOF mass spectrometry confirmed *N. niwae*. Antimicrobial susceptibility testing demonstrated susceptibility to TMP-SMX, imipenem, moxifloxacin, and linezolid, with resistance to amoxicillin-clavulanate; full results are summarized in Table *2*.

Antimicrobial agent	MIC (µg/mL)	Interpretation
Trimethoprim-sulfamethoxazole	0.12/2.4	S
Imipenem	2	S
Moxifloxacin	0.5	S
Linezolid	1	S
Amikacin	≤0.5	S
Tobramycin	≤2	S
Ceftriaxone	≤1	S
Clarithromycin	1	S
Doxycycline	2	I
Ciprofloxacin	2	I
Minocycline	2	I
Amoxicillin-clavulanate	≥256	R

TABLE 2: In vitro antimicrobial susceptibility testing for Nocardia niwae, Case 2

MIC: minimum inhibitory concentration; S: susceptible; I: intermediate; R: resistant.

She was diagnosed with disseminated nocardiosis involving the lung and CNS and was transitioned to combination therapy with intravenous (IV) imipenem, oral TMP-SMX, and oral moxifloxacin. Combination IV therapy was continued for 2-3 months, then transitioned to two-drug oral therapy with linezolid and moxifloxacin (TMP-SMX was discontinued because of worsening hypothyroidism), with a total anticipated duration of antimicrobial treatment of 6-12 months.

Discussion

In addition to these two cases, a literature search (PubMed, search term "*Nocardia niwae*" from inception to March 2026) identified two additional reported cases of disseminated *N. niwae* infection with sufficient clinical detail for comparison [5,6]. A summary of all four cases is presented in Table *3*.

Case	Host	Immune status	Syndrome	Mimicked malignancy	Confirmed malignancy	Outcome	Reference
1	49M	Immunocompromised	Disseminated/CNS/Pulmonary	No	No	Alive	Present study
2	68F	Immunocompetent	Disseminated/CNS/Pulmonary	Yes	No	Alive	Present study
3	63F	Immunocompromised	Disseminated/CNS/Pulmonary	Yes	Yes	Death	Emanuel et al. [5]
4	86M	Immunocompromised	Disseminated/CNS/Pulmonary	Yes	Yes	Death	Datta et al. [6]

TABLE 3: Summary of four reported cases of disseminated Nocardia niwae infection

Case 1: 49-year-old man with HIV infection; patient had multifocal brain abscess requiring craniotomy growing *Nocardia niwae* on culture; alive. Case 2: 68-year-old immunocompetent woman; cavitary lung mass biopsy negative for malignancy but grew *Nocardia niwae* on culture; alive. Case 3: 63-year-old woman receiving corticosteroids and whole-brain radiotherapy for lung adenocarcinoma with brain lesions presumed to be metastases; repeat lung biopsy grew *Nocardia niwae* on culture [5]; died. Case 4: 86-year-old man with axillary squamous cell carcinoma, presumed to be metastatic from a lung primary, treated with chemoradiotherapy, checkpoint-inhibitor immunotherapy, and corticosteroids; *Nocardia niwae* was identified from a right elbow joint aspirate; autopsy found disseminated nocardiosis with no lung carcinoma [6]; died.

M: male; F: female; CNS: central nervous system.

One of our two cases had a landscaping occupation with regular soil exposure, consistent with the known environmental reservoir for *Nocardia* species [1,2]. Both of our cases were diagnosed in Florida at the same hospital, and the case reported by Emanuel et al. [5] was also from Florida, the same region where *N. niwae*

was originally described [4]. The fourth case, reported by Datta et al., occurred in Connecticut [6]. Three of the four cases being located in Florida could reflect a true regional pattern, but a larger number of cases would be needed to confirm the pattern.

Three of the four patients were immunocompromised: HIV infection in our first case, corticosteroids and whole-brain radiotherapy for lung adenocarcinoma with brain lesions in the third case [5], axillary squamous cell carcinoma treated with chemoradiotherapy, checkpoint-inhibitor immunotherapy, and corticosteroids in the fourth case [6]. All four cases had disseminated infection with both pulmonary and CNS involvement on imaging, including the one immunocompetent patient in our report. CNS involvement is only reported in a minority of nocardiosis cases overall [7], though isolated cases continue to be described [8], so seeing it in all four cases here could suggest that *N. niwae* has a stronger tendency to spread to the CNS than other *Nocardia* species. Three of the four cases were also initially read as malignancy, based on pulmonary masses and ring-enhancing brain lesions on imaging [5,6,9]. Two of the four cases had biopsy-confirmed malignancy: lung adenocarcinoma in Case 3 [5] and axillary squamous cell carcinoma in Case 4 [6], although the presumed lung primary in Case 4 showed no carcinoma at autopsy.

Diagnosis in these cases depended on culture with species-level identification, which for newer *Nocardia* species such as *N. niwae* generally requires methods beyond traditional phenotypic panels [1,3]. MALDI-TOF mass spectrometry has emerged as a rapid and reliable method for *Nocardia* identification and was used successfully in both of our cases [10,11]. In our first case, cerebrospinal fluid molecular testing (MicroGenDX) and plasma cell-free DNA sequencing (Karius) both identified *N. niwae* alongside culture, with similar approaches having aided diagnosis in other reported cases of nocardiosis [12,13]. Since *N. niwae* can be mistaken for malignancy on imaging, sending tissue for microbiology in addition to pathology is required for diagnosis.

Antimicrobial susceptibility followed a similar pattern across the isolates tested, consistent with current understanding of susceptibility patterns in the genus [14], summarized in Table *4*. All were susceptible to TMP-SMX and linezolid, and isolates with available data were also susceptible to amikacin and resistant to amoxicillin-clavulanate, with mixed results for fluoroquinolones. Retrospective susceptibility surveillance data reported by Hamdi et al. [15] were useful in guiding empiric antimicrobial selection in both of our cases. TMP-SMX is generally treated as first-line therapy for *Nocardia* infections given its tissue distribution and CNS penetration [7,15,16], which held true across these cases as well. Given how often the disease was disseminated in this cohort, combination therapy was used instead of a single agent in all cases. Linezolid, which penetrates the CNS and is active against *Nocardia* species in general, was part of treatment in both of our cases and has also been used in CNS nocardiosis caused by other species [17,18]. Ceftriaxone has CNS penetration and was susceptible in all three isolates tested. In contrast, larger reported series have found ceftriaxone susceptibility to be more variable and generally lower among *Nocardia* isolates than TMP-SMX or amikacin [7]. The resistance to amoxicillin-clavulanate seen here matches what has been reported for *Nocardia* more broadly [19,20]; the inconsistent fluoroquinolone activity observed across these isolates is consistent with the variable activity this class has shown against the genus as a whole. These observations are preliminary as this report is limited by a small number of cases, incomplete data for some published isolates, and possible publication bias.

Nocardia niwae	Case 1 (present study)	Case 2 (present study)	Case 3 [5]	Case 4 [6]
Tobramycin	S	S	S	N/A
Linezolid	S	S	S	S
TMP-SMX	S	S	S	S
Doxycycline	I	I	I	N/A
Ciprofloxacin	R	I	R	N/A
Amoxicillin-clavulanate	R	R	R	N/A
Moxifloxacin	I	S	N/A	N/A
Amikacin	S	S	S	N/A
Imipenem	I	S	N/A	S
Ceftriaxone	S	S	S	N/A
Clarithromycin	S	S	S	N/A
Minocycline	I	I	S	N/A

TABLE 4: Antimicrobial susceptibility patterns across four cases of Nocardia niwae infection

S: susceptible; I: intermediate; R: resistant; N/A: not available.

Conclusions

Nocardia niwae is an emerging pathogen with a preliminary pattern in reported cases: geographic clustering in Florida, tendency for dissemination with CNS involvement, and mimicking malignancy on imaging, although more cases are required to fully characterize its clinical picture. Diagnosis requires a high index of suspicion in patients presenting with multi-organ disease, tissue cultures, and use of advanced molecular diagnostics. Treatment should begin promptly with antimicrobial agents that achieve good CNS penetration, such as linezolid and TMP-SMX, and can then be narrowed to culture-based targeted therapy.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Adit Chakravarty, Hac-tu J. Chung, Apeksha Kakkar, Pooja Gurram, Minu C. Abraham

Acquisition, analysis, or interpretation of data: Adit Chakravarty, Hac-tu J. Chung, Apeksha Kakkar, Pooja Gurram, Minu C. Abraham

Drafting of the manuscript: Adit Chakravarty, Hac-tu J. Chung, Apeksha Kakkar

Critical review of the manuscript for important intellectual content: Pooja Gurram, Minu C. Abraham

Supervision: Pooja Gurram, Minu C. Abraham

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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Adit Chakravarty and Hac-Tu J. Chung contributed equally to the work and should be considered co-first authors.

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