



Case report

Stroke like presentation of disseminated CNS *Nocardia beijingensis* infection in an immunocompetent patient: Case report and review of the literature

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ABSTRACT

We describe a rare case of pulmonary and central nervous system (CNS) *Nocardia beijingensis* infection in an immunocompetent patient presenting with stroke like symptoms and newly discovered pulmonary and brain mass. Initial work up suggested lung cancer with metastasis to the brain. However, further evaluation revealed disseminated *N. beijingensis*. A literature review of *N. beijingensis* infections in immunocompetent host is also presented.

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Case

A 58-year-old male with no significant medical history, presented to his primary care provider with a two-week history of having trouble finding words, spelling, remembering names, reading, comprehension and more recently headaches and worsening aphasia. The patient reported no travel history, limited outdoor activity, denied alcohol or substance abuse, and quit smoking tobacco twenty years prior. An initial brain MRI without contrast showed a 2.8 × 2.6 cm left temporal mass with a midline shift, prompting a neurosurgery consult. A repeat brain MRI with contrast, and a CT of the chest/abdomen was done to evaluate for malignancy and metastatic disease. Given the presenting symptoms and the midline shift on brain MRI the patient was started on oral dexamethasone.

The CT scan of the chest showed a spiculated left apical lung mass measuring 2.8 × 1.6 cm and a 5.5 mm nodule in the left lower lobe, concerning for a malignant process (Fig. 1A). The brain MRI revealed multiple peripherally enhancing lesions in the left temporal lobe measuring 3 × 2.5 cm along with extensive

vasogenic edema (Fig. 1B). A CT guided lung mass biopsy was negative for malignancy, AFB and fungal stains were negative and no organism was isolated on tissue culture, leaving the underlying etiology unclear. A PET CT scan performed a couple weeks later showed a metabolically active left lung mass that had significantly increased in size to 4.3 cm (Fig. 2A) accompany by multiple new metabolically active parenchymal and pleural nodules in the left upper lobe of the lung, raising further concerns for malignancy.

A few days later the patient presented to the emergency room with complaints of persistent headache and lethargy, despite being on dexamethasone. The brain CT at this time showed an enlarged area of vasogenic edema with left to right midline shift. The patient was subsequently admitted to our neurosurgical unit. On admission the patient was afebrile with stable vital signs. Laboratory evaluation showed leukocytosis, two negative plasma procalcitonin concentrations, negative for HIV antibody, aspergillus AG EIA, urinary histoplasma antigen, negative COVID-19, Influenza A/B and RSV PCR, indeterminate QuantiFERON Gold and negative blood cultures.

A second CT guided lung biopsy of the mass revealed an abscess without evidence of malignancy with tissue sent for culture. The repeat brain MRI revealed enlarging left posterior temporal lobe brain mass now measuring 3.9 × 3 × 2 cm with extensive surrounding vasogenic edema and mass effect, as well as new ring enhancing mass in the right occipital lobe (Fig. 2B). A brain abscess

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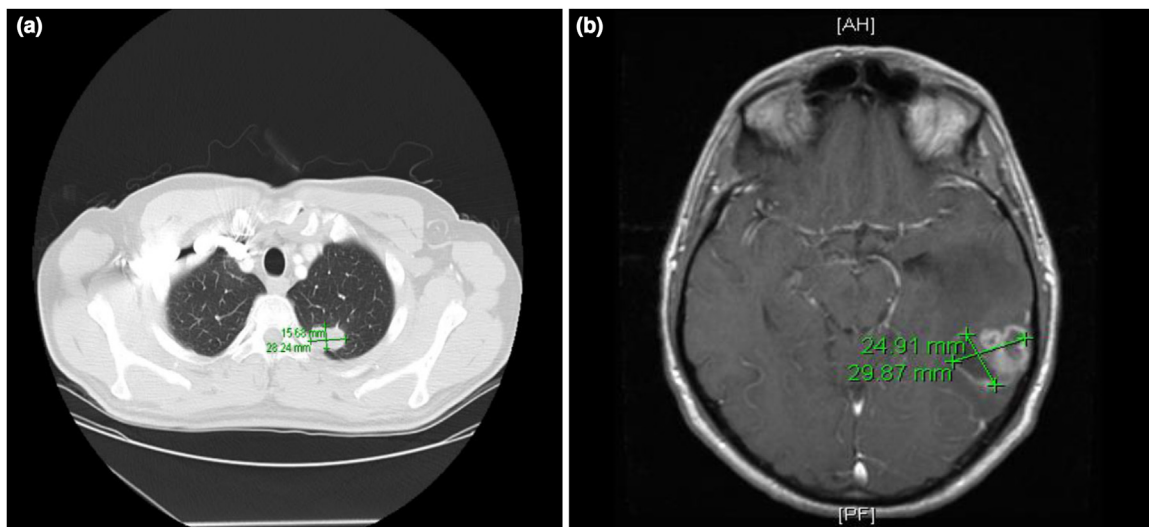


Fig. 1. A: Initial chest CT that visualizes the 2.8 cm lung mass in the left upper lobe. **B:** Initial brain MRI with 3 × 2.5 cm mass.

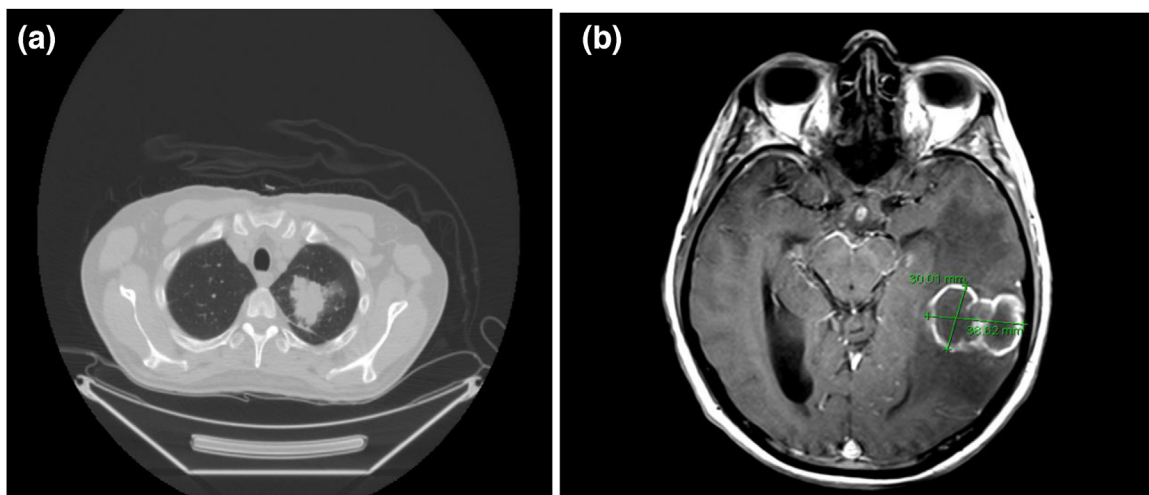


Fig. 2. A: Repeat Chest CT showing markedly increased mass now measuring 4.3 cm. **B:** MRI of brain one month after initial MRI showing enlarging brain mass measuring up to 3.9 cm from previously measured 3 cm lesion with extensive surrounding edema.

was suspected and empiric therapy with vancomycin, ceftriaxone and metronidazole was initiated.

The patient underwent a craniotomy for aspiration of the mass, in which pus was extracted and sent for culture, and several biopsies taken. The second lung biopsy gram stain revealed branching gram-positive rods which led to the addition of intravenous TMP-SMX for possible Nocardiosis. The lung tissue ultimately grew *Nocardia beijingensis* and cultures were sent to a reference laboratory for confirmation and susceptibility testing. Following organism identification, the patient’s antimicrobial regimen was then de-escalated to intravenous TMP-SMX and ceftriaxone and the dexamethasone was weaned over the next several days. Grocott-Gomori’s methenamine silver (GMS) stain of brain tissue revealed numerous filamentous organisms (Fig. 3) consistent with Nocardia infection.

The patient’s mentation initially improved with continuation of antibiotic therapy. Susceptibilities from reference lab revealed *N. beijingensis* susceptible to the current antimicrobial regimen (Table 1). The patient completed an eight-week course of IV TMP-SMX and ceftriaxone and then was to transition to a

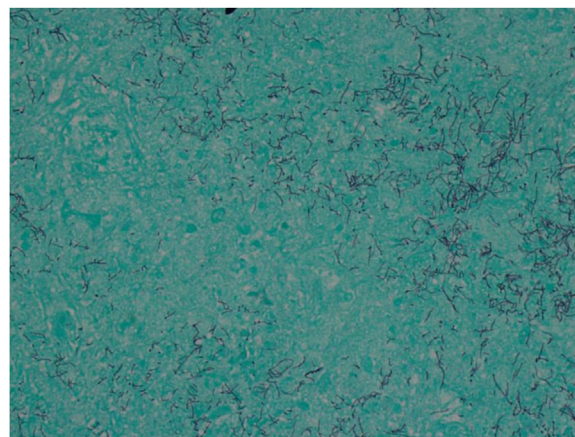


Fig. 3. *N. beijingensis* visualized on the GMS stain from the brain pathology. This isolate was not able to be seen on the brain abscess gram stain and AFB stain.

Table 1

Reported *N. beijingensis* antimicrobial susceptibilities from reference laboratory. Isolate was susceptible to the inpatient regimen of TMP-SMX and ceftriaxone. After six-week of intravenous therapy, transition to an oral regimen of TMP-SMX and azithromycin.

<i>Nocardia beijingensis</i>		
TMP-SMX	< = 0.25	S
Linezolid	< = 1	S
Ciprofloxacin	4	R
Imipenem	< = 2	S
Moxifloxacin	< = 0.25	S
Amoxicillin/Clavulanate	64	R
Amikacin	< = 1	S
Ceftriaxone	< = 4	S
Doxycycline	4	I
Minocycline	2	I
Tobramycin	< = 1	S
Clarithromycin	0.5	S

maintenance therapy of oral TMP-SMX and azithromycin with a plan to continue for a total of one year. The patient's mental status continued to improve, however his hospitalization was complicated by severe *C. difficile* infection that ultimately required subtotal colectomy. Following discharge and completion of intravenous antibiotic therapy, the patient was readmitted with worsening cognition and severe sepsis requiring intubation and pressor support. Sadly, the patient clinically deteriorated over the next several days and expired from sepsis related complications.

Table 2

Summary of *N. beijingensis* Reported Cases in Immunocompetent.

Year	Location	Case Description/Characteristics	Organ Involved	Treatment	Outcome	Ref
2014	Florida	First case in the United States in an immunocompetent host occurred in a 48 yearold Caucasian male	Lung, lymph node	TMP-SMX for 6 months + ceftriaxone for 6 weeks	At 6 weeks, blood counts normalized and inflammatory markers improved	[14]
2015	Israel	55 year old female without underlying lung disease presents with an endobronchial nocardial mass and unresolving community-acquired pneumonia	Lung	Oral TMP-SMX for 3 months + ceftriaxone for 1 month	Complete patient recovery following antibiotic treatment	[15]
2016	Florida	Second case in the United States in an immunocompetent host occurred in a 52 year old African American female	Scleritis	TMP-SMX + amikacin eye drops + polymyxin b-TMP eye drops	3 years later, the patient's best-corrected visual acuity was 20/30 in the right eye, mild cataract noted	[19]
2018	Japan	74 year old female with CT imaging revealing bronchiectasis	Lung	TMP-SMX + minocycline for 6 months	CT finding improved following antibiotic therapy	[17]
2019	Latin America	First case of a CNS abscess in an immunocompetent host occurred in a 58-year-old male presenting with a 6 month headache	CNS	TMP-SMX + meropenem + amikacin	Systemic inflammatory response syndrome due to multisystem infection leading to death after 14 days in the ICU	[20]
2019	Florida	First case in the United States of a CNS abscess in an immunocompetent host occurred in a 60 year old Caucasian female presenting with complaints of altered mentation	CNS	TMP-SMX + ceftriaxone	Repeat imaging of the brain showed improving abscess	[21]
2019	Florida	Adult age unknown. CT imaging show lung mass initially concerning for malignancy. However, post lobectomy mass revealed an abscess	Lung and lymph node	TMP-SMX + ceftriaxone for 6 weeks	Not available	[16]
2020	Virginia	47 year old immunocompetent male with enlarging lung mass	Lung	IV TMP-SMX + imipenem-cilastin transitioned to TMP-SMX + doxycycline	Chest CT at 5 weeks showed 30–40% decrease in lung mass. At 9 months, CT showed near resolution of lung mass	[18]
2020	Japan	68 year old male with military cerebrospinal lesions and right middle lobe atelectasis	Lung, brain, brain stem, spinal cord	TMP-SMX + meropenem, followed by SMX-TMP for 7 months	Mild confusion and irritability, discharged to another facility for long term care	[22]
2020	Maine	60 year old male with primary pulmonary disease and dissemination to subcutaneous tissue and CNS	Pulmonary, subcutaneous, and CNS	IV TMP-SMX + meropenem for 6 weeks transitioned to TMP-SMX for 12 months	2 months after diagnosis, CT show near resolution of lung mass. 5 months later, Brain MRI show decrease in lesion size	[23]
2020	Illinois	57 year old female presented following seizure-like activity. Imaging revealed pulmonary and CNS abscesses	Pulmonary and CNS	IV TMP-SMX for 6 weeks followed by oral TMP-SMX for 12 months	Chest CT at 1 year show near resolution of lung mass. Brain MRI at 6 months showed resolution of vasogenic edema	[24]
2021	Florida	Our Patient. Third case in the United States with pulmonary and CNS disease in immunocompetent host	Pulmonary and CNS	IV TMP-SMX + ceftriaxone for 8 weeks followed by oral TMP-SMX + azithromycin for 12 months	Mentation improved, hospitalization complicated by <i>C. difficile</i> , developed severe sepsis following induction therapy and expired	-

Discussion

Nocardia species are a complex group of organisms that belong to aerobic actinomycetes. *N. beijingensis* is a part of the group *N. abscessus* complex, which also includes *N. abscessus*, *N. arthritidis*, and *N. asiatica* [1]. Nocardiosis is a rare infection with an incidence rate of approximately 500–1,000 cases per year in the United States [2]. However, the incidence may be higher because Nocardiosis has a nonspecific clinical presentation and can be difficult to culture. Presumptive diagnosis can be made if partially acid-fast filamentous branching rods are visualized in the clinical specimen, with a definitive diagnosis made from the isolation and identification of the organism [3]. In our patient case, the presence of pulmonary and CNS lesions on imaging were suspicious, however, the initial biopsy of the lung had a negative AFB and GMS stain, and no organisms were isolated. The second lung biopsy however showed branching gram-positive rods that subsequently grew *N. beijingensis*. Although, the intraoperative cultures from the craniotomy did not grow the organism, the GMS stain of the brain tissue nicely visualized the filamentous morphology consistent for Nocardiosis.

Nocardiosis is a disease caused by the *Nocardia* bacteria, most commonly manifesting as primary cutaneous, pulmonary, and disseminated infection [4]. The most common disseminated site is the brain, but any organ can be involved. While the majority of infections occur in the immunocompromised, about one-third of infected patients are immunocompetent [5].

The first cases of human infection with *N. beijingensis* were reported in 2004 in Thailand and Japan [6]. Similar to other Nocardiosis cases, there have been several reported cases in

immunocompromised patients [6–13]. The first reported case in an immunocompetent host occurred in Jacksonville, Florida in 2014 involving the lung and lymph node [14]. This was followed by additional reports of pulmonary Nocardiosis [15–18] and one case of scleritis in immunocompetent hosts [19]. The first case reports of CNS involvement in immunocompetent patients were reported in 2019 and again in 2020 [20–24]. Table 2 summarizes reported cases of *N. beijingensis* in immunocompetent patients. Interestingly our case is the fifth reported case in the state of Florida.

No one therapy has been proven to be superior at this time, but TMP-SMX is currently recommended as the first line agent. For patients with pulmonary and disseminated disease, a two or three antimicrobial regimen is recommended for empiric treatment. Potential three drug regimens for disseminated disease include TMP-SMX and amikacin plus ceftriaxone or imipenem [5]. Our patient was empirically treated with a two drug regimen of TMP-SMX and ceftriaxone, with both agents exhibiting good penetration into the CNS. Antimicrobial susceptibilities should always be performed to guide therapy. For CNS or multiorgan disease, after three to six weeks of intravenous therapy and clinical improvement, it is appropriate to streamline to an effective oral regimen [25]. Oral options include TMP-SMX and/or minocycline and/or amoxicillin/clavulanate. Disseminated Nocardiosis with CNS disease should receive at least 12 months of antimicrobial therapy [25,26].

Conclusion

This case reports highlights an unusual presentation of Nocardiosis with brain abscess in an immunocompetent patient caused by an uncommon *Nocardia* species. This appears to be the third *N. beijingensis* case reported in the United States with pulmonary and CNS involvement in an immunocompetent patient. We hope this case can be used as a reference for future patients with similar presentations, to aid in identifying Nocardiosis and starting treatment earlier in the disease course.

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Ethical approval

Not applicable. This case reports the care received during hospitalization for a patient with a complicated Nocardia infection. No investigational therapies were given, and all procedures performed were in accordance with the ethical standard of the institution. No protected health information (PHI) was disclosed.

Consent

Written informed consent was obtained from the patient's spouse for publication of this care report and accompanying radiologic and pathology images. A copy of the written consent is available for review by the Editor-in-Chief of IDCases on request.

CRedit authorship contribution statement

Alessandra Diioia: PharmD Candidate, Investigation - case timeline, Writing - Original Draft: Primary author of case manuscript. **Lalit Kalra:** Infectious Diseases Physician for the Case, Writing - Review and Editing, final approval, Supervision. **Lynne C. Krop:** Infectious Disease Pharmacy Specialist/preceptor for first author, Writing - Review and Editing, final approval, Visualization - obtaining appropriate radiographic images and

pathology slide, Supervision, Project administration - formatting and submission/corresponding author.

Declaration of Competing Interest

The authors report no declarations of interest.

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