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Case report

Central nervous system nocardiosis masquerading as metastatic brain lesions

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ABSTRACT

Nocardiosis is an uncommon infection, however it needs to be included in the differential diagnosis, especially in immunocompromised hosts. Central nervous system (CNS) nocardiosis, in particular, is an even rarer entity with a higher mortality. This is a case of CNS Nocardia infection with an atypical presentation that was initially concerning for metastatic disease. In an immunocompromised patient with CNS findings, atypical infectious processes need to be considered. In a patient with concomitant pulmonary findings, an evaluation for Nocardia should be pursued as the lungs are the primary route of entry for this organism. Treatment typically involves a sulfonamide with secondary antibiotic agent, however a combination using meropenem has proved effective here.

Introduction

Nocardia spp. is an aerobic, gram-positive, weakly acid-fast, branching rod-shaped bacteria that is widely found in the environment, i.e. soil. Infections in humans occurs either by inhalation or by direct inoculation of skin. Cell-mediated immunity plays a significant role in eliminating this infection in immunocompetent individuals. A defect in these host defenses, which can occur in patients with AIDS, certain malignancies, organ transplant, immunosuppressive therapy, etc., predisposes a patient to develop localized or systemic infection [4]. A severe form of this represents central nervous system (CNS) involvement, such as meningitis or brain abscess, which can manifest in a variety of ways including headaches, seizures, and focal neurological deficits [1]. *However, because it can have a more insidious presentation, CNS nocardiosis is often mistaken for neoplasia.* We report a case of CNS Nocardiosis in a patient who presented with new onset headaches and lethargy and was found to have multiple brain lesions in the setting of chronic prednisone therapy.

Case report

We report the case of a 54-year-old African-American female who presented to the emergency department with a new headache and altered mental status. She has a medical history of cirrhosis secondary to suspected hepatic sarcoidosis (on chronic prednisone) and hypertension. Computed tomography (CT) imaging of her head showed mass lesions in bilateral cerebellar hemispheres and left orbital frontal lobe concerning for metastatic disease as well as mild obstructive hydrocephalus of the fourth ventricle. During her hospital stay, the patient became increasingly more lethargic requiring intubation and transfer to the neuro-critical care unit. Chest CT showed bilateral lower lobe pulmonary opacities and calcified nodules. Subsequent CT of her abdomen and pelvis were unremarkable for any masses or lesions. Patient underwent aspiration of the larger right cerebellar mass. Acid-fast bacterial culture of aspirate resulted in growth of *Nocardia farcinica*. She was started on intravenous trimethoprim-sulfamethoxazole (TMP-SMX) and meropenem per Infectious Disease specialist recommendations. She was successfully extubated after receiving a short course of steroid therapy to reduce vasogenic cerebral edema. The patients' lethargy began showing improvement with continued antibiotic therapy which was evident by day 3. After the initial two weeks, TMP-SMX was switched to intravenous ciprofloxacin due to the development of severe pancytopenia. Ciprofloxacin therapy was chosen based on susceptibility testing from the isolated *Nocardia farcinica* (Fig. 1). Meropenem was continued. She was treated with intravenous meropenem and ciprofloxacin for 6 more weeks (for a total of 8 weeks), followed by oral ciprofloxacin and sulfadiazine to complete a one year course of treatment. Her chronic prednisone therapy was weaned due to her immunocompromised state which likely predisposed her to develop this infection. Magnetic resonance imaging of her brain done after the first two months of treatment revealed near complete resolution of right cerebellar lesion (Fig. 2), interval resolution of left frontal periventricular lesion, and no evidence of any new lesion. Patient was followed up in clinic and she successfully completed the

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TESTS	RESULT	FLAG
Nocardia Susceptibility Broth		
Organism ID		
	Nocardia farcinica	**Abnormal**
Amikacin		
	1.0 ug/mL or less,	Susceptible
Amoxicillin/CA		
	8/4 ug/mL	Susceptible
Ceftriaxone		
	16.0 ug/mL	Intermediate
Ciprofloxacin		
	0.25 ug/mL	Susceptible
Clarithromycin		
	>16.0 ug/mL	Resistant
Imipenem		
	4.0 ug/mL	Susceptible
Linezolid		
	2.0 ug/mL	Susceptible
Minocycline		
	2.0 ug/mL	Intermediate
Tobramycin		
	>16.0 ug/mL	Resistant
Trimethoprim/Sulfa		
	1/19 ug/mL	Susceptible

Fig. 1. Nocardia Farcinica Susceptibility Chart.

planned one year course of antibiotics without any lasting deficits or symptoms.

Discussion

Nocardia species are saprophytic aerobic actinomycetes found commonly worldwide in soil, where they contribute to the decay of organic matter. While greater than 50 *Nocardia* species have been identified, most systemic disease involves *N. cyriacigeorgica, N. farcinica, N. pseudobrasiliensis,* and species in the *N. transvalensis* and *N. nova* complexes [5]. Greater than 90% of cases of pulmonary or disseminated disease occur in individuals with deficient cell-mediated immunity, particularly those with lymphoma, transplantation, AIDS, or on glucocorticoid therapy [5]. They are thought to follow inhalation of fragmented bacterial mycelia. The most common form of nocardial disease is in the respiratory tract. In half of all cases of pulmonary nocardiosis, disease also appears outside the lungs, the most common site being the brain [5].

Central nervous system *Nocardia* infections typically present as meningitis or subacute abscess. Brain abscesses are typically supra-tentorial, often multi-loculated, and may be single or multiple. When occurring in isolation, *Nocardia* brain abscess presents as a slowly progressive mass lesion, with a reported mortality rate of 55% in immunocompromised patients and 20% in immunocompetent patients; these rates increase to 66% with multiple abscesses [2,3]. *N. farcinica* is a significant cause of disseminated disease among *Nocardia* species and is highly drug resistant. Initial treatment is typically with dual intravenous antibiotic therapy. Usually, a clinical response is seen within 1 week if on appropriate antibiotic therapy. Surgical intervention should be pursued if the patient demonstrates clinical deterioration or no improvement with susceptibility based antibiotic therapy. Therapy can be switched to oral agents after 3–6 weeks depending on clinical course, with a total duration of 6–12 months.

Sulfonamides are the drugs of choice, with the combination of TMP-SMX being the primary therapy in mild to moderate cases. Multi-agent intravenous therapy is recommended by infectious disease experts in severe disease, including disseminated or CNS disease. Amikacin or imipenem are typically added as the second agent, because there is more clinical experience with these agents and appear to be the most active agents in vitro and in animal models [10]. Some reports show TMP-SMX having less than 2% resistance in the United States [7], but other studies demonstrate substantial prevalence of resistance patterns in certain Nocardia isolates [8]. This highlights the importance of obtaining

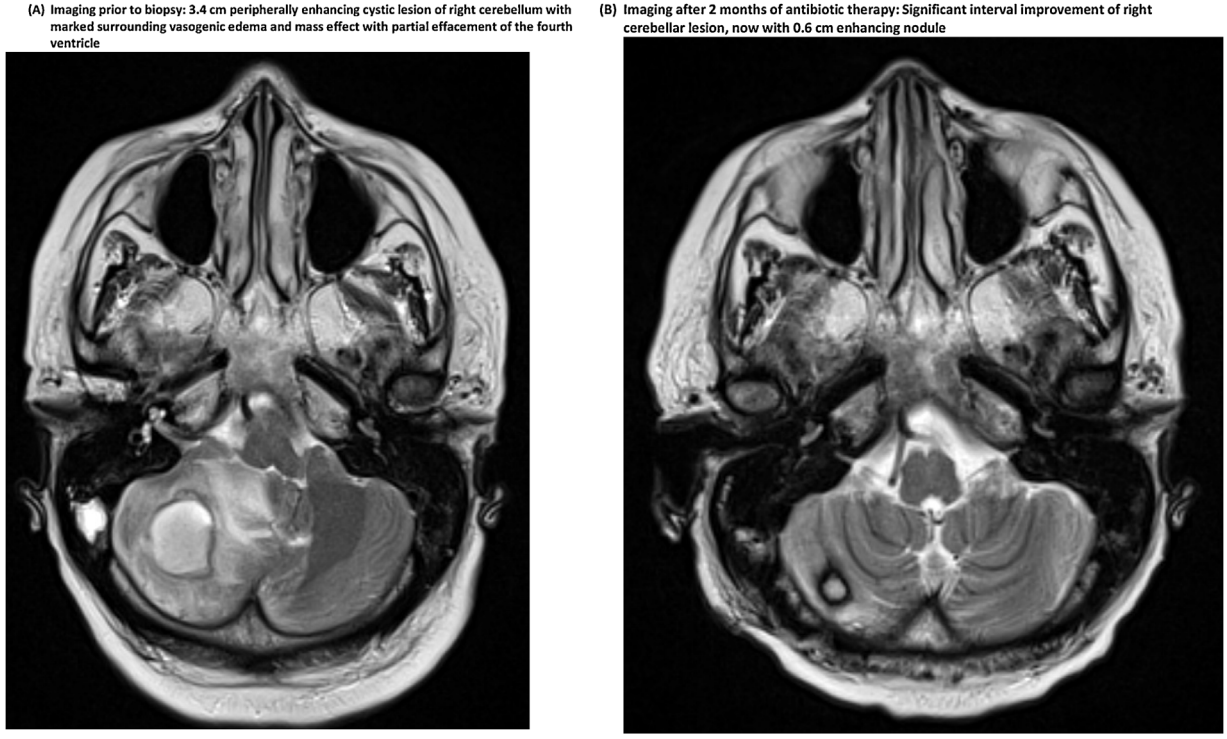

Fig. 2. MRI Brain – T2 Axial.
Imaging prior to biopsy: 3.4 cm peripherally enhancing cystic lesion of right cerebellum with marked surrounding vasogenic edema and mass effect with partial effacement of the fourth ventricle
Imaging after 2 months of antibiotic therapy: Significant interval improvement of right cerebellar lesion, now with 0.6 cm enhancing nodule

susceptibility testing in order to select efficacious therapy early and to have alternative options in the situation of resistance, drug toxicity, or other contraindication. In patients unable to receive TMP-SMX due to hematologic toxicity, *N. farcinica* species can alternately be treated with amikacin, ciprofloxacin, imipenem, and linezolid [5]. For Nocardia farcinica, lowest rates of antibiotic resistance are with linezolid (0%), amikacin (2.9%), TMP-SMX (5.4%), minocycline (9.4%) and imipenem (19.5%) [9]. As demonstrated in Fig. 1, typical susceptibility patterns of this organism include majority being susceptible to amikacin, most to sulfonamides, and resistance against aminoglycosides and third generation cephalosporins.

This case highlights the importance of susceptibility testing to guide therapy when the patient developed an adverse reaction as well as the successful use of atypical antibiotic regimens with meropenem. Meropenem, like imipenem, has good CSF penetration, similar pharmacokinetics, and is associated with a lower incidence of seizures. It has good in vitro activity against several Nocardia species, although one study found that meropenem was less active than imipenem against *N. farcinica* and *N. nova* (11). There are only a few reports using meropenem in combination with other antibiotics to treat nocardiosis, however efficacy has been varying. In our patient the combination of meropenem/TMP-SMX and meropenem/ciprofloxacin both proved to be effective treatments for CNS Nocardia Farcinica. In addition data suggests higher resistance to sulfadiazine therapy without the TMP component, but ciprofloxacin and sulfadiazine was also efficacious here.

Our case of *Nocardia farcinica* brain abscesses had a presentation that was initially concerning for metastatic brain lesions in an immunocompromised patient receiving prednisone therapy. It is important to distinguish between non-infectious brain tumors and *Nocardia* abscess as administration of corticosteroids can contribute to rapid progression of infection, possibly through inhibition of capsule formation [6]. Corticosteroids can however still be used, with caution, to reduce significant cerebral edema and mass effect [6]. In a patient with host defense defects who presents with brain imaging concerning for metastatic disease and lung imaging suggestive of pneumonia, evaluation for disseminated *Nocardia* infection should be done, to prevent any delay in diagnosis and treatment of this condition with high associated mortality. Patients should be appropriately diagnosed and treated, then followed carefully for at least six months after completion of therapy with repeat brain imaging to document resolution of lesions.

Author statement

Hamel Patel: conceptualization, resources, writing – original draft; writing – reviewing and editing.

Bijal Patel: resources, writing - original draft; writing – reviewing and editing.

Sonal Jadeja: writing – reviewing and editing.

Carmen Isache: writing – reviewing and editing.

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