ID Corner

Antimicrobial Management of a *Nocardia farcinica* Brain Abscess

by Lucas Grabowski, PharmD

A patient, whom we'll call LP, is a 64-year-old male who presented to the emergency department with left-sided weakness; new neuropathic symptoms predominantly in his right leg; a history of recent falls; nausea; confusion; low-grade fever; and chills. He had a past medical history of cocaine and alcohol use, and of sarcoidosis, for which he was currently being treated with hydroxychloroquine, etanercept, and low-dose prednisone.

An initial head CT showed a probable ill-defined mass lesion, 2 to 3 centimeters, centered in the right temporal lobe, "with mass effect as described and associated white matter edema." LP was started empirically on intravenous (IV) meropenem and vancomycin. An MRI of the brain revealed a 3-centimeter ring-enhancing lesion in the anterior right temporal lobe and a 6-millimeter ring-enhancing lesion in the anterior medial right occipital lobe. LP experienced a seizure and was subsequently started on levetiracetam for seizure prophylaxis.

The next day, LP underwent a right temporal craniotomy during which the team cultured purulent material and evaluated the abscess. The result of the gram stain of the brain abscess specimen initially showed few gram-positive branching bacilli. Because there were some gram-positive branching bacilli identified, an infectious disease (ID) consultant suspected the microbe was part of the *Nocardia* species and recommended high dose trimethoprim-sulfamethoxazole (TMP-SMX). The microbe was later identified as *Nocardia farcinica*. ID switched the patient's meropenem to imipenem-cilastatin for increased activity against *Nocardia farcinica*. The lab sent the culture to a national reference laboratory for susceptibility testing, to provide guidance for antimicrobial therapy. A few days later, LP was discharged to home on imipenem-cilastatin and trimethoprim-sulfamethoxazole, with the plan to complete 6 to 12 weeks of IV antibiotics, guided by MRI findings, followed by a year-long oral regimen.

LP returned to the hospital that same evening with concerns about completing the complex antibiotic regimen at home. He was readmitted to the hospital pending a plan for possible short-term facility placement. A few days later, susceptibilities returned from the national lab, showing the *Nocardia farcinica* was susceptible to TMP-SMX, but resistant to imipenem (Table 1). ID switched the patient from imipenem-cilastatin to linezolid, a susceptible alternative, and then discharged LP on an oral regimen of linezolid and TMP-SMX.

At a follow-up visit, the patient's MRI showed a new ring-enhancing lesion of the lateral right temporal lobe, and the previous abscess was shown to be almost fully resolved. The patient reported no additional seizures, but did note that he was experiencing intractable nausea and vomiting. His lab work showed severe anemia requiring a transfusion. LP was ultimately switched from linezolid to oral ciprofloxacin, which he has tolerated much better. Subsequent MRIs have shown continued improvement in the right temporal lobe with decreased area enhancement. He continues to have appointments with ID every 6 weeks.

Pathogenesis

Nocardia species are found in soil, organic matter, and water, and are often associated with decomposition of plant material.[1] They are aerobic, gram-positive, branching, rod-shaped bacteria (Figure 1 and 2). *Nocardia* infections are not typically transmitted from one person to another, but rather through inhalation. Nocardiosis is most often characterized as an opportunistic infection, but has been seen occasionally in immunocompetent patients.[2] Patients who are often at risk of nocardiosis include HIV patients with low CD4 counts, solid organ transplant patients, and patients with malignancy. LP was at risk of nocardiosis due to his immunosuppressant medications.

Nocardiosis is sometimes a localized infection, but also has the ability to disseminate.[3] It also has a tendency to relapse and progress despite appropriate therapy. To reduce the risk of treatment failure and progression, comprehensive susceptibility testing should ideally be completed for each *Nocardia* isolate.

There have been up to 54 *Nocardia* species shown to cause disease in humans.[2]

TABLE 1. LP's *Nocardia farcinica* Susceptibility Results

TMP-SMX	Susceptible
Ciprofloxacin	Susceptible
Moxifloxacin	Susceptible
Amikacin	Susceptible
Doxycycline	**Intermediate**
Clarithromycin	**Resistant**
Linezolid	Susceptible
Imipenem	**Resistant**
Amoxicillin/Clavulanate	Susceptible
Ceftriaxone	**Resistant**
Minocycline	**Intermediate**
Tobramycin	**Resistant**

FIGURE 1. *Nocardia farcinica* Growing in a Blood Culture Bottle

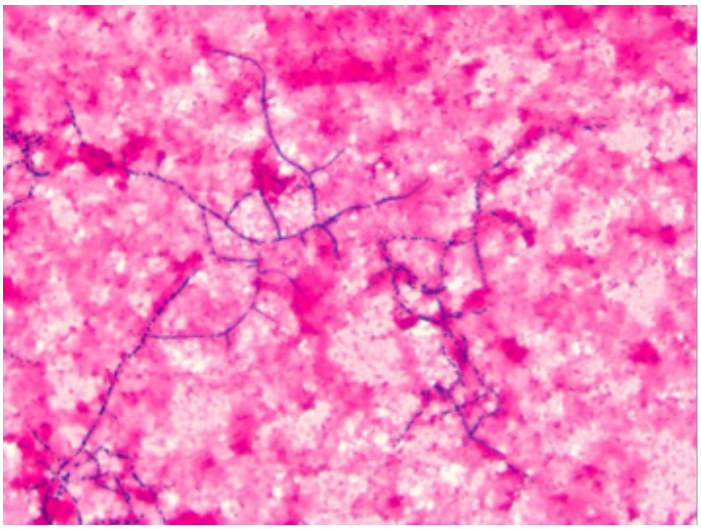

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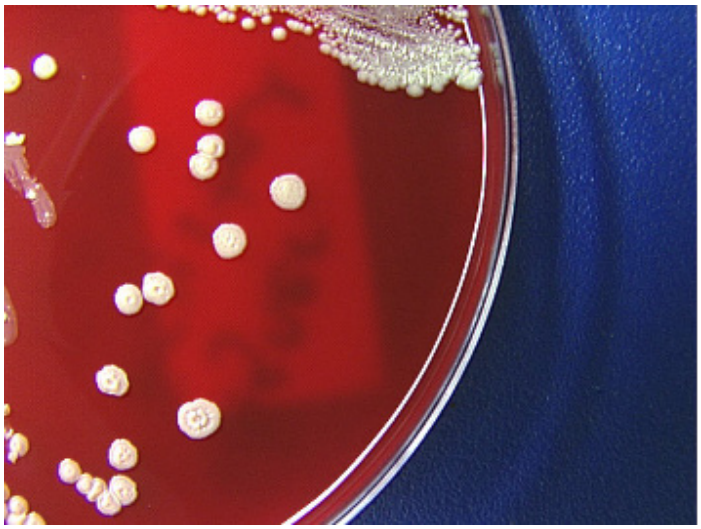
FIGURE 2. *Nocardia farcinica* Subculture on Blood Agar Plate



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Geographical regions play a role in the frequency of occurrence of different species. Some of the most common *Nocardia* species in the United States include *Nocardia nova* complex, *Nocardia brasiliensis*, and *Nocardia farcinica*. Disease manifestations can range from cutaneous infections to severe pulmonary or central nervous system (CNS) infections. Different *Nocardia* species are associated with different types of infections and different extents of disease. For example, *Nocardia brasiliensis* is more commonly associated with a cutaneous skin disease, whereas *Nocardia farcinica* is more often associated with pulmonary and CNS infections.

Nocardia species have a propensity to grow in neural tissue and cause neural disease.[3] Most cases of neural disease occur due to dissemination and can sometimes occur even after the eradication of the infection from the primary site. Infection in the lungs appears to be the most common site that leads to dissemination to the CNS. Nocardiosis in the CNS tends to lead to the formation of parenchymal abscesses in the brain. Abscesses can form in any area of the brain, leading to a wide variety of signs and symptoms. Some common symptoms of a CNS nocardiosis include focal neurological deficits, headaches, and seizures.[4] A patient may start with no symptoms, but, over the course of months to years, begin to show neurological deficits, while remaining asymptomatic from a systemic bacterial infection standpoint.

Treatment

Empiric antibiotic coverage with multiple agents is typically required to treat a severe *Nocardia* infection, because *Nocardia* species have a variability in their resistance to antibiotics. Monotherapy is occasionally used for patients who have a mild to moderate pulmonary disease. With severe infections, patients are often started on empiric combination therapy, and are continued on it until they show clinical improvement, and identification and susceptibilities result.[5] Given its lower risk of relapse or death, trimethoprim-sulfamethoxazole is frequently used as an empiric therapy for suspected *Nocardia* infections.[6] Additionally, TMP-SMX has the ability to penetrate the lungs, brain, skin, and bone, leading to high tissue concentrations in those areas.[7] The recommended dosing varies based on the indication and presence of an immunocompromising condition (Table 2). Other antibiotics that have activity against *Nocardia* species include minocycline, amikacin, meropenem, dapsone, ceftriaxone, cefotaxime, imipenem, linezolid, and fluoroquinolones. The turnaround time for susceptibilities can take longer than for typical culture results, given that *Nocardia* is a slower growing pathogen, and this culture is often sent to a reference lab for susceptibilities. A common empiric therapy regimen for CNS disease is TMP-SMX and imipenem.

Evidence has shown there can be variability among antibiotic classes. Carbapenems specifically have shown different activity against *Nocardia* infections. One study showed that *Nocardia nova* complex was the only *Nocardia* species to have a MIC90 that was shown to be susceptible to imipenem, meropenem, and ertapenem.[8] For *Nocardia farcinica*, imipenem is typically the most active carbapenem, but LP was unable to use this, given the *Nocardia farcinica* he was growing was shown to be resistant to imipenem.

TABLE 2. Example Trimethoprim-Sulfamethoxazole Dosing Recommendations Based off *Nocardia* Indication[3]

Indication	*Dose*
Cutaneous Infection	Oral: 5 -10 mg/kg/day (TMP component) in 2 divided doses
Pulmonary Infection-Immunocompetent	Oral: 5 -10 mg/kg/day (TMP component) in 2 divided doses
Severe Pulmonary Infection, Central Nervous System Infection, or Disseminated Infection	IV: 15 mg/kg/day (TMP component) in 3 to 4 divided doses
Pulmonary Infection-Immunocompromised	Oral: 15 mg/kg/day (TMP component) in 3 to 4 divided doses

Initial treatment for severe infections should be administered intravenously for four to six weeks.[9] A transition to oral therapy and de-escalation to monotherapy can occur in patients who have documented clinical improvement. The duration of therapy depends on each clinical case and the sites of infection.[10] Immunocompromised patients or patients with CNS involvement require a minimum of six months of therapy, with most receiving a year of antibiotic therapy. Frequent check-ins should be completed to monitor for risks of resistance or recurrence of infection. Follow-up imaging can help guide decision making to ensure de-escalation or discontinuation of therapy isn't premature.

Key Takeaways

Providers should suspect a possible *Nocardia* infection when a culture is growing gram-positive, rod-shaped branching bacteria. TMP-SMX is frequently used as an empiric option, given its activity against *Nocardia* species and its ability to penetrate multiple tissues. Patients with a severe *Nocardia* infection or who are immunocompromised should initially be on empiric combination therapy. Susceptibilities, imaging, and the patient's clinical improvement should help guide providers in determining the appropriate time to both de-escalate antibiotics and transition to an oral regimen. Frequent patient follow-up should occur to monitor for relapsing or recurrent infection.

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