**Case Report**

**Nocardia puris** brain abscess in an immunocompromised woman

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**Introduction:** *Nocardia puris* is a rare cause of infection worldwide, with very few published cases. Here we report the first case to our knowledge of brain abscess caused by *N. puris*.

**Case presentation:** Our patient, currently undergoing treatment with rituximab for non-Hodgkin lymphoma, presented with a 2 week history of worsening headache and nuchal rigidity. Magnetic resonance imaging of the brain revealed a ring-enhancing mass in the right temporal lobe. The abscess was surgically resected and the causative organism was identified as *N. puris* by culture and then 16S PCR of the rRNA gene. Our patient was successfully treated with a combination of imipenem and trimethoprim–sulfamethoxazole (15 mg kg⁻¹ day⁻¹) for 3 months, followed by 9 months of monotherapy with trimethoprim–sulfamethoxazole.

**Conclusion:** Treatment of nocardiosis remains challenging, with each species having a unique antimicrobial susceptibility profile. Our patient was successfully treated with a combination of imipenem and trimethoprim–sulfamethoxazole, followed by monotherapy with trimethoprim–sulfamethoxazole.

**Keywords:** brain abscess; imipenem; immunocompromised; *Nocardia puris*; nocardiosis; trimethoprim–sulfamethoxazole.

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**Introduction**

Nocardiosis remains a relatively rare infection, but can cause significant morbidity and mortality, especially in immunocompromised patients. An increasing number of *Nocardia* species have been identified, each with its own antibiotic susceptibility profile, leading to increasing treatment challenges (Brown-Elliott et al., 2006; Schlaberg et al., 2014). To date, there are 103 known species of *Nocardia* (DSMZ, 2013), but only 46 have been validated to cause clinically significant human disease (Conville & Witebsky, 2011). Here, we present a case of *Nocardia puris* causing brain abscesses in an immunocompromised woman.

**Case presentation**

A 72-year-old woman presented at an affiliated hospital’s emergency department due to 2 weeks of worsening headaches. Thirteen years prior to presentation she was diagnosed with non-Hodgkin lymphoma; she has been treated with intravenous rituximab twice yearly, with the most recent infusion 46 days prior to presentation. Twelve years ago she was treated for cryptococcal meningitis and continues to take prophylactic fluconazole. At the time of presentation she described a worsening right frontal headache with associated neck stiffness.

Physical examination was notable for a temperature of 36.8 °C, normal vital signs, nuchal rigidity, and slight left pronator drift. Computerized tomography of the head revealed extensive vasogenic oedema in the right cerebral hemisphere with associated subfalcine herniation and an underlying mass. Magnetic resonance imaging of the brain revealed a 3.2 × 2.4 × 2.2 cm ring-enhancing mass within the medial inferior portion of the right temporal lobe (Fig. 1). Surrounding this mass were several smaller lesions, approximately 1 cm in diameter. She was transferred to our institution for neurosurgical intervention. Operative reports describe copious amounts of purulent material within the mass and successful near-total resection of the mass.

The patient was empirically treated with vancomycin, ceftazidime and metronidazole. Staining of the purulent fluid collected intra-operatively revealed filamentous Gram-variable rods (Fig. 2). Culture and pathology for fungus and flow cytometry for recurrent lymphoma were negative. Aerobic cultures grew *Nocardia*. The culprit organism was identified as *Nocardia puris* by sequencing of the 16S rRNA gene. A 580 bp sequence of the amplified gene product was then entered into the Basic Local Alignment Search Tool, revealing a 100 % match for *N. puris*, GenBank accession number GQ217500 (CLSI, 2008). Antibiotic therapy was changed to imipenem plus trimethoprim–sulfamethoxazole (TMP-SMX) 15 mg kg⁻¹ day⁻¹ based on case reports of prior *N. puris* infections (Lai et al., 2011). The patient was discharged home on post-operative...
day 5 with improvement in headaches and no focal neurological deficits.

The *N. puris* isolate was sent to the National Jewish Laboratory (Denver, Colorado) for susceptibility testing by microbroth dilution technique. The *N. puris* isolate was susceptible to amikacin (MIC ≤8.0), tobramycin (MIC ≤2.0), imipenem (MIC ≤2.0) and minocycline (MIC ≤1.0), TMP-SMX (MIC 1/19), while being intermediately susceptible to amoxicillin–clavulanic acid (MIC 16/8) and linezolid (MIC 8.0). It was resistant to ceftriaxone (MIC >64), cefepime (MIC >32), ciprofloxacin (MIC 8), clarithromycin (MIC 32) (Table 1). Imipenem and TMP-SMX were continued as dual therapy for 3 months. Repeat brain magnetic resonance imaging at 3 months revealed resolution of prior oedema and no evidence of infection. Antibiotic therapy was narrowed to monotherapy with TMP-SMX 15 mg kg⁻¹ to complete 1 year of treatment, and then decreased to 5 mg kg⁻¹ day⁻¹ indefinitely given the patient’s need for ongoing treatment for non-Hodgkin lymphoma.

**Discussion**

To date, there have only been four reported cases of human infection caused by *N. puris*, and this is the first known case in the USA of a cerebral abscess. *N. puris*, isolated from a human abscess, was described as a novel species in 2003 (Yassin et al., 2003). There are two reports of ocular infections, choroiditis and keratitis (Watanabe et al., 2006; Reddy et al., 2010a), and one case of severe pulmonary infection (Tan et al., 2010) caused by *N. puris*.

In 1976 there were approximately 500–1000 nocardiosis cases in the USA (Beaman et al., 1976). While *Nocardia* infections are reported in immunocompetent patients, the vast majority of nocardiosis is an opportunistic infection in the immunocompromised, either from long-term steroid use, malignancy, organ transplant, or HIV infection (Menendez et al., 1997). Improved laboratory techniques for identification have also contributed to increasing numbers of diagnoses. Most laboratories currently use nucleic acid amplification techniques and DNA sequence analysis to make species identifications (Schlaberg et al., 2014). Advances in caring for immunocompromised patients and advances in laboratory techniques for identifying the causative organism of infections will likely increase the reported prevalence of nocardiosis.

Nocardiosis is a result of inhalation or direct inoculation and then haematological spread to distant sites, with central nervous system (CNS) infection being the most severe form of the disease (Kilincer et al., 2006; Mamela et al., 1994). Seventy-one per cent of patients with CNS nocardiosis have coexisting infection outside the CNS (Kilincer et al., 2006). It is not uncommon for patients with CNS nocardiosis to have more than one brain abscess (Brown-Elliott et al., 2006). CNS disease often presents with symptoms of increased intracranial pressure, such as headache, nausea, vomiting and altered mental status, and up to 30 % of patients can present with seizures (Mamela et al., 1994; Brown-Elliott et al., 2006). The mortality rate for a patient with a *Nocardia* brain abscess ranges from approximately 20 % in immunocompetent patients to
isolates were deemed to be multi-drug resistant, with brain abscess et al. et al. et al. et al. 2014. Some investigators et al. and (2012) further reported the susceptibility data of 2198 isolates of various species found that 61 % were resistant to sulfamethoxazole and 42 % were resistant to TMP-SMX (Uhde et al., 2010). Ninety-three per cent of the Nocardia farcinica isolates were resistant to sulfonamides (Uhde et al., 2010). Lai et al. (2011) reported one isolate of Nocardia brasiliensis and one isolate of N. farcinica with resistance to sulfamethoxazole. Schlaberg et al. (2014) found that only 2 % of 2198 isolates were resistant to TMP-SMX, the majority being Nocardia pseudobrasiliensis and Nocardia transvalensis complex. They proposed that this discrepancy with prior studies (Uhde, 2010; Lai et al., 2011) is due to technical differences in susceptibility testing and interpretation, rather than being a true increase in the incidence of TMP-SMX resistance (Schlaberg et al., 2014). Brown-Elliott et al. (2012) further supported this discrepancy in possible TMP-SMX resistance being attributed to technical differences as the MIC of sulfonamides should be based on 80 % growth inhibition endpoints, rather than the traditional 100 % inhibition of other antimicrobials. In their analysis of 552 Nocardia isolates from six geographically diverse laboratories across the USA, they found only 14 isolates (2.5 %) resistant to sulfonamide, three isolates resistant to TMP-SMX, and 11 resistant to sulfamethoxazole (Brown-Elliott et al., 2012). To date, there are no reports of resistance of N. puris to TMP-SMX, amikacin or linezolid. However, our isolate, while susceptible to linezolid, has MIC 8.0, the upper limit of susceptibility, suggesting that linezolid may not be the best antimicrobial choice for empirical therapy against N. puris. When selecting antimicrobial therapy, double or triple coverage may be necessary, particularly with disseminated and/or CNS nocardiosis, until full identification and susceptibility data are available.

In conclusion, this is, we believe, the first case of Nocardia puris brain abscess reported in the USA. The patient was successfully treated with 3 months of dual therapy with imipenem and TMP-SMX, and then transitioned to monotherapy with TMP-SMX to complete a year of treatment. She is currently continuing TMP-SMX therapy.

Table 1. Nocardia puris antimicrobial susceptibilities with MIC data as determined by broth microdilution technique

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC (µg ml⁻¹)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>≤8.0</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>≤2.0</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>&gt;64</td>
<td>Resistant</td>
</tr>
<tr>
<td>Cefepime</td>
<td>&gt;32</td>
<td>Resistant</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤2</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Minocycline</td>
<td>≤1</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>8</td>
<td>Resistant</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>32</td>
<td>Resistant</td>
</tr>
<tr>
<td>Trimethoprim–sulfamethoxazole</td>
<td>1/19</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>16/8</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Linezolid</td>
<td>8.0</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

greater than 55 % in immunocompromised patients (Kilincer et al., 2006; Lowman & Aithma, 2010).

Only three studies have investigated the antibiotic susceptibilities of N. puris. The first, in 2010, had one isolate of N. puris, obtained from an ocular infection. The isolate was susceptible to amikacin, azithromycin and tobramycin, while being resistant to clarithromycin, ciprofloxacin and gatifloxacin (Reddy et al., 2010b). The antibiotics tested in this study were those most commonly found in an ophthalmological form. The second study analysed six clinical isolates of N. puris compiled from four large medical centres in Taiwan from 1998 to 2009. Antibiotic susceptibility testing was performed against amoxicillin–clavulanic acid, ceftriaxone, imipenem, ciprofloxacin, linezolid, sulfamethoxazole and amikacin. All isolates were resistant to ciprofloxacin and five of the six isolates were resistant to ceftriaxone. All six isolates had intermediate susceptibility to amoxicillin–clavulanic acid, but were fully susceptible to imipenem, linezolid, sulfamethoxazole and amikacin (Lai et al., 2011). We used these data to select the empirical regimen of imipenem and TMP-SMX to treat our patient while awaiting the susceptibility results of our clinical isolate.

Since treating our patient, Schlaberg et al. (2014) have reported the susceptibility data of 2198 Nocardia isolates collected in the USA from January 2006 to December 2011. Seven of these isolates were N. puris. Four of the N. puris isolates were deemed to be multi-drug resistant, with resistance to both imipenem and ceftriaxone. One isolate was fully susceptible to all antibiotics tested and two isolates had resistance to ceftriaxone. All isolates were susceptible to TMP-SMX, amikacin, linezolid, minocycline and tobramycin, similar to the findings of Lai et al. (2011). Sulfonamide antibiotics have been the mainstay of therapy for nocardioses since the first successful treatment in the 1940s (Brown-Elliott et al., 2006; Saubolle & Sussland, 2003; Kilincer et al., 2006). However, with disseminated disease or CNS infection, combination therapy with TMP-SMX plus a bactericidal agent such as imipenem, amikacin, minocycline, linezolid or broad-spectrum cephalosporins is indicated (Munoz et al., 2007). Some investigators recommend triple therapy with TMP-SMX and two of the above listed antibiotics (Brown-Elliott et al., 2006). This is supported by some studies showing increasing resistance to sulfonamides. A study of 765 Nocardia isolates of various species found that 61 % were resistant to sulfamethoxazole and 42 % were resistant to TMP-SMX (Uhde et al., 2010). Ninety-three per cent of the Nocardia farcinica isolates were resistant to sulfonamides (Uhde et al., 2010). Lai et al. (2011) reported one isolate of Nocardia brasiliensis and one isolate of N. farcinica with resistance to sulfamethoxazole. Schlaberg et al. (2014) found that only 2 % of 2198 isolates were resistant to TMP-SMX, the majority being Nocardia pseudobrasiliensis and Nocardia transvalensis complex. They proposed that this discrepancy with prior studies (Uhde, 2010; Lai et al., 2011) is due to technical differences in susceptibility testing and interpretation, rather than being a true increase in the incidence of TMP-SMX resistance (Schlaberg et al., 2014). Brown-Elliott et al. (2012) further supported this discrepancy in possible TMP-SMX resistance being attributed to technical differences as the MIC of sulfonamides should be based on 80 % growth inhibition endpoints, rather than the traditional 100 % inhibition of other antimicrobials. In their analysis of 552 Nocardia isolates from six geographically diverse laboratories across the USA, they found only 14 isolates (2.5 %) resistant to sulfonamide, three isolates resistant to TMP-SMX, and 11 resistant to sulfamethoxazole (Brown-Elliott et al., 2012). To date, there are no reports of resistance of N. puris to TMP-SMX, amikacin or linezolid. However, our isolate, while susceptible to linezolid, has MIC 8.0, the upper limit of susceptibility, suggesting that linezolid may not be the best antimicrobial choice for empirical therapy against N. puris. When selecting antimicrobial therapy, double or triple coverage may be necessary, particularly with disseminated and/or CNS nocardiosis, until full identification and susceptibility data are available.

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at 5 mg kg\(^{-1}\) day\(^{-1}\) as prophylaxis owing to the potential need for further chemotherapy to treat non-Hodgkin lymphoma.

References


