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CASE REPORT

Successful medical management of a *Nocardia farcinica* multiloculated pontine abscess

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SUMMARY

A 60-year-old man on chronic corticosteroids developed diplopia, gait instability and facial weakness. Brain MRI revealed a multiloculated pontine lesion. Cerebrospinal fluid (CSF) analysis demonstrated a neutrophil-predominant pleocytosis with elevated protein and low glucose. CSF cultures were negative, as was an extensive infectious diseases evaluation. Neurosurgical intervention was deferred in favour of empiric antimicrobial therapy due to the lesion's inaccessible location. After discontinuation of therapy, the patient reported a severe headache. A subsequent MRI demonstrated intraventricular pus. CSF culture grew *Nocardia farcinica*. The patient received parenteral therapy followed by oral trimethoprim-sulfamethoxazole. At 9 months, he is symptom free. This case illustrates the importance of including *Nocardia* in the differential diagnosis of brainstem abscesses, especially in immunocompromised patients. The availability of antimicrobial agents with excellent *Nocardia* activity and CSF penetration may enable treatment of brainstem abscesses for which surgical intervention has traditionally been considered necessary with medical management alone.

BACKGROUND

Nocardia spp. are Gram-positive bacteria found in soil, water and decaying vegetation. An underlying pulmonary process, HIV infection, malignancy, diabetes mellitus, transplantation and corticosteroid use, among other conditions resulting in deficient cell-mediated immunity, predispose to nocardiosis, although infection can occur in immunocompetent hosts. A possible rise in the incidence of *Nocardia* infections¹ has been attributed in part to advances in transplant medicine and the treatment of cancer and rheumatological disease leading to an increasingly immunocompromised population.²

While cerebral abscesses are a common neurological presentation of *Nocardia* infection, few cases of isolated brainstem abscesses have been reported. We present a case of a *Nocardia farcinica* multiloculated pontine abscess with neutrophilic meningitis to (1) underscore the importance of including *Nocardia* infection in the differential diagnosis for brainstem abscesses, particularly in immunocompromised individuals, given the potential challenges of making the diagnosis and (2) to highlight the successful medical management of a *Nocardia* brainstem abscess with antimicrobial therapy alone.

CASE PRESENTATION

A 60-year-old man with essential thrombocytosis, polycythaemia vera and nephrotic syndrome

secondary to minimal change disease treated with chronic prednisone was admitted to the hospital with diplopia, gait instability and right facial droop. He reported a 1-month history of fever, sweats and malaise. Brain MRI demonstrated a cluster of fluid attenuation inversion recovery (FLAIR) hyperintense, rim-enhancing lesions, 3.1 cm in maximal dimension, in the right posterior pons abutting the fourth ventricle with associated internal restricted diffusion (figure 1A). He was referred to our hospital for neurosurgical evaluation and consideration of brain biopsy.

The patient was married and employed as a maintenance manager for a school district. He reported no history of alcohol, tobacco or illicit drug use. He was born in California and had no history of travel out of state. His father and mother died of lung cancer and pancreatic cancer, respectively.

INVESTIGATIONS

Cerebrospinal fluid (CSF) obtained by lumbar puncture (LP) revealed 1525 white blood cells/mm³ (83% neutrophils), two red blood cells/mm³, protein 120 mg/dL and glucose 40 mg/dL. CSF bacterial, fungal and acid-fast bacilli cultures were negative, as were CSF cryptococcal antigen, *Coccidioides immitis* antibodies, *Mycobacterium tuberculosis* PCR and 16S rRNA gene PCR for bacterial identification. Multiple blood cultures were negative, as were a chest CT scan and whole body fludeoxyglucose positron emission tomography scan. Diagnostic and therapeutic stereotactic aspiration and drainage of the abscess was deferred in favour of empiric antibiotics given the pontine location and potential risks of the procedure. Repeat brain MRI 1 week into therapy with voriconazole, linezolid, ceftriaxone and metronidazole demonstrated a decrease in the enhancement and oedema surrounding the pontine lesion. Antimicrobial therapy was discontinued after 8 weeks. Within days, he developed a severe headache and light-headedness. Repeat brain MRI with contrast showed a near complete resolution of the pontine lesion. An MRI obtained 1 month later for persistent headaches demonstrated FLAIR hyperintense material layering within the lateral ventricles with associated restricted diffusion concerning intraventricular pus (figure 1B). After multiple non-diagnostic LPs, CSF analysis 4 months after initial presentation revealed a persistent neutrophil-predominant pleocytosis with elevated protein and low glucose. Beaded, branching filamentous organisms were seen on Gram and modified acid-fast stain. A positive subculture on Middlebrook 7H11 agar was identified as *Nocardia* spp. The isolate was



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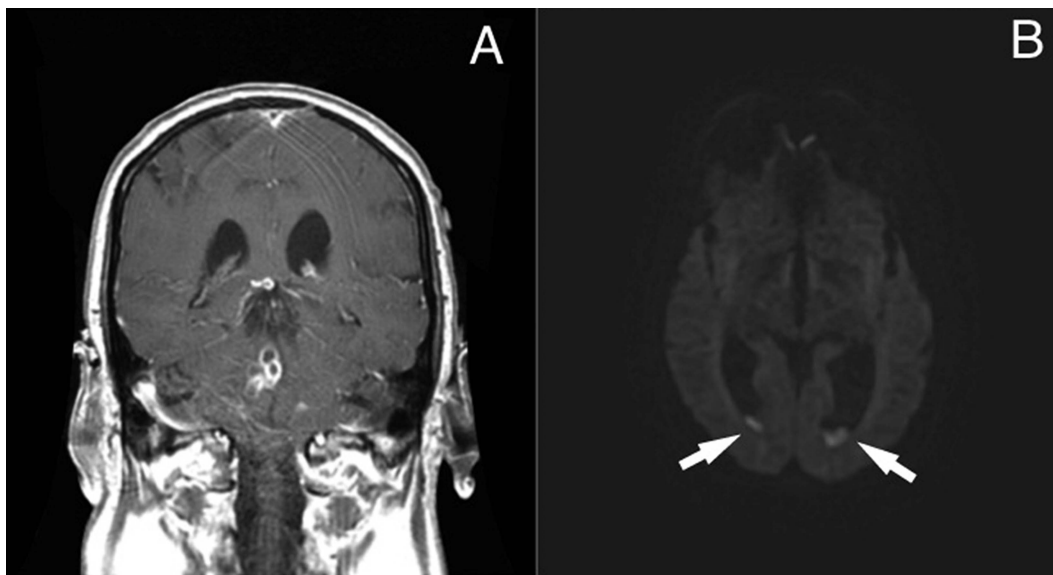


Figure 1 Coronal postcontrast T1 MRI (A) of the rim-enhancing multiloculated pontine abscess abutting the fourth ventricle at the time of initial presentation and axial diffusion weighted imaging (B) at the time of diagnosis demonstrating restricted diffusion within the posterior horns of the lateral ventricles (white arrows) consistent with intraventricular pus.

sent to a national reference laboratory and identified by 16S rRNA gene sequencing as *N farcinica*.

DIFFERENTIAL DIAGNOSIS

On the basis of the patient’s immunocompromised status, marked neutrophil-predominant CSF pleocytosis and ring-enhancing brainstem lesion, a pyogenic bacterial abscess (eg, *Streptococcus*, *Staphylococcus* spp., Gram-negative rods, oral anaerobes), along with *Nocardia*, *Listeria*, *M tuberculosis*, fungal infections (eg, *C immitis*, *Cryptococcus* spp, *Aspergillus* spp, mucormycosis), parasitic infections (eg, toxoplasmosis) and malignancy, were considered in the differential diagnosis.

TREATMENT

The patient was treated with linezolid and meropenem while awaiting susceptibility testing on the *N farcinica* isolate, after which he was changed to ceftriaxone and oral trimethoprim-sulfamethoxazole (TMP-SMX) followed by TMP-SMX monotherapy.

OUTCOME AND FOLLOW-UP

Nine months into TMP-SMX monotherapy, he is headache free with complete resolution of diplopia and improvement in his gait instability and right facial droop.

DISCUSSION

After pulmonary infection, the central nervous system (CNS) is the second most common site of nocardiosis and is associated with a much worse prognosis, particularly in immunocompromised patients.³ The CNS, estimated to be involved in 20–30% of cases,^{4 5} is presumed to be infected via haematogenous dissemination after primary infection, most commonly through the respiratory tract. The primary infection, however, can spontaneously resolve before CNS disease becomes apparent. In one review of 1050 cases from the literature, 38% had isolated CNS infection without evidence of infection at another site, as in this case.⁴

CNS nocardiosis commonly manifests as a focal abscess with or without meningitis, although pure meningitis has also been reported.⁶ Abscesses can be found anywhere in the brain, including the cortex, deep grey nuclei and cerebellum.⁴ Few cases, however, of isolated *Nocardia* brainstem abscesses, which in general comprise <1% of all intracranial abscesses,⁷ have been reported in the literature.^{8–10} We identified only four cases of isolated brainstem abscesses in the literature, ranging in age from 47 to 61 years (table 1). Two of the four occurred in individuals with a predisposing condition. In addition to non-specific symptoms of fever, headache and nausea/vomiting, patients presented with focal weakness, cranial nerve palsies and

Table 1 Summary of the clinical presentation, treatment and outcome of isolated *Nocardia* brainstem abscesses in the literature

Authors	Age	Clinical presentation	Comorbidities	Abscess location	Treatment	Outcome
Kepes <i>et al</i>	61	Hemiparesis evolving into quadriparesis	None	Medulla	Unknown	Death
Herkes <i>et al</i>	47	Occipital headache, CN VI palsy, Horner’s syndrome, bulbar dysfunction	Hodgkin’s disease	Pons, medulla	Radiotherapy and dexamethasone (for presumed lymphoma); no antimicrobial therapy	Death
Herkes <i>et al</i>	61	Fever, headache, nausea/vomiting	Posterior fossa meningioma status post resection complicated by CSF leak	Pons	Imipenem; no surgical intervention	Death
Bertoldi <i>et al</i>	54	Upper respiratory infection, diplopia, left-sided clumsiness	None	Pons	TMP-SMX and cefotaxime; no surgical intervention	Survived

bulbar dysfunction. An antemortem diagnosis of *Nocardia* infection was made in only two of the four patients, of which one, who was treated with antimicrobial therapy alone, survived.

As *Nocardia* spp. are relatively slow-growing bacteria that can be challenging to recover, multiple CSF specimens should be cultured to increase the yield, although it is not uncommon for the bacteria to be recovered only when direct pus is cultured.¹¹ Thus, a positive culture is often unavailable for inaccessible brainstem abscesses. Indeed, despite multiple LPs, a diagnosis was not made in this case until the patient developed ventriculitis with imaging characteristics consistent with intraventricular pus.

There are no randomised clinical trials on treatment of *Nocardia* infections. TMP-SMX has long been considered the standard of care based on observational studies.^{11–13} For more serious infections including CNS disease, empiric coverage with ≥ 2 agents active against *Nocardia* is recommended while awaiting susceptibility testing. A combination of TMP-SMX, amikacin and imipenem or ceftriaxone for CNS disease is often used. If an isolate is susceptible to TMP-SMX, it serves as the backbone for treatment of CNS disease. Linezolid, which also has good CSF penetration and oral bioavailability, is an alternative agent used successfully to treat CNS nocardiosis,¹⁴ although its long-term use may be limited by toxicities including myelosuppression and neuropathy. In a retrospective evaluation of 269 *Nocardia* isolates referred to the Centers for Disease Control and Prevention (CDC), all were susceptible to linezolid.¹⁵

N farcinica is generally considered to be a more resistant species and was originally distinguished from *Nocardia asteroides* based on resistance to tobramycin and cephalosporins.¹⁶ A multicentre study of clinical laboratory isolates found that one of 73 *N farcinica* isolates was resistant to TMP-SMX.¹⁷ In contrast, isolates referred to the CDC for antimicrobial susceptibility testing revealed a high prevalence of sulfonamide resistance among 105 *N farcinica* isolates, with 80% resistant to TMP-SMX.¹⁵ As such, we chose linezolid and meropenem, antibiotics with the greatest in vitro activity against *N farcinica*,¹⁵ as empiric therapy while awaiting susceptibilities. Interestingly, this patient's isolate was susceptible to most antimicrobials, including ceftriaxone, amikacin, imipenem, TMP-SMX and linezolid, which provided a range of options for step-down therapy.

The duration of therapy depends on the patient's immune status, the location of the infection and clinical response. CNS infections should be treated for a minimum of 1 year (typically 6 weeks of parenteral therapy followed by oral therapy), although more prolonged therapy may be required. Premature discontinuation of therapy may increase the risk of disease relapse.¹⁴ In general, surgical excision has been considered essential to the management of *Nocardia* cerebral abscesses.³ In a review of 131 cases, Mamelak *et al*³ recommended surgical excision in cases where the abscess failed to shrink after 4 weeks of therapy, there was clinical deterioration or for any abscess > 2.5 cm. For difficult to access abscesses, which is often the case for brainstem abscesses, stereotactic aspiration and drainage may be more prudent than craniotomy and excision, although the rate of failure for a closed-needle aspiration procedure may be higher for multiloculated abscesses, and multiple procedures may be needed. The availability of antimicrobial agents with excellent activity against *Nocardia* and CSF penetration may enable successful treatment of CNS disease with medical management alone in select cases, as evidenced by our patient who

never required surgical intervention for a multiloculated pontine abscess.

Learning points

- ▶ After pulmonary infection, the central nervous system is the second most common site of nocardiosis and is associated with a much worse prognosis.
- ▶ This case illustrates the importance of including *Nocardia* infection in the differential diagnosis of brainstem abscesses, especially in immunocompromised patients, given that the diagnosis of cerebral nocardiosis can be challenging and is often delayed due to difficulty recovering the organism.
- ▶ The availability of antimicrobial agents with excellent activity against *Nocardia* and cerebrospinal fluid penetration may enable treatment of brainstem abscesses, for which surgical intervention has traditionally been considered necessary, with medical management alone.

Contributors FCC, AM and CL conceived and designed the study and also acquired the data. FCC and CL analysed and interpreted the data. FCC drafted the manuscript. FCC, AM and CL critically revised the manuscript for important intellectual content and have read and approved the final version of the manuscript.

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