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Successful Treatment of Multifoci Nocardial Brain Abscesses

A Case Report and Literature Review

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Abstract: Brain nocardiosis is a serious opportunistic infection with high mortality. It exists more common in the immunocompromised hosts than the immunocompetent patients. Trimethoprim-sulfamethoxazole (TMP-SMZ) has been mostly considered as the choice of the medical treatment. Linezolid is also newly found to be effective to avoid the invasive surgery. The authors reported a case of patient with multifoci nocardial brain abscesses who failed with the combination of linezolid and TMP-SMZ alone but recovered with the surgery intervention and sequential antibiotics for 2 years. The patient lived a high quality life without recurrence and complications during the 30 months follow-up.

Through the literature review, we recommend earlier stereotactic aspiration for diagnosis, combination with surgery intervention and prolonged anti-infection therapy would improve the prognosis.

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Abbreviations: CT = computed tomography, HIV = human immunodeficiency virus, MRI = magnetic resonance imaging, TMP-SMZ = trimethoprim-sulfamethoxazole.

INTRODUCTION

Nocardiosis is a rare opportunistic disease that mainly affects the patients with deficient cell-mediated immunity, including organ transplants, leukemia, diabetes mellitus, alcoholism, underlying malignancy, human immunodeficiency virus (HIV), long-term use of steroid, and autoimmune disease.[1–3] Immunocompromised patients had high morbidity of brain involvement with high mortality.[4] The successful management of nocardial brain abscess remains ununified. Here, we reported an immunocompromised patient with multifoci nocardial brain abscesses, who was successfully treated with the combination of surgery intervention and systemic sequential antibiotics with 30 months follow-up.

CASE REPORT

A 42-year-old man was admitted in our hospital due to a productive cough for 3 months, dizziness, and seizures for 10 days. It was diagnosed with the atypical pneumonia 2 months before the admission, and he was commenced with antibiotics and methylprednisolone. Physical examination showed crackles in the lower field of right lung during the chest auscultation without fever and other physical and neurological abnormality. Laboratory test showed the white blood cell count was 7600 per milliliter. The percentage of neutrophils, lymphocytes, and monocytes were 86.8%, 9.8%, and 3.4%, respectively. Erythrocyte sedimentation rate (ESR) was 38 mm/hour. Skin test for tuberculosis was negative. HIV antibody, hepatitis B surface antigen (HBsAg), and hepatitis C antibody (anti-HCV) were all negative. Serum tumor markers spectrums were normal. Abdominal computed tomography (CT) showed no obvious abnormality. The pulmonary CT showed consolidation and infection in the middle lobe of right lung. Bronchoendoscopy, sputum cytology, sputum cultures, and bronchoalveolar lavage fluid showed no evidence of tumor or pathogen. Lung biopsy suggested chronic inflammation of mucosa with interstitial fibrosis. Brain magnetic resonance imaging (MRI) showed multiple lesions in the left frontal and bilateral parietal lobes with the possibility of granulomatous lesions mimicking metastatic tumors (Figure 1). The diagnosis was pulmonary infection with brain mass. He was commenced on ceftriaxone (2 g every 12 hour, iv) for pulmonary infections and mannitol (25 g every 8 hour, iv) and sodium valproate (Depakote ER, 500 mg twice a day, oral) for improving the neurological symptoms. Eleven days after admission, the symptoms of pneumonia improved, but the neurological symptoms deteriorated with frequent seizures and persistent headaches. Thus, an image-directed stereotactic aspiration of the left parietal lesion was performed. The aspirated fluid revealed pus and the positive culture showed *Nocardia*. We revised the diagnosis and choose the combined treatment of ceftriaxone (2 g, every 12 hour, iv) and trimethoprim-sulfamethoxazole (TMP-SMZ 2#, every 8 hour, oral) (SMZ 0.8 g, TMP 0.16 g). Two weeks later, the repeated MRI showed the size of lesions which undergone stereotactic aspiration was obviously shrunk, but other lesions enlarged (Figure 2A). The antibiotics changed to the combination of TMP-SMZ and linezolid. Four weeks later, the follow-up MRI showed the sizes of lesions slightly shrunk (Figure 2B) but the seizures still persist. Thus, the patient underwent excision of remain abscesses at craniotomy. Postoperatively antibiotic therapy was changed to cefoperazone/sulbactam sodium (2 g, every 8 hour, iv) and TMP-SMZ

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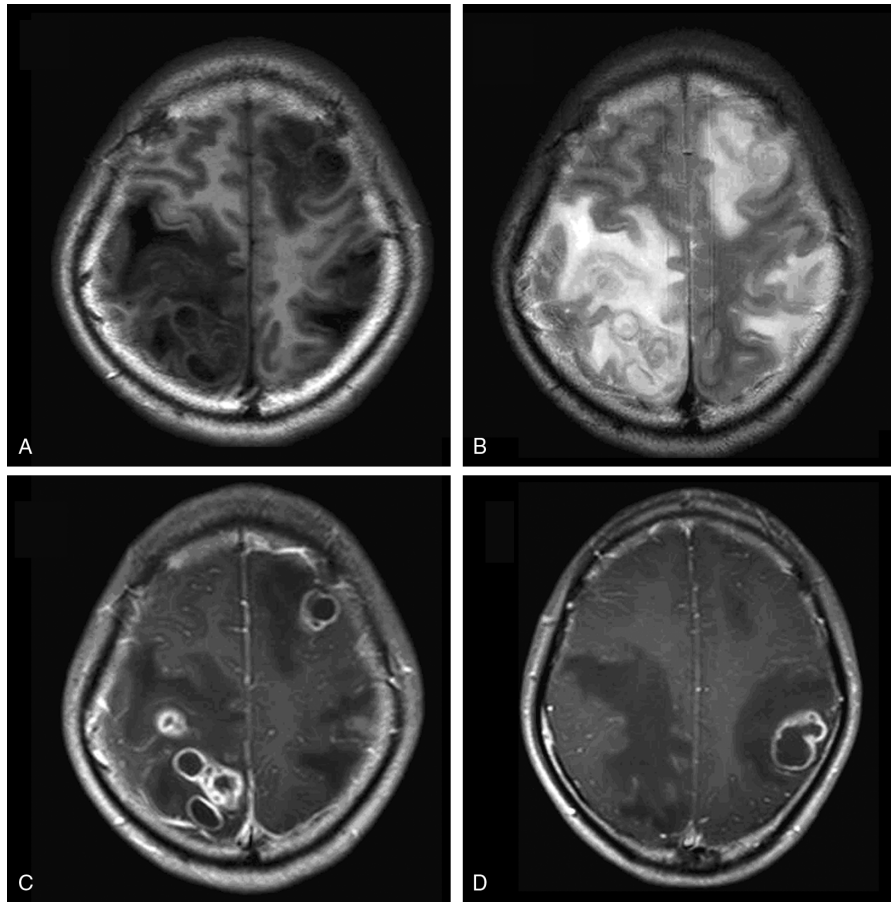

FIGURE 1. MRI found multifoci nocardial brain abscesses. (A) Axial T1-weighted image showed multiple low signal intensity lesions. (B) T2 weighting showed significant edema around the lesions. (C, D) T1-weighted contrast-enhanced image showed multifoci, ring-enhancing abscesses.

(2# every 8 hour, oral) because of the shortage of the supply of linezolid. The seizure was controlled and the patient discharged 4 weeks after operation with TMP-SMZ oral. The 6-month follow-up brain MRI showed 2 residual lesions (Figure 2C), the 12-month follow-up brain MRI showed the lesion on the left frontal lobe disappear, the other lesion lightly shrunk (Figure 2D). So, we prolonged the course of TMP-SMZ to 2 years. There was no recurrence of the abscess in the imaging at 30-month follow-up (Figure 2E, F), and the patient lived well without complications.

DISCUSSION

Nocardia species are gram-positive, aerobic, branching filamentous bacteria belonging to Actinomycetales, which can be found in the soil and dust throughout the world.[5] Three main species cause humans infection, including *N asteroides*, *N brasiliensis*, and *N caviae*. *N asteroides* is the most commonly isolated. *Nocardia* infection commonly arise in the immunocompromised states including organ transplants, leukemia, HIV, steroid abuse, and autoimmune disease.[6] The most common predisposing factors are corticosteroid use (54% of patients) such as in this case and organ transplantation (25%).[7] The pathogen can spread to the central nervous system hematogenously or through inhalation. The involvement of the central nervous system was found in nearly half of all disseminated nocardial infections in the literature.[8,9]

Nocardial brain abscesses is a very severe infection that carries the highest mortality rate among all bacterial cerebral abscesses[10] According to Mamelak study, the mortality rate in immunocompromised patients was 55%, whereas that overall mortality in immunocompetent patients was 20%.[11]

Because *Nocardia* can typically function as a parenchymal abscess in any part of the brain, the clinical presentations of nocardial brain abscesses are controversial, and there are no specific signs or symptoms to confirm the diagnosis. Seizures and focal neurological deficits are the commonest clinical manifestations observed in patients with nocardial brain abscess. The brain imaging mostly manifested as ring-enhancing lesions presumed to be cerebral abscesses. And meningeal involvement, cystic lesions, and subdural hematoma can also be found. Nocardial brain abscesses were often misdiagnosed as malignant brain tumors.[12] In this case, it was special that brain MRI showed the lesion mimicked the tumor mass, which may cause our delay for the diagnosis. Diagnosis was mostly confirmed by the evidence of the pathogen. It was reported 82% of patients confirming the diagnosis by culture of aspirates from the site of infection, including 43% of patients with subsequent culture of cerebral abscess aspirates, 31% with culture of the biopsy specimen, and 8.3% with central system fluid (CSF) culture.[7] So earlier aspiration or biopsy of lesions to get

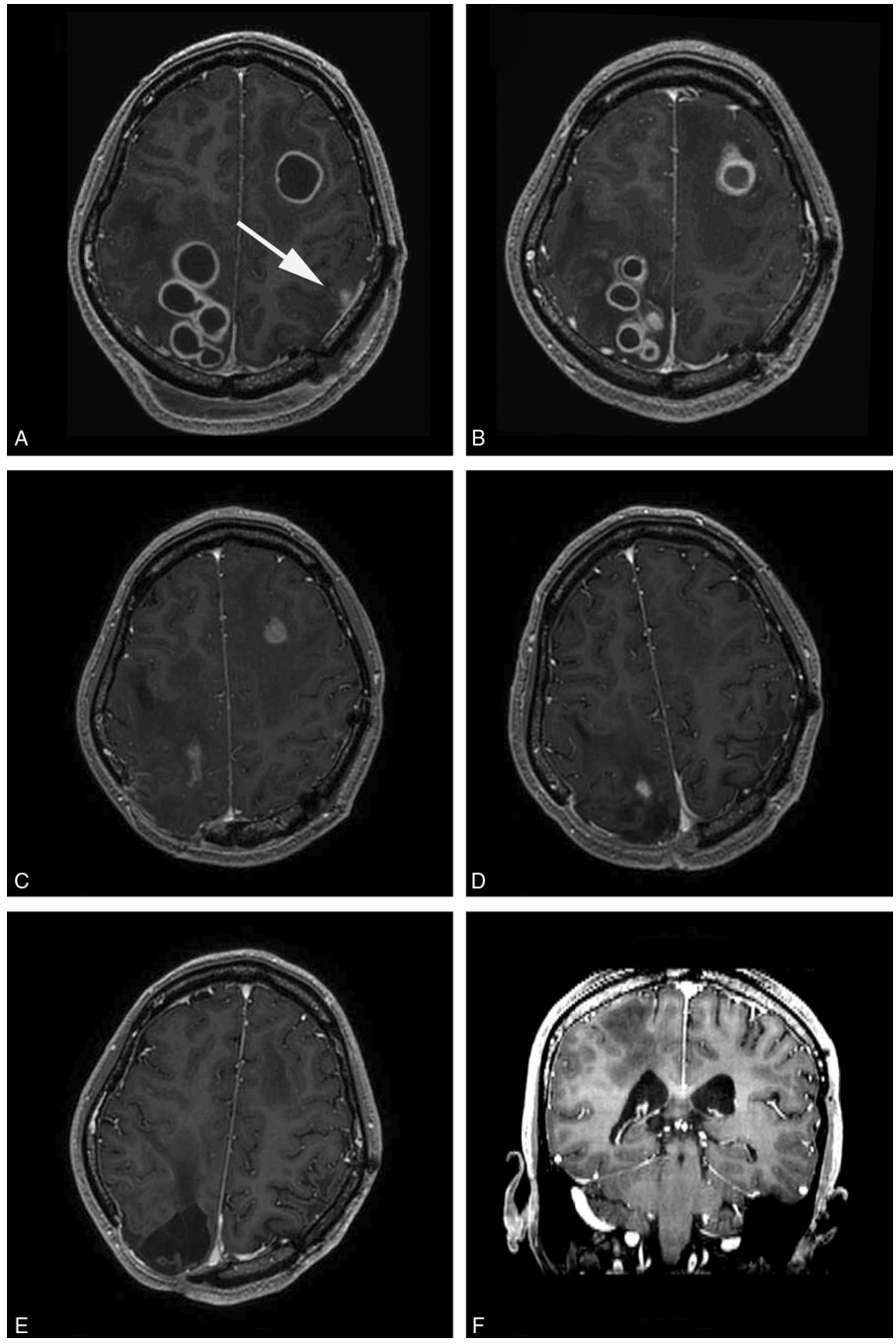

FIGURE 2. (A) T1-weighted contrast-enhanced image showed the lesion where stereotactic aspiration was done was obviously shrunk (arrow), other lesions were enlarged; (B) 4 weeks after linezolid used, the follow-up image showed the multifoci abscesses slightly shrunk; (C) 6-month follow-up image showed residual lesions on left frontal and right parietal lobe. (D) 12-month follow-up image showed a minor residual lesion on right parietal lobe. (E, F) Axial and coronal 30-month follow-up image did not demonstrate any enhancement of a residual mass.

evidence was very essential. In this case, we did not make a definite diagnosis through the clinical manifestation and imaging until we got the evidence of *Nocardia* species infection from the culture of brain tissue.

Like many other authors, we believe the antibiotic therapy of choice for nocardial brain abscess is the synergistic combination of TMP-SMZ.[3,4,7,8] In this case, the use of TMP-SMZ and ceftriaxone did not improve symptoms. As linezolid showed good permeability in the tissues and sensibility of nocardiosis in vitro in many researches,[13–15] it appeared to be an effective alternative for the treatment of nocardiosis while avoiding the surgery intervention.[14–17] Kaswan et al[13] reported a case of lumbar epidural and multiple brain nocardial abscesses. The patient recovered with 2-week treatment

combining linezolid and cotrimoxazol, and discharged from hospital. In our case, we also commence the medical therapy but failed. Surgical management is necessary in most cases. Mamelak et al[11] reviewed cases previously reported and suggested that if the patient's condition deteriorates or if the abscess does not decrease in size within 4 weeks, stereotactic aspiration should be performed to confirm the diagnosis and to decompress the lesion. And if any abscess enlarges after 2 weeks of antibiotic therapy or fails to shrink after 4 weeks of therapy, a craniotomy should be performed to excise the abscess. If the abscess is surgically inaccessible, aspiration/drainage may be repeated, although the likelihood of success is reduced. In this case, the abscesses enlarged after 2 weeks of combined antibiotic therapy, and 4 weeks later, the abscesses failed to obviously shrink although linezolid commenced which was not as effective as reported in that literature.[14,15] The reason may be the sensibility of the bacteria to linezolid in vivo. The craniotomy was performed to excise abscesses immediately as recommended in the literature. We continued SMZ-TMP for 6 months which was reported that sequential targeted antimicrobial medications longer than 6 months lower the mortality and relapse.[7] In the 6 and 12-month follow-up after discharge, brain MRI showed residual lesion. So we extended the course to 2 years. There was no report with the treatment longer than 12 months. At 30 months follow-up, MRI revealed no abscess in the brain. In previous case reports, some patients were alive with complications like motor deficits and hearing impairment.[11] However, this patient lived well without obvious complications.

In summary, Nocardial brain abscesses are a rare but very severe infection that carries the high mortality rate, especially in immunocompromised patients. Through earlier stereotactic aspiration for diagnosis, craniotomy to excise abscesses combined prolonged sequential targeted antimicrobial therapy can successfully shorten the hospitalized time and improve the prognosis.

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