Multiple brain abscesses caused by *Aspergillus fumigatus* in a patient with systemic lupus erythematosus

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**Case Report**

**ABSTRACT**

We report a case of multiple brain abscesses caused by *Aspergillus fumigatus* in a young woman with systemic lupus erythematosus (SLE). The clinical features included progressive headache, visual deterioration and paraparesis. Computed tomography (CT) scan of the brain demonstrated multiple ring-enhancing lesions with surrounding edema at frontal, occipital and parietal lobes. Laboratory tests showed anemia, hypoalbuminemia and marked proteinuria with renal impairment. Brain abscesses with active lupus nephritis were initially diagnosed. Stereotactic guided aspiration of an abscess was achieved and Gram’s stain of pus revealed numerous septate hyphae with dichotomous branching, subsequently grew *A. fumigatus*. Voriconazole was commenced with significant clinical improvement. Brain CT scan performed six weeks and four months after voriconazole treatment revealed less number and smaller in size of the abscesses. *Aspergillus* spp. should be included in differential diagnosis as a potential causative organism of brain abscess in SLE patients. (*J Infect Dis Antimicrob Agents* 2011;29:17-20.)

**INTRODUCTION**

*Aspergillus fumigatus* is a ubiquitous fungus and an opportunistic fungal pathogen of human and animal. It causes infections with a wide spectrum of clinical manifestations, ranging from benign colonization of the lung resulting in allergic disease, such as allergic bronchopulmonary aspergillosis (ABPA), to life-threatening diseases, such as invasive pulmonary aspergillosis (IPA).\(^1\) In a rare occasion, it may hematogenously disseminate and cause endocarditis, endophthalmitis, cutaneous aspergillosis, abscesses in internal organs such as liver, spleen, bone, kidney, myocardium and brain.\(^2\) Cerebral aspergillosis is responsible for 10% - 20% of all cases of invasive

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Aspergillosis and the mortality rate in such patients is extremely high. The major recognized risk factors for acquiring invasive aspergillosis include defects in phagocyte respiratory burst, such as those with chronic granulomatous disease, corticosteroid-induced suppression of macrophage conidiocidal activity, and neutropenia. Systemic lupus erythematosus (SLE) was found to be an underlying disease in about 1% of patients of invasive aspergillosis. In immunocompromised individuals with cerebral aspergillosis, meningism is not common and clinical manifestation may be non-specific which includes alteration of mental status, headache or seizures.

CASE REPORT

A 39-year-old Thai woman with history of SLE, treated with prednisolone for 2 years, presented with progressive headache and visual deterioration for 2 months. She had neither fever nor neurological deficit. Physical examination revealed a young woman with cushingoid appearance. Her temperature was 36.7°C, pulse rate of 120/min, respiratory rate of 20/min and blood pressure of 177/112 mmHg. Her skin showed discoid rash at right pinna. Neurological examination revealed bilateral papilloedema and paraparesis (motor power grade 4/5 at both lower extremities). Complete blood count showed hemoglobin 8.9 g/dl, hematocrit 28.2%, platelet 465,000/mm³, white blood cell counts 5,430 cells/mm³ with 30.2% neutrophil, 52.7% lymphocyte, 7.2% monocyte and 9% eosinophil. Renal function test showed blood urea nitrogen (BUN) 20.5 mg/dL and creatinine 1.4 mg/dL. Liver function test showed total bilirubin 0.1 mg/dL, aspartate transaminase 24 IU/L, alanine transaminase 15 IU/L, alkaline phosphatase 68 IU/L, albumin 2.8 g/dL and globulin 3.2 g/dL. Urinalysis showed pH 8, specific gravity 1.010, protein 4+, sugar-negative, ketone-negative, white blood cell 1-2 cells/HPF, red blood cell 5-10 cells/HPF, and no cast. Serum complement level was decreased. A computed tomography (CT) scan of the brain was performed and demonstrated multiple ring-enhancing lesions with surrounding edema at frontal, occipital and parietal lobes (Figure 1). Brain abscesses with active lupus nephritis were diagnosed and she was treated empirically with intravenous ceftriaxone, metronidazole and TMP-SMX for coverage of common causative bacteria including streptococci, enterobacteriaceae, anaerobes and Nocardia spp. Although her symptoms of headache, visual deterioration and paraparesis were slightly improved, brain CT scan after 1 week of treatment demonstrated no decrease in size of the lesions. Therefore, stereotactic guided aspiration of abscess was achieved and three milliliters of yellow-green colored pus was collected intraoperatively. Gram’s stain of the aspirated pus revealed numerous septate hyphae with dichotomous branching. Antimicrobial agents were therefore discontinued and Amphotericin B (1 mg/kg/day) was commenced. Pus culture was subsequently reported as A. fumigatus and the antifungal agent was changed to voriconazole. Brain CT performed 6 weeks and 4 months after voriconazole treatment showed disappearance of some lesions and smaller in size of the remaining abscesses (Figure 2). The patient continued voriconazole for 1 year with marked improvement.

DISCUSSION

This is a case of cerebral aspergillosis in SLE patient. Aspergillosis is relatively less common than the other infections in patients with SLE. Differential diagnosis of brain abscess in SLE patient normally includes cerebral nocardiosis, listeriosis, mixed bacterial brain abscess, tuberculosis and cryptococcosis. Although cerebral aspergillosis in SLE is relatively rare, the mortality rate is high. Therefore, high index of
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Suspicion to achieve prompt diagnosis and treatment is crucial and an attempt to get tissue histopathology for definite diagnosis by invasive interventions is the key milestone. A systematic review by Lin et al. reported an overall case fatality rate of 58% in 1,941 patients with invasive aspergillosis. The mortality was highest in patients with bone marrow transplant recipients and those with disseminated or cerebral aspergillosis (approximately 88%). A. *fumigatus* is the most common reported species that causes invasive aspergillosis which was also isolated from our patient. Other pathogenic species include *A. flavus, A. niger,* and *A. nidulans.*

Although it has been shown in a randomized controlled trial that voriconazole was superior to amphotericin B deoxycholate for treatment of invasive aspergillosis, and voriconazole became the primary antifungal treatment for invasive aspergillosis, most of the cases were invasive pulmonary infection. Randomized controlled trial to compare treatment outcomes in patients with cerebral form of aspergillosis is lacking and therefore warranted. Furthermore, the Infectious Diseases Society of America (IDSA) Practice Guidelines for Diseases Caused by *Aspergillus* suggested that intracranial Aspergillus abscess is not well-penetrated by systemic antifungal agents. Stereotactic procedures for abscess drainage should be considered. In addition, an open-label study showed that voriconazole in combination with surgical intervention gave favorable outcomes in 35% and a long-term survival of 31%. Voriconazole is therefore the treatment of choice for cerebral aspergillosis. Our case successfully underwent cerebral abscess drainage and received antifungal treatment with voriconazole and the outcome was favorable.

Figure 1. Computed tomography of brain showed multiple ring enhancing lesions with perilesional edema.

Figure 2. Computed tomography of brain showed disappearance and smaller in size of cerebral abscesses after treatment with voriconazole for 4 months.
We report here a case of cerebral aspergillosis presented with multiple abscesses in the brain successfully treated with voriconazole and stereotactic guided abscess aspiration. *Aspergillus* spp. should be considered as a potential pathogen of brain abscesses in patients with SLE receiving corticosteroid therapy.

References