Disseminated invasive aspergillosis of the brain and spine

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ABSTRACT
We report a case of 27-year-old female with steroid using presented with progressive headache for 2 months followed by lower back pain. Computed tomography of the brain revealed brain abscess at multiple sites and MRI of thoracolumbar spine showed spondylodiscitis at T9-10 level. Open brain biopsy was done and the histopathology demonstrated fungal with septate hyphae. Voriconazole was administered as a drug of choice. After 2 weeks of the treatment, symptoms were improved and follow-up imaging was improved also. (J Infect Dis Antimicrob Agents 2011;29:83-7.)

Note: This case had been presented and discussed in the Interhospital Case Conference on Infectious Disease (ICCID), 13 October 2011, Chon Buri, Thailand.

INTRODUCTION
Invasive aspergillosis is a life-threatening infection in immunocompromised patients such as those who receive chemotherapy or immunosuppressive therapy, including corticosteroid.¹ The incidence of invasive aspergillosis has increased.² Although pulmonary involvement is a common presentation, invasive extrapulmonary aspergillosis can occasionally be observed and this condition is associated with poor prognosis.³⁴ Herein, we report a case of disseminated aspergillosis involving brain and spine without evidence of apparent pulmonary infection.

CASE REPORT
A 27-year-old woman with multiple sclerosis was admitted to provincial hospital because of subacute headache. Her headache localized at temporal area and radiated to occipital area. The characteristics of pain were dull and progressive. She sometimes awoke at night because of a headache. She neither had fever nor vomiting. The physical examination was unremarkable except for right hemiparesis from underlying multiple sclerosis.

One year ago, she presented to the provincial hospital with right hemiparesis. Multiple sclerosis was...
diagnosed and initially treated with a high dose of steroid. The dose of steroid was tapered to 10 mg of prednisolone. She had stable minimal right hemiparesis.

During this presentation, computed tomography (CT) of the brain demonstrated rim enhancing lesions at left frontal area with surrounding edema and another lesion at right cerebellar area. Her blood culture for bacteria was negative. She was treated for bacterial brain abscess with ceftriaxone and metronidazole. During the admission, she developed back pain at lower back area. MRI of T-L spine revealed spondylodiscitis at T9-10 level without spinal cord compression. After intravenous antibiotic treatment for 2 weeks, her headache was slightly improved. A follow-up CT of the brain found a new lesion at left cerebellar area. She was referred to a secondary care hospital. At that hospital, she was presumptively treated with intravenous trimethoprim/sulfamethoxazole for nocardia brain abscess. The follow-up magnetic brain imaging of brain and spine after two weeks of treatment showed no improvement. She was referred to King Chulalongkorn Memorial Hospital for further diagnostic procedures. The total duration of this illness was 3 months before arrival at our hospital.

On physical examination, she was afebrile. There were no pheripheral signs of endocarditis, no point of tenderness and no visible abnormality at her back. On the neurological examination, there were right hemiparesis with decrease pinprick sensation at the right side. Her white blood cell count was 13,820 mm$^3$ with 81.8% neutrophil and 13.4% lymphocyte. The hemoglobin was 14.5 g/dL and platelet count was $352 \times 10^9$/L. Chest radiography was normal. Anti HIV was nonreactive and serum cryptococcal antigen was negative. Blood culture for bacteria, mycobacterium and fungus were also negative. Spinal bone biopsy was done under fluoroscopy. The pathology from bone biopsy was mild chronic inflammation and negative for malignancy and granuloma. The patient was then sent for brain biopsy. There was encapsulated abscess $3 \times 3$ cm with multiloculation at left frontal lobe. The histopathological examination revealed suppurative inflammation with granulomata and dichotomas branching with septate hyphae organism. Cerebral aspergillosis was diagnosed based on morphologic findings on the brain pathology. Intravenous voriconazole (6 mg/kg every 12 hours) was started on the first day and continued (5 mg/kg intravenous every 12 hours).

Follow-up imaging after two-week treatment of intravenous voriconazole, all brain abscesses were decreased in size. She was discharged from hospital with oral voriconazole for 400 mg per day. Prednisolone was discontinued. After two months of treatment, the symptoms of headache and low back pain disappeared. Her MRI of the brain and T-L spine were all significantly improved. Improvement of the lesions at brain and spines could be demonstrated.

**DISCUSSION**

Cerebral aspergillosis accounts for about 10% of all cases of invasive aspergillosis. After the lung, the central nervous system (CNS) is among the most frequent secondary sites of invasive aspergillosis. It is also the most serious form, with a mortality rate of more than 90%. Aspergillus can reach the CNS by three different routes; hematogenous spread from a remote extracranial focus, extension from a contiguous extracranial location and direct introduction of aspergillus by a neurosurgical procedure iatrogenically. The common portal entry before dissemination is the lung. Our patient had a disseminated form of invasive aspergillosis without chest symptoms. There was a report of isolated CNS aspergillosis without lung lesions.

It is difficult to differentiate between pyogenic
Figure 1. MRI of the brain shows brain abscess at left frontal and both cerebellar area with surrounding edema.

Figure 2. MRI of T-L spine: Spondylodiscitis at T9-10 level that progressed in the follow-up imaging 1 month later after antibacterial treatment (A and B).

Figure 3. Dichotomas branching, septate hyphae of *Aspergillus*. (H&E stain, × 400)

Figure 4. Septate hyphae. (GMS stain, × 400)
and fungal infection from radiologic findings. In fungal spinal osteomyelitis MRI may demonstrate hypointense lesions of the vertebral bodies on T1-weighted sequences with lack of hyperintensity within the discs on T2-weighted images, and preservation of the intranuclear cleft on T2-weighted images. However, in our patient, there was no sign of fungal infection from imaging.

The outcome of CNS aspergillosis is usually unfavorable with mortality rates exceeding 90%. Now, voriconazole, a new broad spectrum triazole, is a first line therapy for treatment of invasive aspergillosis. Successful treatment of cerebral aspergillosis was first reported in 1997 in a patient with acute leukemia. High drug concentrations of voriconazole in CSF of guinea pigs and immunocompromised patients have been reported. The concentrations of voriconazole in bone tissue were high and similar to those seen with fluoroquinolones or rifampicin, which are known as drugs having a good bone diffusion. Our patient was treated with voriconazole and showed favorable outcome.

In conclusion, disseminated aspergillosis should be considered in the differential diagnosis of brain abscess in patients with immunocompromised status.

References


