ABSTRACT

We report a case of 57-year-old diabetic man presented with progressive neck pain for 4 months followed by weakness and numbness of right arm. MRI of the cervicothoracic spine revealed osteomyelitis and diskitis of the C6-T4 spine with epidural and prevertebral phlegmon. Open bone biopsy and decompression of the T4-5 spine was done and the histopathology demonstrated degenerated fungal hyphae within necrotic cartilage. Bone tissues grew *Aspergillus fumigatus*. Amphotericin B was administered as a primary drug, followed by voriconazole. However, the treatment was subsequently discontinued due to drug-induced hypersensitivity. Amphotericin B was re-administered for 4 weeks, followed by oral itraconazole. After 2 months of the treatment, neck pain, weakness and numbness were improved. To our knowledge, this is the first case report of vertebral aspergillosis from Thailand. (*J Infect Dis Antimicrob Agents* 2011;28:197-202.)

Note: This case had been presented and discussed in the Interhospital Case Conference on Infectious Diseases (ICCID), 18 March 2011, Bangkok, Thailand.

INTRODUCTION

*Aspergillus* spp. is a rare etiology of vertebral osteomyelitis but the disease may lead to devastating outcome.\(^1,2\) We here described a case of vertebral aspergillosis, complicated with epidural abscess that was successfully treated with long-term oral itraconazole.
CASE REPORT

A 57-year-old Thai man, from Ubonratchatani province, presented with progressive neck pain for 4 months. Patients’ underlying diseases included diabetes mellitus (DM), hypertension, dyslipidemia and a remote history of pulmonary tuberculosis (TB), for which he received a completed a course of anti-tuberculous chemotherapy. Four months prior to admission, he developed progressive neck pain radiating to right upper extremity and a subsequent onset of weakness and numbness of the hand. He initially received an evaluation at a provincial hospital where a wedge-shaped mass-like lesion at the left upper lobe of the lung and the extended area of osteomyelitis of the C6-T4 spine were identified from magnetic resonance imaging (MRI) (not shown). Despite bronchoscopy, the diagnosis remained unestablished. Anti-tuberculous regimen was begun for clinical suspicion of spinal TB. However, severe drug hypersensitivity had developed soon after the treatment. He was then referred to our hospital for further investigation and treatment. On admission, physical examination revealed neck tenderness by manual compression with limited flexion and extension of the lower cervical to the mid-thoracic area. A grade 4 weakness of the right triceps muscle was also noted together with decreased pinprick sensation over his right arm. Chest examination revealed left-sided tracheal deviation and decreased breath sound over the left upper lung. Complete blood count revealed a hematocrit of 35.6%, white blood cells of 12,750/mm³ (neutrophil 80%, lymphocyte 16%, monocyte 4%), and platelet of 346,000/mm³. The second MRI of the cervicothoracic spine (not shown) showed no significant change of the vertebral and pulmonary abnormalities. He underwent open bone biopsy. The pathology showed granulomatous inflammation on the T4-5 disc but stains and cultures for bacteria, mycobacteria and fungus were all negative. Following one month after closed observation without specific antibiotic therapy, he subsequently experienced progressive weakness of the right hand. Repeated MRI was undertaken (Figure 1) and showed worsening spondylodiskitis from the C5 to T5 levels along with increased thickness and pressure effect of epidural and prevertebral phlegmon, mild cord compressions at the C5-6 and T4-5 levels, and segmental atelectasis of the left upper lobe in the region of the suspected mass-like lesion. CT scan of the chest (not shown) was subsequently done and confirmed the presence of atelectasis of the apicoposterior segment left upper lobe that resulted from complete occlusion of the left apicoposterior segmental bronchus. Besides mild thickening of the overlying pleura and extrapleural fat, no associated pleural effusion or adjacent chest wall involvement was seen. He subsequently underwent micro-decompressive laminectomy of the T4-5 spine and the second bone biopsy. The histopathology of bone tissue revealed degenerated fungal hyphae within necrotic cartilage (Figure 2A). *Aspergillus fumigatus* was isolated from fungal culture of bone tissues (Figure 2B). The patient was initially aimed for long-term oral voriconazole treatment but severe maculopapular rash occurred 2 weeks after the treatment initiation. Voriconazole was discontinued and intravenous amphotericin B was started. After 2 weeks of the treatment, the symptoms including neck pain, weakness and numbness of the right upper limb improved and ESR level decreased. However, he developed gradual worsening of renal function. Amphotericin B was discontinued. He subsequently received oral itraconazole solution of 400 mg daily. Six months after antifungal therapy, the follow-up MRI (Figure 3) revealed markedly improved spondylodiskitis with some residual abnormalities at the T4-5 level. Patient currently remains on long-term oral itraconazole treatment.
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Figure 1. (A) Sagittal T1-weighted MRI with fat suppression and intravenous contrast administration revealing a long segment of spondylodiskitis from the C6 level down to the T5 level. Corresponding subligamentous disease and pus spreading are seen up to the C2 level (white arrows), along with anterior epidural soft-tissue component (black arrows) which causes multi-focal spinal cord compressions.

(B) Coronal T2-weighted MRI with fat suppression showing segmental atelectasis of the left upper lobe in which multiple dilated bronchi are seen (white arrow). Note that the dilated bronchi are filled with hyperintense mucus. Mild mediastinal shift to the left is seen.

Figure 2. GMS stain of bone tissue showed degenerated fungal hyphae within necrotic cartilage (A) and microscopic morphology (B) showing atypical structure of *Aspergillus fumigates* with secondary conidiophores (black arrow) connected with the primary conidiopore.
DISCUSSION

In the present report, we illustrated a case of vertebral aspergillosis that occurred in a patient with long-standing diabetes mellitus. Despite a considerable number of published cases worldwide, this is the first case report from Thailand. Consistent with previously reported cases of vertebral aspergillosis, from which back symptoms was a classic presentation, our patient initially presented with a prolonged onset of pain and numbness over the cervical and thoracic spine but in spite of invasive procedures, the final diagnosis was initially unestablished until the second attempt of open bone biopsy. This finding highlights the fact that the disease is difficult to diagnose and can easily be missed, as the invasive procedure is not always widely available in the resource-limited setting and tissue culture might provide low diagnostic sensitivity, as well as delayed result. In the present case, empirical treatment of TB was begun prior to referral to our hospital but soon after the treatment, adverse effect occurred. Our experience reflects a rather common medical practice in Thailand where empirical treatment of TB was usually begun due to a higher incidence of the infection in the current era of TB endemic. As the diagnosis in the present case is quite challenge and the morbidity from the disease was quite substantial from the disease itself as well as severe adverse drug effect, our experience underscores an importance in recognizing...
the diagnostic step toward a definite result of invasive fungal disease.

Of interest, our patient had a remote history of pulmonary TB which resulted in bronchostenosis and subsequent development of postobstructive atelectasis and bronchiectasis at the left upper lobe. Although initial bronchoscopy failed to reveal evidence of fungal infection, fungal colonization within the mucus-filled dilated bronchi remained possible. Lack of inflammatory sign in the adjacent pleura or chest wall, however, made the possibility of contiguous spread of the infection from pre-existing pulmonary focus less likely. According to recent case series, hematogenous infection is the most common route of disease acquisition, particularly among immunocompromised population. As diabetes mellitus is a known condition that potentially causes impaired polymorphonuclear function, the possibility of hematogenous spread is not excluded but this speculation is not documented due to lack of tissue diagnosis to confirm presence of the organism in the lung tissue.

Of interest, diabetes mellitus was recently noted as “newly recognized factor” of invasive aspergillosis in developing countries but the true incidence of the infection within this population remains unknown. Between types of invasive aspergillosis that occurred among individuals with diabetes mellitus, vertebral involvement is rather rare, compared to sinus/rhino-orbital infections. However, cases of vertebral aspergillosis in diabetic patients have occurred, including those with pre-existing structural lung lesion from previous tuberculosis, from which aspergilloma was present at the time of diagnosis in one report. In the present study, we showed that the disease morbidity can be substantial in the absence of appropriate treatment which consists of surgical debridement and/or decompression of the spine and antifungal therapy. According to Infectious Disease Society of America (IDSA) guidelines, treatment of Aspergillus osteomyelitis with either amphotericin B or voriconazole is recommended as a primary option while itraconazole may be used as an alternative agent. Due to adverse drug effect related to both agents, oral itraconazole was given in this case with a long-term satisfactory response at 6 months of follow-up.

In conclusion, we have reported a case of vertebral aspergillosis caused by A. fumigatus in a diabetic patient. Long-term treatment with oral itraconazole has resulted in gradual clinical and radiographic improvement.

References
7. Korovessis P, Repanti M, Katsardis T, Stamatakis M. Anterior decompression and fusion for Aspergillus