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CLINICAL CASE REPORT

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Multiple Brain Abscesses Due to *Aspergillus Fumigatus* in a Patient With Liver Cirrhosis

A Case Report

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Abstract: Invasive cerebral aspergillosis always developed in immunocompromised host. Early diagnosis may save life in this critical condition; however, it is difficult to reach. Herein, we presented an unusual case of invasive cerebral aspergillosis in a cirrhotic patient.

A 47-year-old man presented with progressive deterioration of consciousness for three days. The patient had a history of alcoholic liver cirrhosis, Child-Pugh class C. Magnetic resonance imaging (MRI) of brain showed multi-focal parenchymal lesions, which was consistent with multiple brain abscesses. The diagnosis of invasive cerebral aspergillosis was made by molecular based laboratory methods including Aspergillus galactomannan antigen assay and oligonucleotide array. Despite treatment with the antifungal agent, Amphotericin B, the patient died at the ninth day of hospitalization.

Our findings suggest that liver cirrhosis can be one of risk factors of invasive cerebral aspergillosis, and support the diagnosing usefulness of MRI, Aspergillus galactomannan antigen assay, and oligonucleotide array.

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Abbreviations: CSF = cerebrospinal fluid, MRI = magnetic resonance imaging.

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INTRODUCTION

Invasive cerebral aspergillosis usually developed in immunocompromised host.[1–3] Early diagnosis may save life in this critical condition; however, it is difficult to reach. Herein, we presented an unusual case of invasive cerebral aspergillosis that was diagnosed by image, and molecular-based laboratory methods.

CASE PRESENTATION

A 47-year-old man presented with progressive deterioration of consciousness for 3 days. The patient had a history of alcoholic liver cirrhosis, Child-Pugh class C. On arrival, his vital signs were as follows: a temperature of 38.2°C, pulse rate of 112/min, respiratory rate of 23/min, and blood pressure of 115/74 mm Hg. Laboratory examinations were as follows: white cell count 22900/mm^3, platelet 52000/mm^3, creatinine 0.86 mg/dL, asparate aminotransferase 55 IU/L, sodium 130 mmol/L, glucose 151 mg/dL, ammonia, 30 umol/L, C-reactive protein of 89 mg/L (reference value <3 mg/L). Radiography of the chest revealed multiple patches over bilateral peripheral lung fields. Computed tomography of brain did not disclose any evidence of intracerebral hemorrhage. Magnetic resonance imaging (MRI) of brain showed multifocal parenchymal lesions with signal change involving subcortical regions of bilateral superior frontal gyri, left lateral occipital gyrus, bilateral cerebellar parenchyma, and left lenticular nucleus (Figure 1), which was consistent with multiple brain abscesses. In support of our clinical diagnosis, we used ELISA and PCR to detect *Aspergillus* antigen and DNA, respectively. Cerebrospinal fluid (CSF) Platelia *Aspergillus* galactomannan antigen test showed a value of optical density index >7.46. However, for the PCR we used oligonucleotide array for rapid screening in which the gold standard for *Aspergillus* species confirmation relies on the internal transcribed spacer sequencing and the 28s rDNA sequencing.[4] In this case, the internal transcribed spacer result was *Aspergillus fumigatus* 99.5% (549/552) and 28s rDNA sequencing result was *A fumigatus* 99.5% (578/581). At the same time, the culture of sputum specimen grew *A fumigatus*, and serum *Aspergillus* galactomannan antigen test also showed a positive result (optical density index ≥ 0.5). Despite treatment with the antifungal agent, Amphotericin B, the patient had rapidly developed shock with acute respiratory failure. The patient died at the ninth day of hospitalization. However, eventual fungal culture results of CSF remain negative after 4 weeks.

DISCUSSION

Invasive cerebral aspergillosis is an uncommon disease, and most of reported cases developed in severe immunodeficiency patients, such as transplant recipients, steroid users, and cancer

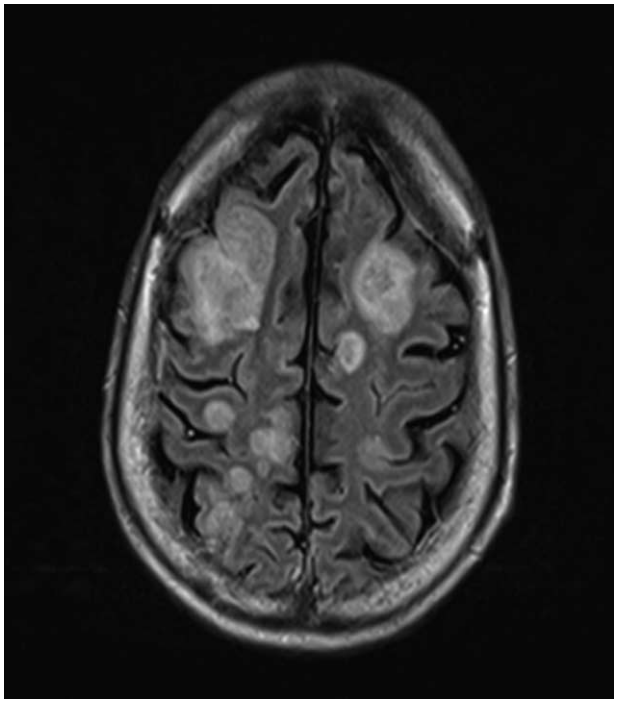

FIGURE 1. Magnetic resonance imaging showed multifocal parenchymal lesions with hemorrhage in the brain (arrows).

patients.[1–3] In contrast, liver cirrhosis—the only one immunocompromised condition for the present case—is not traditionally considered an important risk factor of invasive cerebral aspergillosis. Based on a literature search in PubMed/Medline, Jeurissen et al[5] identified only a total of 43 cases with cirrhosis and/or liver failure who have developed invasive aspergillosis between 2002 and 2012. Among them, lung was the most frequent organ involved (n = 42), whereas other organs including skin, esophagus, pericardium, myocardium, stomach, kidney, and brain were less involved with only 7 patients being reported. Although invasive aspergillosis rarely develops in cirrhotic patients without conventional risk factors, our report and previous studies[5–7] should suggest that clinicians should keep in mind this possible invasive aspergillosis, including aspergillus brain abscess as possible differential diagnosis among patients with liver cirrhosis.

Because the clinical manifestations of intracerebral aspergillosis are nonspecific, early diagnosis to prompt direct treatment is difficult. However, other options for early diagnosis of invasive aspergillosis should be explored. Ideally, culture of sterile CSF specimen is the method of choice and is considered the ''gold standard'' for definitive diagnosis. Current methods to obtain CSF specimen from this critically ill patient were hindered unless an aggressive, risky, and invasive approach is exercised. Alternatively, MRI and molecular diagnostic methods offered an attractive approach that helped us to save the life of this patient and to reach a definitive diagnosis in speedy manner.[4] In our case, characteristic MRI findings of *Aspergillus* brain abscess, and the positive *Aspergillus* galactomannan antigen assay provided useful information in diagnosing invasive aspergillosis. In addition, a supportive test, oligonucleotide array, had helped us to accurately and rapidly identify the mycotic infection to the species level as *A fumigatus*. Based on these findings, it is evident that using oligonucleotide array test can make the diagnosis of invasive aspergillosis more easy and rapid than before. However, the unavailability of this test constrains its application as a diagnostic method of choice in conventional laboratories.

CONCLUSIONS

Our findings suggest that liver cirrhosis can be one of risk factors of invasive cerebral aspergillosis and support the diagnosing usefulness of MRI, *Aspergillus* galactomannan antigen assay, and oligonucleotide array.

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