Fusarium Brain Abscess in a Patient with Diabetes Mellitus and Liver Cirrhosis

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Abstract-

Purpose: Invasive mycosis caused by the *Aspergillus, Fusarium,* and *Mucor* can be fetal, especially in the immunocompromised patients with central nervous system (CNS) involvement. Here we present a case of CNS *Fusarium* infection, and this is the first reported case of *Fusarium* brain abscess in Taiwan.

Case report: A 65-year-old woman presented with fever and conscious disturbance for 3 days. Neurological examination showed stupor consciousness, neck stiffness, multiple cranial nerves palsy, and bilateral Babinski signs. Magnetic resonance imaging showed multifocal lesions involving medulla oblongata, pons, bilateral cerebral peduncles, and bilateral cerebellar peduncles. Cerebrospinal fluid (CSF) study revealed neutrophil predominant pleocytosis, but both blood and CSF culture were negative. We treated patient with ceftriaxone and vancomycin initially as empiric therapy for suspected bacterial meningoencephalitis. However, chronic sinusitis with fungal ball and brain abscess were later found. Despite antifungal treatment and surgical intervention, patient expired 3 months after admission. Fungal culture of the brain abscess disclosed Fusarium species 2 weeks after her death.

Conclusion: CNS *Fusarium* infection should be considered when an immunocompromised patient presenting with fever, conscious change, cranial nerve palsies, and angioinvasion suggested by brain imaging. To properly manage the disease, early effective antifungal therapy and neurosurgical intervention are important.

Key Words: Brain abscess; Fusariosis; antifungal therapy, Voriconazole.

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INTRODUCTION

Invasive mycosis caused by the Aspergillus, Fusarium, and Mucor can be fetal, especially in the immunocompromised patients with central nervous system (CNS) involvement. The portal of entry is mostly airborne, with subsequent blood stream dissemination or direct invasion from the infected sinuses[(1)]. The consequences of these fungal infections often result in cranial nerves palsies and stupor consciousness, as well as focal destruction of

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the skull.

To properly manage the disease, early effective antifungal therapy and neurosurgical intervention are important[2]. Moreover, differential diagnosis of the fungal type, including Aspergillus, Fusarium, and Mucor, might be cardinal in determine the treatment regimen and their outcome. Aspergillus and Fusarium have thin and septate hyphae, and their common host factors are those with neutropenic condition and patient who receives organ or stem-cell transplantation. However, Mucor has broad hyphae with hyposeptate, and it could infect immunocompromised and diabetic patients[1]. Here we present a case of CNS Fusarium infection.

CASE REPORT

A 65-year-old woman with diabetes mellitus and liver cirrhosis was brought to our emergent department (ED) with fever and conscious disturbance for 3 days. Initially, she suffered from fever and severe headache for 3 days. Symptomatic treatment had been given in the local clinic, however, right facial swelling, right eye congestion with discomfort, and blurred vision developed later, followed with conscious disturbance. On admission, physical examination revealed fever (body temperature of 38.1 °C), blood pressure of 130/60 mmHg, and tachycardia (heart rate of 119 beats per minute). Her Glasgow coma scale (GCS) was E2M5V2. Neurological examination revealed stupor consciousness, and neck stiffness 4 fingerbreadths. Grossly she had complete ptosis, ophthalmoplegia, proptosis, and congestion of right eye. Her pupils were anisocoric (5 mm without light reflex at the right and 3.5 mm with light reflex at the left). There was also left abducens palsy, right peripheral facial palsy, and bilateral Babinski signs. There was no focal weakness of limbs. Brain computed tomography (CT) scan without enhancement showed ill-defined low densities in bilateral cerebellum and pons. Magnetic resonance imaging (MRI) showed multifocal lesions involving medulla oblongata, pons, bilateral cerebral peduncles, and bilateral cerebellar peduncles (Fig. 1). Her complete blood count showed anemia (hemoglobin concentration 8.5 g/dL), leukocytosis (white blood cell count 14,400 /μL mainly with segmented neutrophil 89%), and thrombocytopenia (platelet count 97,000 /μL). Her biochemistry data were as follows: randomized glucose 883 mg/dL, C-reactive protein 18.07 mg/dL, sodium 125 mEq/L, and ammonia 153 μg/dL. Cerebrospinal fluid (CSF) results were as follows: leukocytes, 308 /mm^3 (78% neutrophils); protein, 330 mg/L; and glucose, 89 mg/dL (simultaneous blood glucose, 883 mg/dL). Ceftriaxone and vancomycin were given initially as empiric antibiotics for possible bacterial meningoencephalitis.

Patient's left eye became ophthalmoplegic without light reflex on the 4th day of admission. Her conscious remained stupor. Chronic sinusitis with possible fungal infection was suspected according to the orbital CT (Fig. 2), and amphotericin B was soon added. But galactomannan antigen assay, blood, and CSF culture were

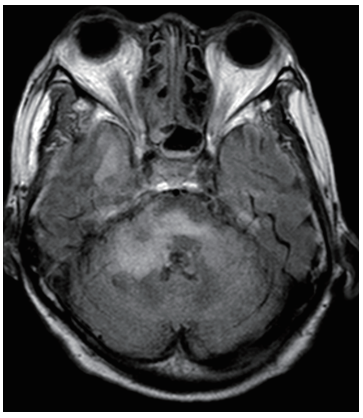

Figure 1. Brain T2/FLAIR magnetic resonance images revealed multifocal lesions involving medulla oblongata, pons, bilateral cerebral peduncles and bilateral cerebellar peduncles.

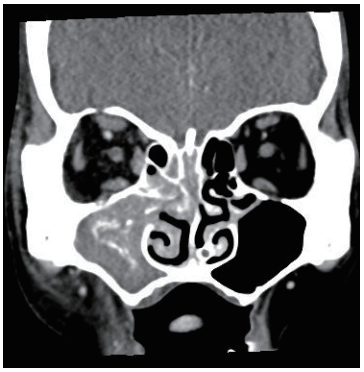

Figure 2. Orbital computed tomography revealed mucosal thickening or fluid accumulation in bilateral ethmoid, sphenoid and right maxillary sinuses.

all negative. Biopsy and surgery were not done at that time because of unstable condition.

Bilateral multiple sinusectomy was done on the 16th day, numerous fungal balls were found in bilateral ethmoid and right maxillary sinuses (Fig. 3). The pathology report showed numerous thin hyphae with regular branching, and Aspergillus was suspected (Fig. 4). Although continuous antifungal therapy with amphotericin B was administered, brain MRI on 42th day showed abscess formation on right cerebellopontine angle and segmental narrowing of right internal carotid artery, suggesting of angioinvasion by fungus. Operation for brain abscess removal was done on the 50th day. Pathology suggested either mucormycosis or degenerated aspergillosis (Fig. 5). Liposomal amphotericin B was used since 51st day because of impaired renal function. However, her condition became more deteriorated after abscess removal, and finally expired due to multi-organ failure 3 months after admission. Fungal culture of the abscess disclosed Fusarium species 2 weeks after her death.

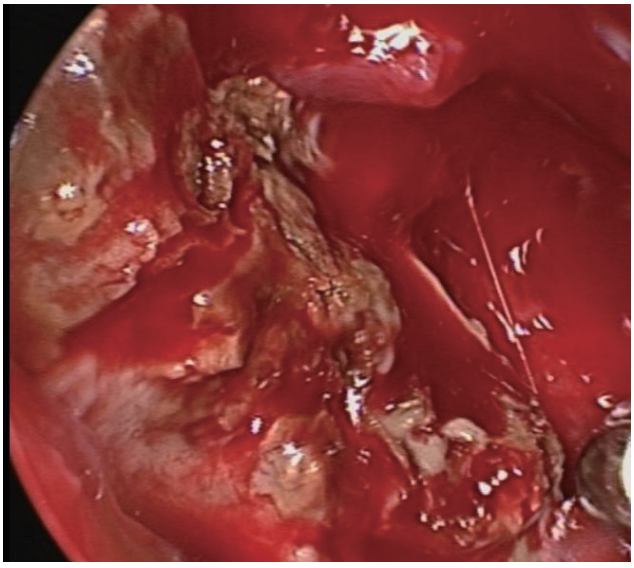

Figure 3. Bilateral multiple sinusectomy disclosed fungal balls in bilateral ethmoid and right maxillary sinuses.

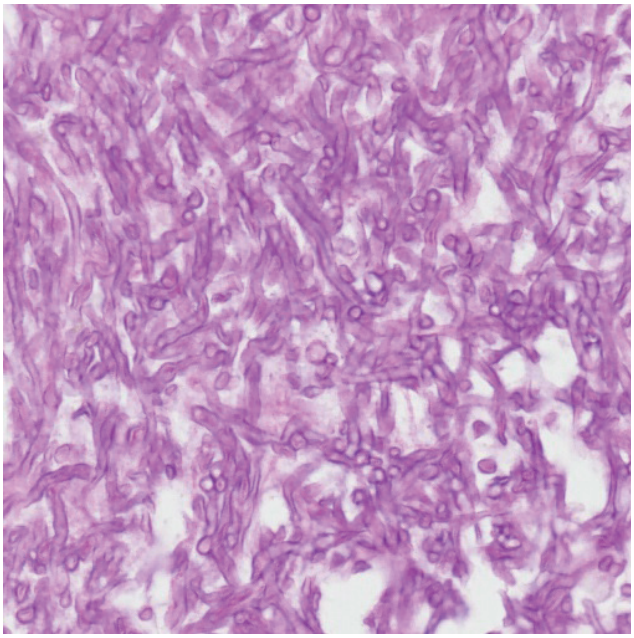

Figure 4. The fungal balls were composed of thin hyphae dichotomized in acute angles. (H&E stain, 200X)

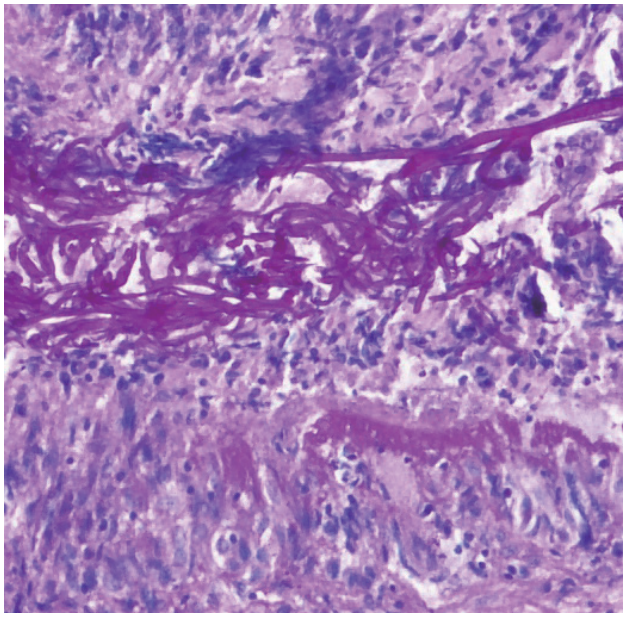

Figure 5. The specimen from brain abscess showed necrotic tissue with numerous thin hyphae. (Periodic acid-Schiff stain, 200X)

DISCUSSION

Fusarium belongs to the genus of Deuteromycetes (fungi imperfecti) and is an important plant pathogen, but it has limited role in human infection. Although rare, it was first isolated from skin lesions of burn patients in

1964[3]. In 1973, the first case of dissemimated fusariosis was reported in a child with acute leukemia[4]. In the literature, there were cases of invasive fusariosis, and most patients were immunocompromised with underlying hematological malignancy, HSCT (hematopoetic stem cell transplant), solid organ transplantation, burn, neutropenia, glucocorticoid exposure, or end-stage liver disease[5]. Clinical presentations were focal to the skin in immunocompetent but usually disseminated among immunocompromised, involving lungs, sinus, bones, and skin, however, Fusarium brain abscess infection is rare[6-7]. Our patient is the first reported case of Fusarium brain abscess in Taiwan.

Reviewing the literature[5], there were cases of Fusarium infection in patient with hematological malignancies had history of diabetes mellitus. In another case report[6], the patient infected with Fusarium brain abscess had underlying diabetes mellitus and acute leukemia but failed stem cell transplantation. Our case is the first case of patient who had diabetes mellitus and liver cirrhosis as the predisposing immunocompromised condition infected with Fusarium without underlying hematological malignancies or post-transplantation status. Other immunocompromised condition had not been discussed in the past.

There was no specific emphasis on the CSF data in Fusarium brain abscess in the literature. There was a case report of Fusarium brain abscess whose CSF data showed pleocytosis with 100% PMN leukocytes, low glucose level, and high protein level[7]. In our patient, CSF study showed pleocytosis with polymorphonuclear (PMN) leukocytes predominance (78%) is not a typical finding for fungal infection and often misinterpreted as a possibly partially treated bacterial infection, then delayed the initiation of antifungal therapy. In fact, it is not uncommon in invasive fungal infection such as mucormycosis, aspergillosis and fusariosis presenting with modest PMN predominance in CSF study. Concomitant bacterial infection should always be considered and ruled out by optimal evaluation. We performed CSF study for three times and the results for CSF culture all showed negative findings,which may point out the concomitant bacterial infection is less likely.

Tissue culture is a gold standard for diagnosis of fusariosis, and Aspergillus galactomannan antigen assay, 1,3-D-glucan test could be used to aid in the diagnosis of invasive fusariosis[7-8]. In patients with disseminated fusariosis, blood cultures were only positive in 60% of cases[9]. In our case, blood and CSF culture for fungus were negative, and Fusarium species grew in tissue culture after patient expired. Novel biomarkers or PCR technique for detection of fusariosis are needed.

Parenchymal involvement is a key feature of Fusarium brain abscess[10]. Brain MRI showed ring-enhancing lesion in the brain parenchyma, meningeal enhancement may also be seen if patient developed meningoencephalitis[6]. Besides, Fusarium are highly angioinvasive and may cause hemorrhagic or ischemic infarction events[1]. Segmental narrowing of the vessels could be seen on MRA (magnetic resonance angiography) due to its characteristic of vascular invasion[7].

Although amphotericin B and itraconazole are commonly used in fungal infection, elevated dose levels of voriconazole against Fusarium species is suggested because of wide voriconazole susceptibility ranges for the Fusarium species[10-11]. Moreover, combination of liposomal amphotericin B with voriconazole or other azoles is not better than voriconazole alone[12-13]. We treated our patient with amphotericin B since 4th day, and shifted to liposomal amphotericin B since 51st day due to its lesser nephrotoxicity. However, we did not use any azoles since admission because of probable mucormycosis or aspergillosis suggested initially by pathologist. Unfortunately, though with aggressive early sinusectomy and abscess removal, our antifungal regimen with only amphotericin B and lysosomal amphotericin B was proved to be ineffective.

CNS Fusarium infection should be considered when an immunocompromised patient presenting with fever, conscious change, cranial nerve palsies, and angioinvasion suggested by brain imaging. Although accurate diagnosis of fusariosis requires tissue culture, voriconazole should be considered as empirical therapy for possible fusariosis. Early diagnosis, surgical debridement of the involved tissue, and antifungal therapy are crucial for invasive fusariosis.

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