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Disseminated zygomycosis with involvement of the central nervous system

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Abstract

Zygomycosis of the central nervous system (CNS) can manifest in three distinct clinical forms, as rhinocerebral zygomycosis, as disseminated zygomycosis with CNS involvement, and as isolated cerebral zygomycosis. We present a case of a 2-year-old boy with leukaemia and disseminated zygomycosis, caused by *Absidia corymbifera*, involving the brain, spinal cord, lung and liver. The child received treatment with liposomal amphotericin B and posaconazole for 6 months. Although the lesions of the lungs and liver resolved, those of the CNS persisted and the child is in a vegetative state. A review of the literature after 2004 identified ten additional cases of disseminated zygomycosis with cerebral involvement, all but one of which had concurrent lung infection. The most common underlying disease in these cases was haematological malignancy and the mortality rate was 70%. Disseminated zygomycosis with cerebral involvement is a fatal disease. Early recognition and prompt intervention with combined medical and surgical treatment may improve the outcome.

Keywords: Amphotericin B, CNS, disseminated, posaconazole, spine, zygomycosis

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Introduction

Zygomycosis is an invasive, life-threatening fungal infection that mainly affects immunocompromised hosts. Zygomycetes can invade virtually any tissue or organ, resulting in a variety of clinical presentations. The central nervous system (CNS) can be invaded by Zygomycetes either contiguously from adjacent paranasal sinuses, or haematogenously from a remote site of infection. Zygomycosis of the CNS can present in three distinct clinical forms, as rhinocerebral zygomycosis, as disseminated zygomycosis with CNS involvement, and as isolated cerebral zygomycosis. Rhinocerebral zygomycosis is the most frequent form of CNS zygomycosis and has been well described in the literature [1], whereas disseminated zygomycosis with brain involvement and isolated cerebral zygomycosis are rarer forms of the disease. In this report, we present a boy with acute myeloid leukaemia and disseminated zygomycosis with involvement of the CNS and we review the relevant literature.

Illustrative Case Report

A 2-year-old boy was admitted to hospital because of acute myeloid leukaemia. Two days after admission, he received induction chemotherapy with cytosine-arabinoside, thioguanine and idarubicin. Two weeks later, while on antimicrobial treatment for a febrile episode, his fever recurred and his leukocyte count was 310 cells/μL. The antimicrobial regimen was changed to meropenem and teicoplanin, and liposomal amphotericin B (L-AmB) (5 mg/kg) was added. Over the next 3 days the patient developed multiple focal seizures. Computed tomography (CT) of the brain revealed a ring-enhanced lesion extending into both parietal lobes and the patient was started on corticosteroids and phenyntoin (Fig. 1a). Chest CT showed extensive infiltrates in both lungs with bilateral pleural effusion. A CT scan of the abdomen revealed two low density areas in the liver (Fig. 1b). Subsequently, the patient developed status epilepticus and quadriparesis, was intubated and was transferred to the intensive care unit. Direct microscopy of the pleural fluid revealed fungal hyphae. All cultures from blood, pleural fluid, bronchoalveolar lavage and cerebrospinal fluid were negative for bacteria and fungi. Serum galactomannan and polymerase chain reaction (PCR) for *Aspergillus* were negative. A brain

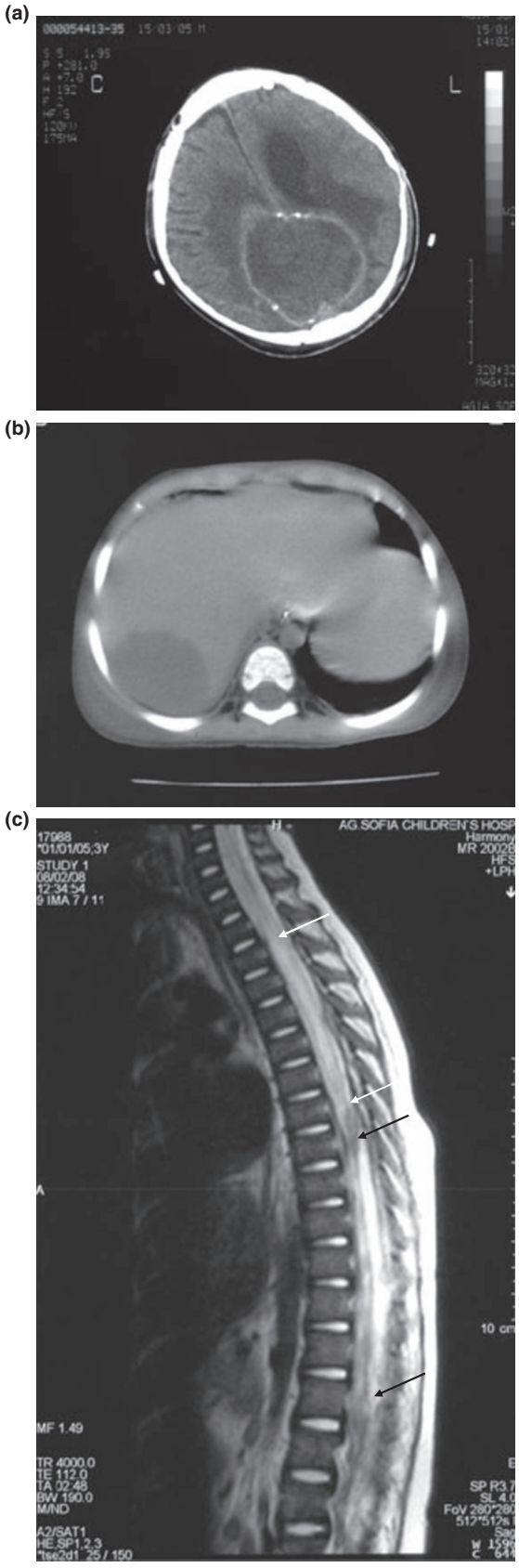

FIG. 1. (a) Computed tomography (CT) scan showing a large, hypodense, interhemispheric mass lesion with ring contrast enhancement compressing both lateral ventricles with extensive surrounding oedema. (b) Abdominal CT scan showing two low density areas, one in the right liver lobe and the other in the border between the right and left lobes. (c) Spine magnetic resonance imaging T2-weighted image showing extensive intramedullary oedema of the thoracic spinal cord (white arrows) and epidural fluid entrapment at the thoracolumbar junction (black arrows).

biopsy revealed fungal hyphae consistent with *Aspergillus*. The child was treated with voriconazole and caspofungin along with intraventricular AmB for 1 month. He remained febrile and his clinical condition was unchanged. Magnetic resonance imaging (MRI) of the brain revealed new lesions and MRI of the spine showed hypodense lesions extending from the cervical to the lumbar spinal cord area (Fig. 1c). In light of these findings, paraffin-embedded brain tissue was re-examined using a semi-nested PCR specific for Zygomycetes and sequencing of the amplicon identified the fungus to be *Absidia corymbifera* [2]. The patient was then treated with posaconazole (25 mg/kg) and L-AmB (7 mg/kg) for 6 months. He defervesced, the lung and liver lesions disappeared, but the brain and spinal cord lesions remained unchanged. Six months after discontinuation of antifungal therapy, the patient is alive but in a vegetative state and his leukaemia is in remission.

Discussion

The case presented here underlines the diagnostic and therapeutic difficulties involved in the management of cerebral fungal infections. The diagnosis of CNS zygomycosis is often difficult because the clinical and radiological findings are non-specific. For a definitive diagnosis, histology and culture are needed. Histological identification of fungus, however, may be incorrect and cultures are positive in <70% of cases [3]. In our patient, the fungus had been misidentified as *Aspergillus* based on hyphal morphology, which resulted in the administration of inappropriate treatment for a month. The correct identification of fungus as *Absidia corymbifera* was made by PCR in paraffin-embedded tissue after conventional means had failed to allow the diagnosis. In addition to the diagnostic difficulties, the management of fungal infections with CNS involvement is problematic as a result of the poor response of the CNS to standard antifungal therapy. With the administration of L-AmB and posaconazole, the lung and liver lesions resolved, whereas those of the CNS remained unchanged.