A Case Of Invasive Aspergillosis in a Patient with No Identifiable Immunodeficiencies

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Abstract
Invasive fungal infections usually affect patients with immunodeficiencies and very rarely patients with no known or identifiable risk factors. Diagnosis could be delayed in patients without previously known immunodeficiencies due to a low index of suspicion, leading to a delay in treatment and a potential poor outcome. We report a case of a postpartum woman with no history of immuno-compromised disease who developed left hemiparesis with evidence of invasive aspergollosis affecting the nervous system, and leading to fatal outcome. The patient had a mass-like lesion in the neuroimaging with soft tissue shadowing in the chest x-ray leading to initial diagnosis of tuberculosis. The brain biopsy showed changes consistent with a diagnosis of aspergillosis. The source of the aspergillus infection was not clear. Aspergillus infection should be considered in patients with no identifiable immunodeficiencies who have abnormal brain imaging and chest x-ray, as early treatment may alter the outcome.

Introduction

Central nervous system (CNS) aspergillosis is one of the opportunistic fungal infections that affect immuno-compromised hosts, such as patients with; prolonged neutropenia, haematopoietic stem cell transplant, solid organ transplants particularly lung and liver, and acquired immunodeficiency syndrome (AIDS) [1,2]. It remains a rare entity in patients without known immunodeficiencies [1,2,3,4]. It can have a variety of presentations including aseptic meningitis, multiple cranial abscesses, mycotic aneurysms, ischaemic and haemorrhagic infarcts and solitary mass-like lesion [1,2,3,5]. The main source of the infection is usually inhalation of spores making lungs the primary site of infection leading to haematogenous dissemination to other organs. Direct extension can occur from the para-nasal sinuses and orbits, and direct inoculation at the time of surgery. Aspergillosis affecting the nervous system could present with altered mental status, seizures and focal neurological deficits, and has varied neuro-imaging features [4,6]. We report a patient with no known immunodeficiencies who presented with aspergillosis affecting the CNS.

Case report

A 27-year-old Pakistani woman who moved to the United Kingdom six months before presented with three days of headaches with left sided jerky movements of shoulder and left facial drooping. A day before admission, left arm and left leg weakness was noticed. Three weeks before the presentation the patient had uneventfully delivered a full term healthy baby. The general physical examination including the chest was recorded as normal. Neurological examination revealed evidence of mild left sided hemiparesis, with normal symmetrical reflexes and down-going plantars. Initial basic investigations revealed a normal full blood count, differential count, erythrocyte sedimentation rate, C- reactive protein, urea, sodium, potassium, liver function test, glucose and calcium.

On admission a brain computed tomography (CT) showed evidence of hypo-density in the right frontal area (figure 1). Magnetic resonance imaging (MRI) brain showed almost homogenous circumscribed hyper-intensity in the right hemisphere on T2 weighted and diffusion weighted sequence with hypo-intense signal on T1 weighted sequence (figure 2). Magnetic resonance Venogram reported as normal. At this stage it was felt these changes could represent an anterior circulation ischaemia. Patient was given aspirin and kept under observation.

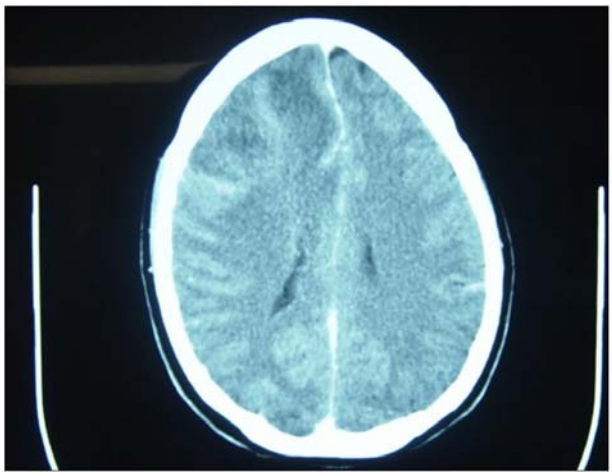

Figure 1 Axial CT brain showing evidence of hypodense area in right frontal area with minimal midline shift

Forty-eight hours later the patient's Glasgow Coma Score (GCS) dropped to 6, with the developing of a dense hemiplegia on the left side. The right pupil became fixed and dilated (6mm) with divergence of the right eye. The left pupil was of normal size (2mm) and reacting to light. These signs were consistent with right trans-tentorial herniation with compression of rostral brainstem. CT brain showed an increase in the size of right hemispheric hypo-density, along with compression of midbrain and significant midline shift. Mannitol was given and right hemicraniectomy was conducted urgently. The brain was oedematous on opening the skull and a partial right frontal lobectomy was performed, and a frontal lobe sample was sent for histological analysis.

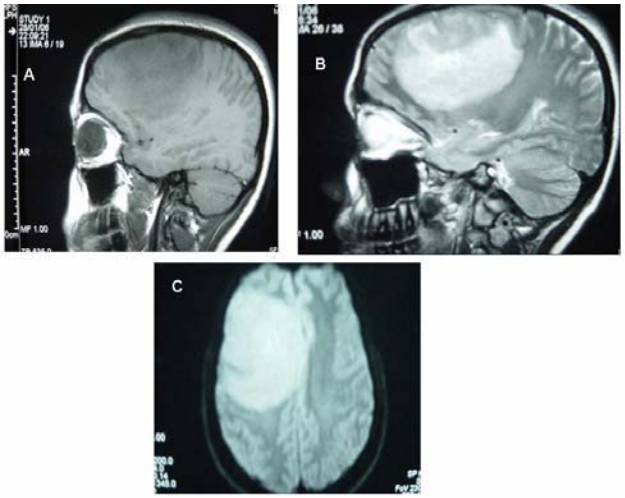

Figure 2 A) Sagittal T1W MR showing uniform hypo-intensity B) Sagittal T2W MR brain showing almost homogenous circumscribed hyper-intensity in right hemisphere C) Axial Diffusion Weighted MR showing an area of hyper-intensity

The chest x-ray was reviewed at that stage and a soft tissue shadowing in the right mid-zone along with calcified lymph nodes and mottled appearance was reported. On the basis of the abnormality in the chest x-ray and the CNS presentation it was thought that tuberculosis is the likely diagnosis, and after consultation with the respiratory team anti-tuberculous treatment was started. HIV screening was negative.

After the procedure the patient's condition improved with GCS of 11. She started communicating with family members and both pupils became reactive to light, but dense left-sided hemiparesis remained. Two days later the clinical status took a turn for the worse with GCS dropping to 3, intracranial pressure rising to 25cm H2O and then to 35cm of H2O and became intractably high. At this stage the results of biopsy came back showing evidence consistent with aspergillosis, (figure 3) and amphotericin B was started. Brain CT at this stage showed extensive mass herniating out from the right hemicraniectomy site. Unfortunately she expired 24 hours later.

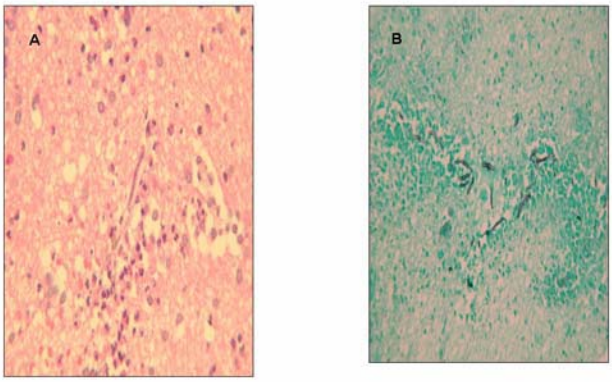

Figure 3 A) Hematoxylin & Eosin stain shows brain with fungal hyphae in the centre, and associated neutrophils B) Grocot's methenamine silver staining shows septae and branching of hyphae

Discussion

Aspergillus species are ubiquitous moulds found in organic matter [3]. More than one hundred species have been identified, with the majority of human illness being caused by Aspergillus fumigatus, Aspergillus flavus, Aspergillus terreus and Aspergillus niger [7]. The transmission of fungal spores to the human host is usually via inhalation, but not always. Aspergillus may cause a broad spectrum of disease in the human host, ranging from hypersensitivity reactions to direct angioinvasion. Aspergillus primarily affects the lungs with haematogenous dissemination, which can cause endophthalmitis, endocarditis, abscesses in the myocardium, kidney, liver, spleen, soft tissue, bone and CNS [1,2]. Invasive Aspergillosis has a significantly high mortality rate of 30-95% [1,2,3] even higher with CNS disease, approaching the 100% [8]. Treatment mainly comprises of voriconazole, amphotericin B, itraconazole and capsofungin [9]. A major reason for the devastating prognosis in CNS aspergillosis is the delay in diagnosis and poor penetration of antifungal drugs into the CNS, with the exception of voriconazole [9].

Our patient is not known to have, and we could not find, an immuno-deficiency disorder, but she may have had undiagnosed disease such as chronic granulomatous disease. The rapid course of her illness made it difficult to ascertain her immune status. However, the neuro-imaging showed unusual features, as cases that have been described before had ring enhancement lesions, especially in patients with no known immunodeficiencies, and can be solitary or multiple lesions [4,6]. This case expands the spectrum of imaging features in patients with cerebral aspergillosis and demonstrates that a large circumscribed mass can be a feature of intracranial aspergillosis in patients with no risk factor. We presume that the lesion in this case resulted from either a thrombosis (angioinvasion and haematogenous spread results in combination of arterial and venous blood flow impediment with resultant infarct) or a rapidly enlarging mass-like lesion. We hypothesize that our patient probably developed aspergillosis via the nasal route leading to pulmonary involvement first, then spreading to the brain. The infection may possibly have been acquired nosocomially in the maternity hospital during delivery, with a construction site nearby and building work going on, although no other cases were reported in our hospital. Nosocomially acquired aspergillosis has been reported before in immuno-suppressed patients, usually from an airborne source and associated with hospital construction or contaminated ventilation systems [10].

As the patient was not diagnosed until biopsy results came back four days after admission, no anti-fungal drugs were given until the last 24 hours, as the clinical diagnosis was tuberculosis. Clinically she deteriorated so rapidly despite aggressive surgical treatment. A delay in diagnosis, a fulminant course, and poor outcome are common in such cases [1,2,3,8,11].

The lesson to be learned from this report is that, in addition to tuberculosis, aspergillosis should be considered in cases with unusual neuro-imaging appearances and abnormal CXR findings, even in patients with no known

immuno-deficiencies, and treatment should be started as soon as possible hoping for a better outcome.

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