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Aspergillus Meningitis in a Seven-year-old Girl with AIDS: a Case Report

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Abstract

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A seven-year-old girl presented with one-month history of fever and progressive weight loss, and a two-week history of multiple generalized tonic-clonic seizures with associated somnolence. She had vomited three times since the onset of seizures. She was initially managed at a church for what the parents thought was epilepsy but was eventually taken to two private hospitals where she received various drugs without any improvement. She presented in our hospital where a diagnosis of aspergillus meningitis was eventually made from cerebrospinal fluid analysis. Despite the commencement of fluconazole on the fourth day of admission, the patient died five days later. This case report focuses on the importance of this rare disease in immunocompromised children, as well as the diagnosis and limitations in management in a resource poor setting.

Keywords: Aspergillus, meningitis, AIDS

Introduction

ADVANCED HIV disease is characterised by opportunistic infections due to organisms that are not usually invasive such as *Pnuemocystis jirovecii* and *Toxoplasma gondii*. While the commonest fungal infection in HIV infected individuals is candidiasis, the cryptococcus is the commonest fungal cause of meningitis, and other fungal meningitides are less commonly reported.[1-4]

Fungal meningitis in patients with AIDS is associated with high mortality and morbidity. Aspergillus meningitis in particular is usually an aggressive disease associated with high case fatality rate just like other fungal meningitides, especially in Africa.[5-8] This may be because patients with profound immunosuppression may not present with fever or typical features of meningeal irritation, thereby causing a delay in diagnosis.[9-10]

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This communication reports the diagnosis of aspergillus meningitis in a patient hitherto unknown to be HIV positive. It also outlines the possibilities in diagnostic tests even in a resource poor setting.

Case Report

OA, a seven-year-old girl, presented at the Emergency Paediatric Unit of our hospital with one-month history of fever and progressive weight loss, and a two-week history of multiple generalized tonic-clonic seizures of varying duration (5-15 minutes on the average) that aborted spontaneously. There was no post-ictal loss of consciousness but the mother noticed undue somnolence since the onset of seizures. She had vomited at least three times in the last two weeks but had no diarrhoea. Her appetite had become significantly reduced in the last two weeks, although feeds which were mainly pap had been fortified with milk.

She had been admitted to various hospitals at least thrice, for diarrhoeal illnesses since she was six months old. Her stools had never been bloody, mucoid or contained worms. The mother had an exanthematous illness that was slightly pruritic when she was pregnant with OA. Our patient was the fourth and last child in a monogamous family where

both parents lived together. The mother, who was a civil servant, however provided the major financial support for the family while OA's father was unemployed. There was no previous history of seizures in the child and the other siblings. There was no family history of epilepsy or diabetes mellitus. There was no history of contact with anyone suffering from chronic cough. No history of sexual abuse or blood transfusions.

Evaluation of OA revealed severe wasting, pyrexia (T=37.8°C), grade 3 finger clubbing and no pedal oedema. Central nervous system revealed an unconscious child (Glasgow Coma Score 12), with positive Kernig's and Brudzinski's signs, no features of cranial nerves deficit but muscle tone was slightly increased. The spine was normal in shape. The abdominal examination only revealed an enlarged liver with a span of 15cm. The respiratory and cardiovascular systems were normal.

Cerebrospinal fluid analysis revealed white blood cell (WBC) count of 15/mm^3 with 85 percent lymphocytes, elevated protein (209mg/dl), and low glucose (1.5mmol/L; random blood glucose (RBS) 6.2mmol/L). There were no acid-alcohol fast bacilli seen and gram stain revealed no organisms. The chest X-ray was normal. A revised provisional diagnosis of bacterial meningitis, possibly tuberculous was made while culture results were awaited. As this revealed no growth, it was subjected to further specialized studies to include fungal culture.

Ceftriaxone administered intravenously in a single daily dose of 100mg/kg/day was commenced together with other supportive care. The patient *however continued to deteriorate and* keratoconjunctivitis was noticed on the 3rd day. It was on the 4th day of admission that a CSF culture showed aspergillus species but further speciation was not possible. Amphotericin B 1mg/kg was prescribed but was not available at our centre or in the immediate vicinity, therefore oral fluconazole at 5mg/kg every six hours was prescribed and given via a nasogastric tube. HIV screening was positive but the parents did not consent to be screened. Patient deteriorated despite the therapy; she became more deeply comatose with the Glasgow coma score consistently below 6. Decorticate posturing, dilated and sluggish pupils were noticed on the last three days before she finally died on the 9th day of admission. Our suspicion of complications such as ventriculitis, hydrocephalus and cerebral aspergillosis was not confirmed in this patient due to lack of access to brain MRI at that time.

Discussion

Invasive aspergillosis has been reported in individuals with immunocompromised status as one of the rare opportunistic infections usually resulting from *Aspergillus fumigatus* and *Aspergillus flavus* infection.[11,13] Symptoms of aspergillus meningitis are non-specific but could include headache, fever, personality changes, seizures and coma. Aspergillus meningitis may present either in the acute or chronic stage of the disease.[11,13]

Our patient presented with a low grade fever of one month's duration at the time of presentation, had had several episodes of seizure, and was somnolent. These features were consistent with the chronic form of meningitis which could occur in patients with severe immunocompromise as in AIDS.[13] These symptoms are also common in tuberculous meningitis which was one of the first diagnostic considerations. The lack of prior knowledge of the HIV status of the patient, the endemic nature of tuberculosis in our environment as well as the rarity of aspergillus meningitis led to a diagnosis of tuberculous meningitis. To the best of our knowledge, this case was the first to be reported in a Nigerian child. With the increasing number of children living with HIV and progressing to AIDS in the country, fungal meningitis should be thought of, as a differential to tuberculous meningitis even when the HIV status of the patient is unknown.

The significance of the chronic cough in OA could not be established; however, it is known that pulmonary aspergillosis can disseminate to the CNS and other sites in patients with severe immune compromise as in AIDS.[14-16] OA also had keratoconjunctivitis which can be one of the ocular manifestations of the fungus.[18] The keratoconjunctivitis may also be due to hypovitaminosis A, cytomegalovirus infection or toxoplasmosis as reported by previous workers.[17,18] There may be no sign of pulmonary involvement at the time of the CNS disease, as in our patient.

The non-specific symptoms of the illness create delays in diagnosis. Difficulties in diagnosis also arise from the limitations of the investigative tests such as chest X-ray and CT scan. Despite the availability of new antifungal agents in developed countries, these reasons partly account for the low survival rate of 30 percent-50 percent seen in CNS aspergillosis.[14] In all, a high index of suspicion is required to enable an early diagnosis of fungal meningitis especially in children in whom the manifestations may be atypical.

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