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Case Report

Cryptococcal antigenemia in a Nigerian child with advanced HIV disease: a case report

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ABSTRACT

Cryptococcal infection in Nigeria's advanced HIV disease (AHD) population is not uncommon but is sparsely reported in children. The dearth of data on cryptococcal disease in our paediatric population suggests it is an uncommon clinical entity and may cause delayed diagnosis and preventable deaths. It is pertinent that cognizance be done of this clinical entity in our paediatric population. We report a 16-month-old HIV-positive child with complaints of weight loss of 3 months, cough of 1 month, fever, passage of watery stool, fast and difficulty in breathing for 1 week. She was initially managed as a case of paediatric AIDS with septicaemia and was receiving ceftriaxone and cotrimoxazole. The diagnosis was subsequently reviewed to paediatric AIDS with cryptococcal disease as the cryptococcal antigen screening test was positive and oral fluconazole commenced. However, the patient deteriorated and eventually died. This case report suggests a significant knowledge gap in the occurrence of cryptococcosis in our paediatric population and as a matter of urgency the need to conduct studies targeted at ascertaining the burden of cryptococcosis in children living with AHD in Nigeria.

Keywords: Cryptococcal disease, AHD, Children

INTRODUCTION

The advanced HIV disease (AHD) population including all children living with HIV younger than five years are at risk of opportunistic infections (OIs) such as tuberculosis (TB), pneumocystis pneumonia, histoplasmosis, and cryptococcal meningitis (CM).[1,2] Cryptococcal disease is a serious opportunistic infection commonly encountered in people living with AHD and is a major contributor to illness, disability, and mortality, affecting one million people annually.[1,3] The spectrum of clinical presentation ranges from asymptomatic infection to a severe life-threatening disease that can present as a space-occupying lesion, meningitis, meningoencephalitis or even affect the respiratory system causing atypical pneumonia.[4] The most common presentation is CM, estimated to have caused 181, 100 deaths among people living with HIV as of 2014 and accounted for 15% of all the people dying from HIV-related deaths globally.[1] A recent analysis of the global burden of CM estimated an incidence of 223,100 cases annually, with 73% of these cases occurring in sub-Saharan Africa.[2] Nigeria has the highest burden of CM in Africa estimated at 57,866 cases/year with a prevalence rate of 16.8% to 36%.[3] Similarly, cryptococcal antigenemia is commonly reported in Nigeria with a prevalence rate of 1.4% to 19.67% but all from studies targeted at adults living with HIV/AIDS.[3] Studies and/or case reports on cryptococcal

diseases in children are rarely conducted or reported in our setting. We report a 16-month-old HIV-positive Nigerian with cryptococcal disease.

CASE REPORT

A 16-month-old female presented at our facility, the university of Calabar teaching hospital (UCTH) with complaints of progressive weight loss of 3 months, cough of 1 month, fever, passage of watery stool, fast and difficult breathing of 1 week. There was a positive history of contact with an adult with a chronic cough; the mother had been coughing for more than a month. Both the child and parents reside in Calabar.

Antenatal care was unsupervised, and delivery was done at home. She was on both breast milk and artificial milk (miksi-full cream adult milk) from birth before pap was added at 2 months of age. Breastfeeding was stopped 2 months before presentation, and she was started on family diet thereafter which was taken 3 times a day. She received BCG immunization two weeks after birth. Mother had never had HIV testing before this presentation.

On examination, she was acutely ill, dyspnoeic (flaring of alae nasi, intercostal and subcostal recessions), with a respiratory rate of 32 cycles per minute and had widespread coarse crepitations bilaterally, febrile (temp: 37.9^{o}c), and wasted (prominent rib cage, hanging axillary and gluteal folds). She was lethargic and had head lag with reduced tone globally. There was no pedal oedema, no convulsions, and no signs of meningeal irritation. SPO_2 in room air was 84%, which improved to 98% on oxygen at 2 L/min. The pulse rate was 126 beats per minute. First and second heart sounds were heard on auscultation with no added sounds. She had oropharyngeal thrush. The abdomen was flat with a non-tender hepatomegaly of 6 cm.

Her anthropometric measurements were all low for her age; weight was 7.2 kg (<-3Z score), length-74 cm (<-2Z score), occipitofrontal circumference-41 cm (<-3Z score), mid-upper arm circumference-11 cm, weight for length<-3Z score.

On admission, a working diagnosis of paediatrics AIDS with septicaemia to rule out pulmonary TB was made given that HIV antibody screening for both patient and mother was positive. Other investigations done were stool and gastric aspirate for gene Xpert (negative for MTB), and cryptococcal antigen screening (positive). Dry blood spot for HIV PCR was not done as logistics of collection and analysis were not completed before demise. Also, urine TB-Lipoarabinomannan assay was not done as there was no strip at the time. Other investigations including full blood count, blood culture, urinary Histoplasma antigen assay, cerebrospinal fluid analysis and chest X-ray were not done before demise due to gross financial constraints. Moreover, the patient was too ill to be moved to the radiology centre where a chest X-ray could have been done free, and there was no mobile X-ray unit. She was commenced on intravenous ceftriaxone 100mg/kg daily and cotrimoxazole 5 mg/kg daily. A nasogastric tube was passed for feeding and rehydration solution for malnutrition (ReSoMal) was also commenced.

Cryptococcal antigen screening test result was retrieved on day 2 and diagnosis was reviewed to paediatric AIDS with cryptococcal disease. Suspension fluconazole 8 mg/kg stat was commenced and continued at 4 mg/kg daily thereafter.

The diarrhoea resolved by day 2, however, the patient's general clinical state continued to deteriorate with gasping respiration and deepening unconsciousness before demise eventually on the 4th day of admission. Autopsy was declined by the parents.

DISCUSSION

As of 2021, 1.9 million Nigerians including adults and children were living with HIV. Of the 1.9 million, 170,000 are children aged 0-14, representing a significant proportion of the Nigerian population living with HIV [UNAIDS]. However, cryptococcal disease is documented to be uncommon in children and may be missed particularly in our setting which is rife with other clinical entities like TB, pneumonia, diarrhoeal disease, and malnutrition.[1] These intricacies are worsened by the impediments to the prompt diagnosis of fungal diseases in our setting.[3] Favourable outcomes often depend on several factors including the presentation time and the attending physician's ability to establish a diagnosis promptly and initiate appropriate antimicrobials.[5] However, in some cases, reverse is the case, especially in resource-limited settings like ours where the accessibility to specialist care may be hampered by poor health-seeking behaviour, financial constraints, and the lack of funding for health care.

Our case report typifies the above narrative and emphasizes the need for routine screening of children with AHD for opportunistic fungal pathogens. The need to drive awareness of fungal diseases must go beyond the hospital environment or the training of clinicians only, to educating the public. In addition, the challenge of financial constraints and the poor availability of free/subsidized healthcare for the less privileged is an urgency that needs to be addressed. Unfortunately, this twin played out in this case; the very late presentation was probably due to their lack of funds, and ignorance as seen by the prior poor health-seeking behaviour during pregnancy and delivery. Severe acute malnutrition (SAM), seen from the globally low for age anthropometric measures, further complicated the patient's clinical state as SAM is a poor prognostic factor in paediatric HIV/AIDS. This is because SAM is associated with increased antimicrobial translocation,

immune exhaustion, and impaired immune recovery even when ARVs are commenced.[6] Even though the diagnosis of cryptococcal disease was arrived at a day after admission, this short delay is unlikely to account for the demise of this patient. Moreover, syrup fluconazole was commenced immediately after cryptococcal disease was diagnosed. Aspiration as a cause of death in this child was also unlikely as nasogastric tube feeding was commenced on day one due to the malnourished state of the patient. The barrage of investigations reeled out for the patient to carry out was not done due to financial constraints and this may have limited other measures of intervention that would have been deployed by the attending clinicians and masked the cause of death in this patient though we presume it may have been due to multiorgan failure following but not limited to fungal sepsis. This reiterates what seems to have been a major limitation in the management of this patient including the delayed presentation at our facility.

CONCLUSION

Cryptococcal disease may not be uncommon in the Nigerian paediatric population as it appears. There is an urgent need to drive awareness and diagnosis of this life-threatening fungal disease in our paediatric population through research investigating the occurrence of cryptococcosis in the paediatric AHD population of Nigeria.

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