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Case report

Fatal disseminated histoplasmosis in a Nigerian woman: A case report

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ABSTRACT

Disseminated histoplasmosis (DH) is the most severe clinical presentation of histoplasmosis, commonly associated with the advanced HIV disease (AHD) population. Our case report highlights the need for the deployment of point of care test kits for the diagnosis of histoplasmosis in resource limited settings including Africa and Nigeria in particular. Our case is a 56-year-old HIV positive (CD4 count of < 200 cells/microliter) Nigerian woman with complaints of cough, weight loss and easy fatigability all of several month's duration, who had self-interrupted her care prior to the onset of presenting complaints. The anti-TB regimen was commenced based on chest CT and chest X-ray findings despite negative GeneXpert results while awaiting urine *Histoplasma* antigen assay results. A positive *Histoplasma* antigen assay was communicated to the attending clinician 2 weeks after patient's demise. Delays in the diagnosis of disseminated histoplasmosis in our locality is a major factor contributing to fatal outcomes. The availability of point of care kits for the detection of *Histoplasma* in our facilities will aid in prompt diagnosis and invariably avert preventable deaths.

Introduction

Histoplasmosis is a serious fungal disease endemic in the USA and Latin America with increasing cases now reported in previously non-endemic areas for histoplasmosis including Western Africa, Southern Africa, Eastern Africa, Central Africa and South East Asia [1-3]. Histoplasmosis in humans is caused by *Histoplasma capsulatum* var *capsulatum* (Hcc) and *Histoplasma capsulatum* var *duboisii* (Hcd). The former causes classical histoplasmosis which occurs worldwide while the latter causes African histoplasmosis predominantly found in the African continent [1]. Although histoplasmosis cases were reported in the African continent prior to the advent of HIV/AIDS, more cases of histoplasmosis have been reported in Africa since the advent of HIV/AIDS with HIV/AIDS formally classified as an AIDS defining illness in 1987 [1,4]. Histoplasmosis is primarily an infection of the lungs acquired via the inhalation of microconidia, but can become disseminated in the immunocompromised especially in the advanced HIV disease (AHD) population [1,4]. Its diagnosis is yet challenging in resource limited settings like ours due to poor awareness on the part of clinicians and the lack of capacity and infrastructure in the area of diagnostics [1,4]. Besides, the clinical features of histoplasmosis mimics tuberculosis (TB) and can lead to misdiagnosis or delayed diagnosis which often results in poor clinical outcomes [1,4,5]. We report a 56-year-old woman who was managed as a

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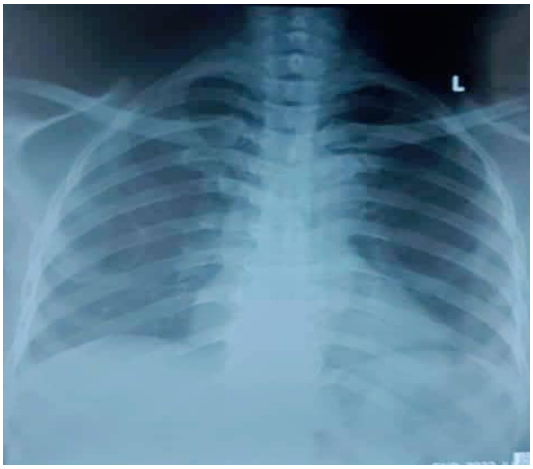
case of TB despite negative Gene Xpert results and later discovered to be *Histoplasma* positive after her demise.

Case report

A 56-year-old HIV positive Nigerian woman whose occupation was trading presented at the Alimosho general Hospital (ALGH) for HIV testing services with complaints of cough, weight loss and easy fatigability all of several months' duration. She had on her own interrupted her care at the Lagos University Teaching Hospital prior to the onset of these complaints. An impression of Advanced HIV disease (AHD) with pulmonary TB was entertained even before the outcome of other screening was done. CD4 cell count done using Lateral flow assay showed < 200 cells/microliter, urine TB lipoarabinomannan was negative and serology test for cryptococcal antigen also negative. Commencement of antiretroviral drugs was delayed pending further review with results of chest X-ray and sputum GeneXpert which were ordered for at her presentation. Her urine sample was also collected for *Histoplasma* antigen assay. Patient presented on day three with the following investigation results for further review of her clinical condition: sputum GeneXpert showed MTB/RIF not detected, chest X-ray showed thin walled cavitatory lesions in the right lower lung and hilar fullness bilaterally **(Figure 1),** hepatitis B surface antigen was positive while anti – hepatitis C antibody and syphilis test were negative. ESR was 124mm/hour (1 – 20mm/hour), white blood cell count was 6.4 × 10^9/L (4-10x10^9/L), with granulocytes count of 86.9%. Packed cell volume and haemoglobin were 28.6% (35-45%) and 8.9g/dL (12 – 16g/dL) respectively. Serum electrolyte, urea and creatinine showed sodium 142 mmol/L (135-144 mmol/L), potassium 3.7 mmol/L (3.5-5.0 mmol/L), bicarbonate 19 mmol/L (22-28 mmol/L), chloride 112mmol/L (98-106 mmol/L), urea 3.2 mmol/L (2.6-6.7 mmol/L), and creatinine 1.5mg/dL (0.6 – 1.1mg/mg/dL). Liver function test showed total protein 7.2g/dL (6 – 8g/dL), total bilirubin 150.3µmol/L (3 – 17µmol/L), conjugated bilirubin 53.04µmol/L (2 – 7µmol/L), albumin 4.3g/dL (3.5 – 5.5g/dL), aspartate aminotransferase 66IU/L (5-40 IU/L), alanine aminotransferase 19IU/L (5-40 IU/L) and alkaline phosphatase 299IU/L (22-92 IU/L). A chest CT scan was requested for while awaiting urine *Histoplasma* antigen assay results. She presented on day 9 with her chest CT scan report showing features suggestive of atypical pneumonia with TB as a strong differential. The decision to promptly commence the patient on anti- TB drugs pending the outcome of the review of her urine sample for histoplasmosis was made and activated. She was referred to the DOT clinic where she was enrolled into care as a drug-sensitive TB case and promptly commenced on regimen 1 of anti-TB drugs, the issuance of the same being for two weeks. A positive *Histoplasma* antigen assay result was communicated to the attending clinicians on day 28 and an attempt at bringing the patient in for necessary care was activated. Daily efforts at reaching out to the patient were done but her phone lines and that of the next of kin as indicated on her case file were reported unavailable by their network providers. On day 32, two officers of the social welfare department of ALGH and one adherence counseling officer of the department of community health ALGH were mobilized and charged with the responsibility of tracking the patient to her home address as supplied on her records with the facility and bring her in for the needed care as earlier narrated. After several hours spent on trying to locate her whereabouts in her immediate community and with collaborative efforts from community leaders her home was located where the news of her demise was broken and her grave by the side of a house. The date of her demise corresponded with day 15 from the first day she presented. The chest CT film and report were not added to this case summary as they were taken away by the patient.

Figure 1. Opacities in the right lung fields and hilar fullness bilaterally.



Discussion

The demise of our index patient was not due to the challenge of poor awareness or a low index of suspicion, neither was it really a misdiagnosis as it were because histoplasmosis was considered from the outset and urine sample collected for *Histoplasma* antigen assay. The Patient's demise happened on day 15 while the result of *Histoplasma* antigen test for urine collected on day 1 was sent to the attending clinician on day 28. This is a huge time lag (2 weeks) for a patient with disseminated histoplasmosis who needed urgent intervention as at the time she presented. The reason for this delay may be due to the fact that samples had to be pooled and ran in batches to minimize cost as the ELISA kits for *Histoplasma* antigen testing though available are quite expensive and not in routine use in most of the laboratories across our tertiary institutions [6,7]. As a matter of fact, the diagnosis of DH in our case report was made possible through the fungal surveillance program driven by the Medical Mycology Society of Nigeria. Prompt diagnosis is critical in ensuring favorable clinical outcomes in patients with invasive fungal infections otherwise outcomes are always fatal [2,4,8]. Although we cannot generalize this opinion, our index case suggests the fact that we have made some progress in improving awareness and index of suspicion for histoplasmosis in our setting with a few hurdles to surmount, particularly in the area of diagnostics. A point of care device for the detection of *Histoplasma* at the time of presentation would have been invaluable in salvaging the life of the deceased. Unfortunately, these kits (Mira Vista) are very expensive and to the best of our knowledge not currently available in any of our tertiary health care facilities. Although it has been reported to have variable sensitivity, the use of a blood smear may have helped in this case but was never utilized. Moreover, a trained microscopist is needed to make a diagnosis of DH on the blood smear [8]. Culture was not done due to the lack of biosafety level 3 facility [1]. Besides, considering the rapid evolution in the clinical presentation of our index case, culture wouldn't have been helpful as it requires about six weeks to establish the growth of *Histoplasma* in a culture medium. We acknowledge the fact that the demise of our index case may have been caused by other opportunistic pathogens or complications from AHD due to her low CD4 cell counts and non-compliance to HAART prior to presentation. Besides her liver function tests were markedly deranged which also suggest fulminant hepatitis secondary to hepatitis B virus infection. However, the derangement of other organ systems and the involvement of the liver in DH [4,9,10] strongly suggest DH as the cause of death in our index case.

Conclusion

DH is often associated with fatal outcomes. Prompt diagnosis and timely antifungal therapy are key to averting mortalities. The availability and easy accessibility of point of care kits in our setting will go a long way in reducing mortality rates from histoplasmosis which is now increasingly being reported in Nigeria.

Conflict of interest statement

The authors declare that they have no conflicts of interest regarding the publication of the present study.

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Authors' contributions

OOO conceptualization, participated in writing, review and editing, BEE conceptualization literature review and writing-original draft and main manuscript, review, and editing, ROO conceptualization, review, and editing.

Ethical consideration

Not applicable.

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