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Case report

Cryptococcus laurentii fungaemia in a tertiary hospital in Nigeria: Case reports

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ABSTRACT

The non-neoformans *Cryptococci* are increasingly causing opportunistic infections in both immunocompetent and immunocompromised individuals worldwide. Non-neoformans *Cryptococci* are skin and mucous membrane colonizers as well as environmental fungi. *Cryptococcus laurentii* and *Cryptococcus albidus* cause more than 80% of non-neoformans *Cryptococcal* infections are gaining recognition as human pathogens because of the advancements in diagnostic techniques. Here, we report 2 cases of *C. laurentii* fungaemia in an immunocompetent adult and a preterm neonate in Nigeria. The first case was a 51-year-old man with 31% second-degree mixed-thickness burns. He fully recovered with the addition of fluconazole early in its treatment. The second case was a preterm neonate in whom fungaemia was diagnosed after a fatal outcome had occurred. These two cases highlight that the new identification and susceptibility diagnostic techniques allow for earlier diagnosis and better treatment of unusual fungal infections. However, the timely and early commencement of empirical antifungal drugs improves patient outcomes.

Introduction

The non-neoformans *Cryptococci* are *C. laurentii*, *C. albidus*, *C. luteolus*, *C. curvatus*, and *C. humicolus*, however, *C. albidus* and *C. laurentii* are responsible for 80% of human infection [1-3]. They are saprophytic, encapsulated basidiomycetous yeast found in soil contaminated with pigeon faeces [1,2], and are increasingly causing opportunistic infections like arthritis, fungemia, endophthalmitis, pneumonia, meningitis; skin and soft-tissue

infections, among others, globally [2-8]. *Cryptococcus laurentii* is a skin and mucous membrane colonizer, widely isolated from soil, water, air, wood, and pigeon excreta [4]. The inhaled, ingested, or inoculated spores or desiccated yeast of *C. laurentii*, into an injured skin, result in infection [8].

Cryptococcus laurentii affects both immunocompromised and immunocompetent hosts,

however, the risk of infection is increased in immunosuppressed individuals, neutropenic patients, those with indwelling intravenous devices, and those on prolonged steroids, and antibiotic use [4,5,9,10,11]. Due to the improvement in our clinical laboratory diagnostics, we are reporting two (2) cases of *Cryptococcus laurentii* bloodstream infections in Nigeria, in addition to the twenty-four cases of *C. laurentii* that have been documented in the literature. This report aims to iterate that *C. laurentii* exists in Nigeria. The absence of earlier reports may be because of a lack of modern laboratory equipment to diagnose other yeast apart from *Candida albicans*.

Case 1: This is a 51-year-old man referred from a private facility to Lagos University Teaching Hospital (LUTH) on 12th October 2021 due to a burn injury following a gas cylinder explosion that happened four days before his admission. There was the involvement of the upper limbs, abdomen, chest, and face, but no associated loss of consciousness, or difficulty in breathing. He was immediately rushed to a private hospital where he was diagnosed with 31% second-degree mixed-thickness burn. He was rehydrated with intravenous fluids, and given intravenous (IV) ceftriaxone 1g 12 hourly, metronidazole 500mg 8 hourly, as well as analgesics. He was at this hospital for 4 hours before he was referred on request by the relatives for expert management. He had no significant past medical history and was not a known diabetic, hypertensive, or retroviral disease patient. No history of blood transfusion or previous hospital admission except for this time, and no history of drug allergy. He is married in a monogamous setting, smokes cigarettes about 5 sticks per day for 31 years and occasionally drinks alcohol. Physical examination showed a man in acute painful distress, conscious, febrile (39°C), not pale, anicteric, acyanosed, not dehydrated, with mixed thickness burns involving the face, chest, upper part of the abdomen, and both upper limbs and had no pedal edema

Cardiovascular examination showed that pulse was full and regular with a rate of 110 beats per minute. The blood pressure was 109/80 mmHg. His respiratory system revealed vesicular breathe sounds globally. The abdomen was full and moved with respiration, there was no area of tenderness and no palpable organomegaly. He was admitted into the spontaneous vertex delivery. She was immediately taken to a private hospital where she was admitted and treated with no clinical

Burns and Plastic unit for specialized care. Laboratory investigations such as blood culture, full blood count (FBC), electrolyte urea and creatinine (E, U, Cr), viral markers, and wound swab microscopy culture and sensitivity (m/c/s) were ordered. A central venous line was inserted and IV amoxicillin-clavulanate 1.2mg 12 hourly, I V metronidazole 500 mg 8 hourly, and analgesic IV paracetamol 1g 8 hourly were commenced. Other supportive management included daily wound dressing with honey dressing, nutritional rehabilitation with high protein calories, and the elevation of both upper limbs using skin traction. The complete blood count showed a white blood cell count (WBC)- of 9700/mm³, neutrophil (N)- 76%, lymphocyte 7.8%), and packed cell volume (35%). Random blood sugar was 70 mg/dl. Plasma sodium: 143 mmol/l; potassium: 2.9 mmol/l; Chloride:99 mmol/l; urea: 4.3 mmol/l and creatinine: 67.5 µmol/l. The wound swab culture yielded no growth. He was negative for Hepatitis B and Hepatitis C virus. The fever persisted despite the antibiotics therapy and a repeat FBC revealed neutrophilic leucocytosis (WBC of 33,560/mm³, N-97%), Oral fluconazole 200 mg daily was empirically added to his treatment.

The blood culture sample collected was incubated in BactAlert®3D (Biomérieux) automated machine at the Medical Microbiology Laboratory and flagged positively within 72 hours of incubation. The Gram stain showed large yeast cells and the subculture grew mucoid, glistening colonies. Vitek® 2 version 8.0 (Biomérieux) was used for its identification and sensitivity. The yeast was identified as *Cryptococcus laurentii*, sensitive to Fluconazole, Voriconazole, and Amphotericin B. The fluconazole 200 mg daily was continued for eight (8) weeks. The fever subsided 3 days after the commencement of fluconazole. His overall clinical conditions improved with re-epithelization of the wound.

Case 2: An 8-hour-old female neonate delivered at home at the gestational age of 35 weeks was admitted to the neonatal ward of LUTH through the children's emergency room (CHER). As a result of fever, inability to cry, and difficulty in breathing since birth. She was delivered at home on 30th December 2021 at 10p.m through

improvement and was referred to LUTH. They arrived eight (8) hours after delivery.

History taking done at LUTH showed that the pregnancy was uneventful. Mother had antenatal care in a private facility and had no history of maternal fever, premature rupture of membrane, or rashes in pregnancy, the mother described a profuse itchy vaginal discharge with associated dysuria two weeks before the delivery.

On admission, baby was febrile (Temperature 38.7°C), cyanosed, with severe respiratory distress (evidenced by the subcostal recession, and flaring of alae nasi) that necessitated her to be placed on nasal continuous positive airway pressure. She weighed 1900 grams and had altered consciousness, Blantyre coma scale was 2/5, She also had global hypotonia, depressed reflexes and tachypnoea (RR-56cpm); the random blood glucose was 29 mg/dl which was corrected, and full blood

count showed leucocytosis (WBC 25,000/mm³, with an absolute neutrophil count of 15,180/mm³. Cefotaxime and amikacin were commenced empirically after the blood culture sample was collected. The patient died 20 hours after admission before the blood culture flagged

The blood culture was incubated into the BactAlert® 3D (Biomérieux) automated machine at the Medical Microbiology laboratory of LUTH. It flagged positively within 48 hours and microscopy showed large oval yeast cells that grew at 37°C on Saboraud's dextrose agar yielding cream-coloured, mucoid, glistening, colonies. The Vitek 2 (Biomérieux) version 8.0 was used for identification and sensitivity. *Cryptococcus laurentii* was identified, sensitive to Fluconazole, Voriconazole, and Amphotericin B.

Reported cases of *C. laurentii* fungaemia

Age and sex	Co-morbidity/ Risk factors	Diagnostic methods	Antifungal therapy	Outcome	Reference
27 days, M	premature	Blood culture, biochemical tests	amphotericin b, flucytosine	Recovered	[15]
27, F	-	Blood culture	fluconazole	Recovered	[15]
42, F	Cervical cancer	blood culture, biochemical test, molecular techniques	fluconazole	Recovered	[16]
76, M	myocardial infarction, arterial hypertension, previous haemorrhagic stroke	blood culture, Vitek 2, biochemical test, Indian ink	Amphotericin B	Recovered	[5]
39, F	membranoproliferative glomerulonephritis, immunosuppressive therapy	Blood culture, Vitek 2	Itraconazole	Recovered	[17]
neonate, F	low-birth weight	Blood culture, API 32C	Amphotericin B, removal of central venous catheter	Recovered	[8]
16, M	ganglioneuroblastoma	blood culture, API 32C, API 20C AUX, sequence analysis	Amphotericin B	Recovered	[18]
Neonate, M	Prematurity	Blood culture, Vitek 2, maldi-tof	Liposomal amphotericin b	Recovered	[7]
Neonate, F	Prematurity	blood culture, vitek 2, pcr-sequencing	Liposomal amphotericin b	Recovered	[19]

17, M	leukemia, neutropenia	Blood culture	fluconazole	Recovered	[20]
Neonate	contaminated umbilical cord	Blood culture, vitek 2	Fluconazole	Recovered	[21]
26, M	solid tumor	Blood culture	catheter removal, fluconazole	Recovered	[22]
50, M	NHL	Blood culture	catheter removal, deoxycholate amphotericin b	Death	[22]
57, M	AML	Blood culture	catheter removal, deoxycholate amphotericin b	recovered	[22]
5 months, M	Prader willi syndrome	blood culture, api 20c aux, MALDI-TOF, Sensititre yeastone	liposomal amphotericin b	Recovered	[23]
47, F	AML, allogeneic hematopoietic stem cell transplantation	Blood culture, Vitek 2	Amphotericin B	Recovered	[24]
68, F	Diabetes mellitus, breast cancer	Blood culture, Vitek 2	Amphotericin Bb	Recovered	[12]
35, F	hodgkin lymphoma	blood culture, api 32c	Fluconazole	Recovered	[25]
35, M	HIV	Blood culture	Amphotericin B, Fluconazole	Recovered	[26]
NR	Neutropenia	Blood culture, Vitek Jr	amphotericin b	Recovered	[27]
NR	Neutropenia	Blood culture, Vitek Jr	NR	Death	[27]
NR	Neutropenia	Blood culture, Vitek Jr	NR	Recovered	[27]
30, F	post-operative infection	Blood culture, Vitek 2	Amphotericin B	Death	[28]
3 months, M	prematurity, down syndrome	Blood culture	Amphotericin B	Death	[29]

M, male; F, Female; NR, not reported; -, negative; HIV, Human Immunodeficiency virus; AML, acute myeloid leukemia; NHL, non-hodgkin lymphoma; MALDI-TOF, Matrix-assisted laser desorption/ionization-time of flight

Discussion

Non-neoformans *Cryptococcus* cause life-threatening infections and are increasingly becoming more common because of the improvement in diagnostic procedures [12]. In reported case 1, the patient had fungaemia which may have resulted from the loss of anatomic skin barriers, and the inserted intravascular catheter. The skin barrier is one of the defence mechanisms used to prevent the invasion of the host by pathogens.

This patient had 31%-mixed thickness burns, making him vulnerable though he was immunocompetent. The breach in skin integrity allowed this pathogen to gain entrance and spread haematogenously in the body. This may be the reason *C. laurentii* was isolated from the blood culture. Several cases of *C. laurentii* affecting the immunocompetent have been reported [4,13,14]. A case of arthritis of the knee following a penetrating wound from a thorn was reported by Huang et al [4] Likewise, in Spain, a non-inflammatory primary

cutaneous lesion was also reported [13]. In both cases, the patients failed to respond to the antibiotics treatment but fully recovered after instituting antifungal therapy when the fungus was isolated from the culture [4,13]. In this case report, the fever persisted despite the antibiotics therapy and an appreciable response was noticed when the clinician instituted the empirical fluconazole therapy even before a diagnosis of fungaemia was made. For the second case report, the preterm neonate has low birth weight, poorly developed anatomical barrier and immune cells which are the major risks for fungal infection [8]. In addition, the questionable delivery process and condition may have also served as additional risk factors. The mother's copious vaginal discharge during the course of the pregnancy that was not microbiologically confirmed may be caused by *C. laurentii* due to maternal-to-child transmission of the infection. Therefore, for this neonate, the portal of entry of this fungal pathogen remains unknown. In Taiwan, *C. laurentii* fungemia in an extremely low birth weight preterm neonate was reported with a favourable outcome when antifungal was initiated early [8]. Unfortunately, in this case, patient demise occurred before laboratory results could be obtained.

This presented case attests that infection due to *C. laurentii* exists in Nigeria, the prevalence may be higher than this. The absence of previous reports may be due to misdiagnosis. The microbiology laboratory of Lagos University Teaching Hospital (LUTH) was recently upgraded to improve its diagnostic capacity.

Conclusions

The new identification and susceptibility diagnostic techniques allow for earlier diagnosis and better treatment of unusual fungal infections. However, the timely and early commencement of empirical antifungal drugs improves patient outcomes.

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