

Cryptococcus Laurentii Sepsis Presenting as Purpura Fulminans in a Two-Year-Old Child

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

We report a case of sepsis caused by *Cryptococcus laurentii*, a rare human pathogen [1], presenting as purpura fulminans. *Cryptococcus laurentii* was isolated in blood culture and identified by Vitek -2 yeast identification system. The patient was successfully treated with standard management protocols, including amphotericin B.

Keywords: *Cryptococcus laurentii*; fungal sepsis; purpura fulminans; erythematous rash.

ABBREVIATIONS

Hb : Hemoglobin
TLC : Total Leucocyte Count
CRP : C-Reactive Protein
PT : Prothombin Time
INR : International Normalized Ratio
APTT : Activated Partial Thromboplastin Clotting Time

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ESR : Erythrocyte Sedimentation Rate
LDH : Lactate Dehydrogenase
IL-6 : Interleukin -6

1. INTRODUCTION

Cryptococcus laurentii (*C. laurentii*), is a non-neoformans cryptococcus species that has rarely been associated with human infection. However, opportunistic infections caused by *C. laurentii*, *Cryptococcus albidus*, *Cryptococcus curvatus*, *Cryptococcus humicolus*, and *Cryptococcus uniguttulatus* have become more common in recent years [2]. *C. laurentii*, a basidiomycetous encapsulated yeast, has been found in pigeon droppings and cloacal samples. It causes both deep-seated infections like fungal sepsis and meningitis, as well as superficial infections like keratitis [3,4]. The majority of *C. laurentii* fungal sepsis cases have occurred in immunocompromised individuals.

We describe a case of fungal sepsis caused by *C. laurentii* in a two-year-old child who was treated successfully.

2. CASE HISTORY

A two-year-old male child was admitted to our institution with complaints of fever of 2 weeks duration, erythematous rash and multiple fluid-filled lesions distributed over the surface of the body from five days prior to admission. Parents gave history of multiple hospital admissions and treatment before admitting to our institution. As per history given by Parents, the child was apparently healthy before developing fever and had no recurrent illness.

The erythematous rash was first noted at the lateral aspect of the left thigh, lesions were small – about 1 cm in diameter which later increased in number and size to coalesce and spread to cover a large tract especially over the lower limbs, the trunk and abdomen. The patient simultaneously also had multiple fluid-filled lesions distributed over abdomen, trunk and limbs which were painful and warm to touch.

There was no history suggestive of any congenital or acquired immune deficiency disorders such as recurrent pneumonia, frequent sinus infection, ear infection, meningitis, recurrent deep skin infection, delayed growth.

On examination the patient was conscious, irritable, with vitals as: Pulse rate -120/min, good volume, Respiratory rate- 40 /min, SpO₂-98% at room air CRT less than 3 seconds BP-

100/70 mmHg (normotensive for age)—and a temperature of 102 F. Anthropometric measurements were: weight -13 kg (median to +1sd normal for age), length -88 cm (median to +1sd normal for age) Mid-upper arm circumference -13 cm (median to +1sd normal for age).

Local examination revealed a large bluish-purple colored coalesced ecchymotic lesion at the anterolateral aspect of right thigh measuring 15 x 10 cm tender, with clear margins with no discharge or any bleeding, multiple tense bullae were also present over similar areas all over the body (Figs. 1, 2 and 3).

With a clinical diagnosis of purpura fulminans, the patient was managed accordingly in the PICU with—empirical appropriate antibiotics (vancomycin) along with other supportive therapy owing to suspicion of staphylococcal sepsis. Meningococcus infection was ruled out, as nasopharyngeal swab culture and blood culture were negative for the organism [5,6]. Culture of the aspirate from bullae were positive for *Pseudomonas aeruginosa* for which intravenous Meropenem was started. This was not consistent with his blood culture as it grew *C. laurentii*. Skin biopsy from right thigh lesion was s/o Erythema Multiforme. HIV and COVID-19 status of the child was negative, skin lesions were managed with local dressings [7,5].

Blood culture was done using the BacT/Alert® system. The instrument flagged his bottle as positive for growth on day 3 of incubation in BacT/Alert. Subsequently, a direct smear from the bottle was made, which on Gram staining demonstrated a field full of pus cells with gram positive round budding yeast cells (BYCs). Subculture was done from the blood culture bottle on blood agar and Sabouraud's Dextrose Agar (SDA) in view of BYCs seen on direct Gram stained smear from blood culture bottle and both were incubated at 37°C for 18-24 hrs. After 24 hours of incubation, blood agar showed white, small, circular, smooth, easily emulsifiable and beta-haemolytic colonies. SDA subculture showed growth of white, smooth pasty and creamy colonies. Gram staining from both the culture plates revealed Gram positive round BYCs. An India ink stained preparation was

made from the SDA tube as well, which showed capsulated BYCs. A provisional diagnosis of fungal sepsis by *Cryptococcus* species was made, and the child was initially started on

intravenous Fluconazole on day 4 of admission. Finally, *Cryptococcus laurentii* was detected as the cause of sepsis via Vitek 2 Compact (Biomérieux, France) automated system.

Table 1. Initial investigations done revealed anemia and deranged inflammatory markers

| Parameter | Day 1 | Day 4 | Day 10 | Day 18 |
|-------------------------------|-------------------------------|--------|-------------------------------|-----------|
| Hb (g/dl) | 8.6 | 7 | 6 | 7 |
| Tlc (cells/mm ³) | 5000 | 2820 | 2200 | 5000 |
| Platelet (platelets/ μ l) | 100000 | 100700 | 130000 | 177000 |
| CRP (mg/dl) | 62 | 48 | 30 | 28 |
| PT (secs) | 18.8 | 17 | 18 | 17.9 |
| INR (secs) | 1.45 | 1.3 | 1.2 | 1.39 |
| APTT (secs) | 56 | 55 | 57 | 49.2 |
| ESR (mm) | 80 | 82 | 78 | 76 |
| Triglycerides (mg/dl) | | 198 | 164 | |
| LDH (U/L) | | 356 | | 323 |
| IL-6 (pg/ml) | | 6.5 | | |
| Serum Ferritin (ng/ml) | | 730 | | 1000 |
| Blood Culture | <i>Cryptococcus laurentii</i> | | <i>Cryptococcus laurentii</i> | No growth |

Day 1 of Admission:



Fig. 1. Multiple fluid filled bullae all over the body



Fig. 2. Ecchymotic purpuric rash over right thigh



Fig. 3. Erythema with central areas of black gangrenous necrosis which has a surrounding erythematous border

The child continued to have intermittent high-grade fever spikes and new bullae lesions. In view of this, Liposomal Amphotericin B was administered on day 8 of admission in addition to intravenous Fluconazole and was continued for another two weeks. On day 14, the child showed a reduction in episodes of fever and also in the severity of the rashes, with no fresh lesions being noticed. A repeat blood culture was sent, which showed no growth of any pathogenic organism. Clinical improvement and microbiological clearance on administration of intravenous Liposomal Amphotericin B was strongly suggestive of the fact that—*Cryptococcus laurentii* was the pathogen causing sepsis in our patient.

3. DISCUSSION

Cryptococci are found in pigeon feces and are transferred to humans mostly by inhaled fomites. *C. neoformans* saprophytes have long been thought to be nonpathogenic [1,2]. Together, *Cryptococcus laurentii* and *Cryptococcus albidus* are thought to be responsible for 80% of recorded cases. Including the present report, there are a total of 15 case reports of disease in humans caused by *C. laurentii* infection, out of which 3 case reports are from India [1,2]. A Case report of *C. laurentii* fungemia in low birth weight preterm infant from India has been reported recently [8]. Only one case of *C. laurentii* has been reported in a child (8 year old) who had cutaneous *c. laurentii* infection and was successfully treated with oral Fluconazole for 8 weeks [1]. The practice guidelines for the management of cryptococcal infection

recommends the use of azoles for non-central nervous system cryptococcal infections, including cutaneous disease [1]. In this child, we gave a combination of intravenous Fluconazole and Liposomal Amphotericin B. Risk factors associated with *C. laurentii* infection are invasive devices, prior steroid exposure, prior immunosuppressant exposure, prior azole exposure, low CD4 count, exposure to pigeon excreta and neutropenia [2]. Dissemination from a pulmonary source or transfer through intravenous catheters are two possible origins of fungemia.

After the initial pulmonary infection, it has the potential to spread to other organ systems, especially in immunocompromised patients. Disseminated disease is often the first sign of cryptococcosis in many patients.

According to previous research, the most common clinical manifestation is bloodstream infection. Infection typically manifests as febrile illness, with some cases presenting with hemodynamic changes and skin manifestations, as in our case. Isolation of the organism from blood culture is considered as diagnostic in cases of fungemia [9].

In the clinical microbiological laboratory, detecting a white pasty mucoid colony on SDA is often the first indication of the presence of cryptococci, and this suspicion is further strengthened when Gram positive round BYCs are seen on Gram staining and when encapsulated budding yeasts are seen in India

ink preparation of the colony. There are 37 members of the genus *Cryptococcus*, and virtually all members of the genus assimilate inositol, produce urease, and are non-fermenters. In particular, the identification of *C. laurentii* can be confirmed through the use of various biochemical tests, and most clinical laboratories use a range of biochemical tests contained in commercially available kits. A negative caffeic acid test, lack of KNO₃ utilization, and utilization of lactose and melibiose can indicate *C. laurentii* other species [10]. Alternatively, confirmation of this yeast can also be done via Vitek-2 compact automated system [10,3].

Lack of validated standard treatment for this yeast might have been due to the limited number of cases reported worldwide. Studies correlating in vitro antifungal susceptibility test results and treatment outcomes do not exist [2]. Amphotericin B had been the most successful drug to treat *Cryptococcus laurentii* fungemia till now. Besides fungemia, *C. laurentii* has been reported to cause peritonitis, cutaneous infection, lung infection and eye infection [10].

In this case, the parents of the child gave history of multiple hospital admissions of the child and treatment from various sources over a substantial period of time. He may have acquired the fungemia nosocomially from another hospital prior to presentation to our hospital. The fungus after entering the blood stream of the child caused sepsis, leading to the persistent episodes of fever and purpura fulminans causing the rashes, boils and blisters all over the body of the child. The child was successfully treated with intravenous Amphotericin B for 2 weeks.

4. CONCLUSION

To the best of our knowledge, the present report is the first to describe *Cryptococcus laurentii* sepsis presenting as purpura fulminans in a child from India. This case report has been prepared to bring out the fact that this organism must also be searched for/considered in patients with sepsis – especially those who are in an immunocompromised state. Further, improved culture and identification techniques can contribute to the timely and correct diagnosis of such unusual fungal infections, further leading to increased recovery of these patients. The reporting of such patients may help to broaden

the current spectrum of clinical manifestations of this disease.

CONSENT

As per international standard or university standard, Parental written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard, written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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