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A CASE REPORT: A DECEIVING DIAGNOSIS OF PRIMARY CUTANEOUS CRYPTOCOCCOSIS IN AN IMMUNOCOMPETENT HOST

Medical Microbiology

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ABSTRACT

Cryptococcosis is a fungal infection caused by Cryptococcus species, most commonly affecting immunocompromised individuals, but may be found in immunocompetent patients too. Typically, Cryptococcus neoformans is known for causing pulmonary and central nervous system infections in immunocompromised individuals. The skin involvement in an immunocompetent host is an unusual manifestation. While cutaneous manifestation is usually a secondary sign of the disseminated disease, our patient presented with primary cutaneous cryptococcosis. We present a case of 37 year old female, who was diagnosed to have cutaneous cryptococcosis by staining techniques and classical culture techniques.

KEYWORDS

Fungal infections, primary cutaneous cryptococcosis, immunocompetent

INTRODUCTION

Cryptococcosis is a fungal infection caused by Cryptococcus species, most commonly in immunocompromised individuals, especially in patients with HIV, organ transplant, and cancer chemotherapy.(1)

Cutaneous cryptococcosis can present with a variety of skin manifestations. The most common presentation of disseminated cutaneous cryptococcosis is umbilicated papules on the head or neck; other cutaneous manifestations include abscesses, cellulitis, pyoderma gangrenosum-like lesions, acneiform pustules, vegetating crusted plaques, whitlow, and a combination of polymorphic lesions. (4)

Case Report

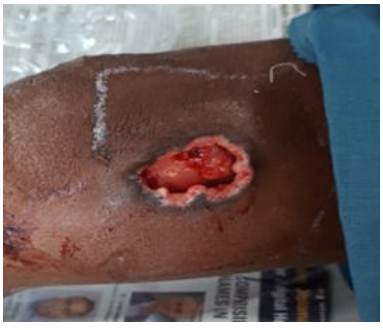
A 37 year old female, who works in the forest, presented with history of multiple abcsesses over her body since 3 months along with fever. She also had history of breathlessness with bilateral pedal edema since 1 month.

Initially the abscess started with a swelling of 2x2cm on the left elbow which was incised and drained. This was followed by formation of multiple abscesses over the right arm, forearm, left breast and right knee. The abscesses were associated with pain and discharge and were drained.

The patient also had history of breathless ness since 1 month which was gradually progressive (MMRC grade 3), along with generalised edema of the body with significant bilateral pedal edema, with pain and swelling up to the knees since 1 month. The patient also had history of fever which was on and off since 1 month, more in the evening and early morning but not associated with chills. The fever followed by profuse sweating. There was no history of cough, but was associated with weight loss of 6 kg in 3 months. Patient had no history of abdominal pain, jaundice, vomiting or any loose stools. She had normal sensorium, no seizures or syncope. No chest pain, palpitation and no altered bowel movements. Patient has no known comorbidities. Patient had undergone several incision and drainage procedures in civil setup prior to reporting at our centre.

CECT thorax revealed mediastinal and right hilar adenopathy with non-homogenous enhancement. All her lab parameters were normal and her HIV and other viral markers were negative.

On general examination the patient was conscious and oriented, with normal vitals, although she had pallor and bilateral pitting pedal edema with left side palpable axillary lymph node. Multiple abscesses were noticed over right arm, left side chest and right knee with scars **(Figure 1, 2)**.

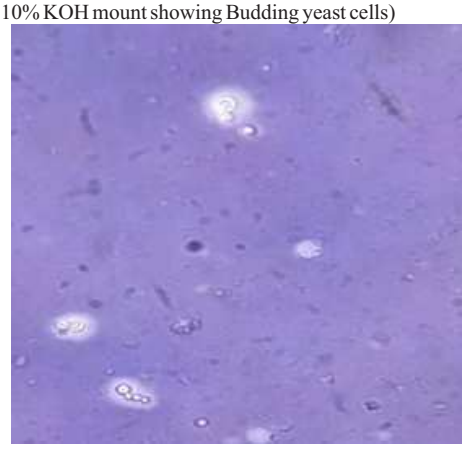


(Figure 1, Ulcerative lesion over right thigh)

(Figure 2, Lesion over right shoulder)

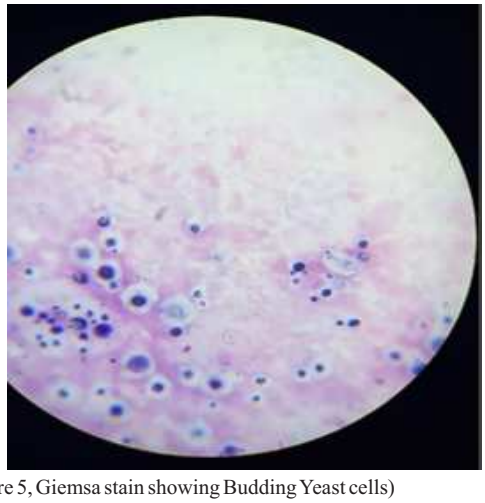
A differential diagnosis of tuberculosis was made and pus was again aspirated and sent for culture sensitivity before starting treatment with piperacillin tazobactam injection. Her workup for tuberculosis was negative. Skin biopsy was received for bacterial and fungal cultures. 10% KOH mount, Gram stain, ZN stain, India ink stain and Giemsa stain were done. 10% KOH mount revealed few budding yeast cells like organism **(figure 3)**, which was further confirmed to be capsulated in the India Ink stain **(figure 4)** with narrow based budding.

(Fig 3, 10% KOH mount showing Budding yeast cells)



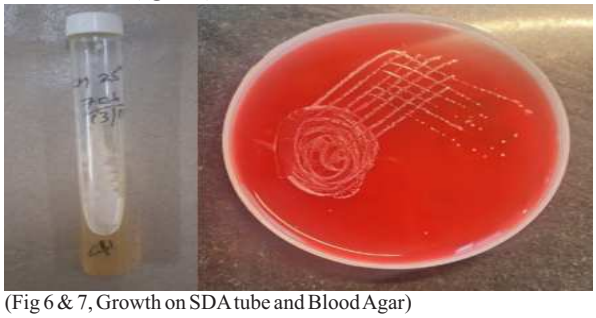
(Fig. 4, India Ink stain showing capsulated organisms with narrow based budding)

Gram, ZN and Giemsa stain **(figure 5)** also showed budding yeast like cells. The sample was inoculated on SDA (plain and with Chloramphenicol, at 25°C and 37°C), Blood and Mac Conkey Agar and LJ media.

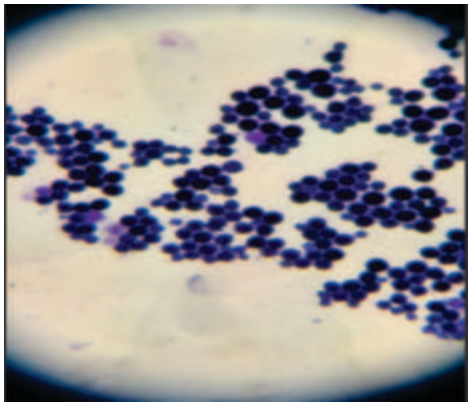


(Figure 5, Giemsa stain showing Budding Yeast cells)

LJ media had no growth whereas the SDA tube **(figure 6)** and blood agar **(figure 7)** showed cream colored pasty yeast like growth. A Gram stain was done from both the growths and gram variable budding yeast cells were seen **(figure 8)**.



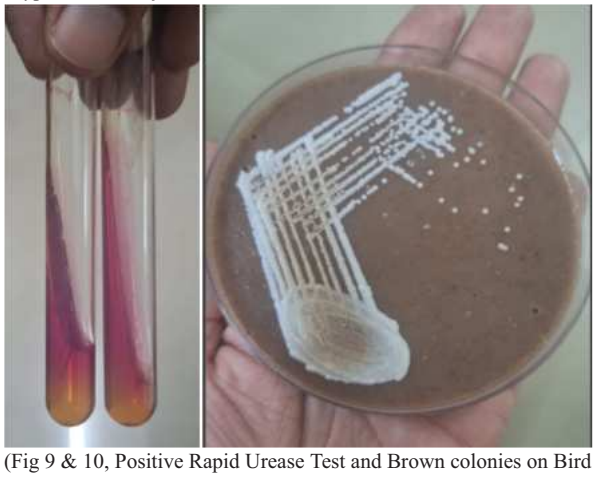
(Fig 6 & 7, Growth on SDA tube and Blood Agar)



(Figure 8, Gram stain from Growth showing Gram variable Budding yeast cells)

A diagnosis of Cryptococcus spp was made.

A rapid urease test was performed along with sub culture of the growth onto Bird Seed Agar to further speciate the organism. Rapid urease came out to be positive with a color change within 30 mins **(figure 9)** of inoculation and the growth on BSA turned to be brown after 48 hrs of inoculation and incubation at 37°C **(figure 10)** and a confirmation of *Cryptococcus neoformans* was made.



(Fig 9 & 10, Positive Rapid Urease Test and Brown colonies on Bird Seed Agar)

Vitek ID and AFST, also confirmed *Cryptococcus neoformans*, susceptible to Amphotericin B.

With the help of culture, a confirmatory diagnosis of Primary Cutaneous Cryptococcosis (PCC) was made and the patient was started on Liposomal Amphotericin B.

Even though cutaneous manifestations of PCC usually differ from secondary cryptococcosis, but it should be kept in mind that almost any type of lesion can be seen in disseminated cryptococcosis. Therefore it is mandatory to exclude secondary cryptococcosis with careful investigations. Furthermore, the possibility that initial skin lesions could be the cause of systemic cryptococcosis should be taken into account. In order to rule out a systemic infection, additional tests were carried out on our patient following the diagnosis of *C. neoformans*. These tests included serum cryptococcal antigen detection, chest radiography, and abdomen US, and blood cultures. Lumbar puncture was not conducted in this case since there were no signs or symptoms of central nervous system involvement, the serum antigen detection was negative and there was no additional evidence of central nervous system nor systemic dissemination. Additionally, patients with skin lesions caused by *C. neoformans* should have comprehensive investigations conducted to rule out immunodeficiency diseases. In this case, HIV antibodies and HIV p24 antigen were negative, leading to the diagnosis of PCC in an immunocompetent patient.

DISCUSSION

Cryptococcosis is one of the most common opportunistic infections

affecting immunosuppressed patients, involving the CNS or lungs, as either a sub-acute or chronic disease. *Cryptococcus gattii* and *Cryptococcus neoformans* are the two species that are commonly isolated. The majority of individuals affected by *C. neoformans* are either on corticosteroid therapy, have HIV infection, have undergone transplantation, or have a compromised cell-mediated immune response.On the other hand, *C. gattii* species have a limited geographic distribution, being isolated from decomposing wood in tropical and subtropical areas and from eucalyptus trees. They seem to be more virulent affecting immunocompetent as well as immunosuppressed patients. (1)

Cryptococcus neoformans is an environmentally, worldwide distributed encapsulated yeast. It is usually retrieved from soil that has been contaminated by dust, decomposing wood, fruits, vegetables, and avian excrement, particularly pigeon droppings (2).

Cryptococcosis is an infection caused by Cryptococcus species, most commonly seen in immunocompromised individuals, particularly those undergoing cancer chemotherapy, organ transplants, and HIV. (3)

The primary or secondary cutaneous condition is polymorphic, which may present as papules, purpura, vesicles/blisters, pustules, nodules, tumors, ulcerations, necrotizing panniculitis/cellulitis, abscesses, acne-like lesions or molluscum contagiosum-like lesions. Due to the polymorphic presentation, there can be a delay in the diagnosis leading to unfavorable outcomes. (1, 4)

PCC is determined as cryptococcal infection that is only located on the skin. Little has been done in recent years to identify the underlying cause of PCC in immunocompetent hosts as opposed to their immunocompromised counterpart, given the trend of increasing numbers of cases of cryptococcosis reported in immunocompetent hosts, who are "apparently healthy" following extensive clinical investigation. A typical clinical presentation of a Cryptococcus cutaneous infection does not exist. The most typical presentation is asymptomatic or mild itching and the development of painful nodules; however, ulcers may also be seen. (5)

In 1972, Noble and Fajardo proposed three diagnostic criteria for the diagnosis of PCC. (6)
1. Absence of infection in other organs
2. *Cryptococcus neoformans* must be isolated from skin
3. Absence of extracutaneous infection within
4. Weeks after the primary cutaneous cryptococcosis diagnosis

Primary cutaneous cryptococcosis is a rare clinical condition in itself and if left uncontrolled, it can lead to disseminated disease. The diagnosis is predicated on the lack of invasive symptoms in other sites. (7)

Due to the relatively low number of cases, guidelines have not fully defined a standard treatment for PCC in immunocompetent hosts. The three most often prescribed medications for PCC are fluconazole, itraconazole, and amphotericin B. A standard treatment for PCC in immunocompetent hosts has not been fully defined by guidelines, due to the relative rarity of cases. Fluconazole, itraconazole and amphotericin B are the most commonly used drugs to treat PCC (8).

CONCLUSION

PCC may be a challenging clinical entity to identify. Our patient was working in the forest which may have been the source of her infection. Here, we have evidenced the need for comprehensive diagnostics in cases of long-lasting skin lesions, particularly those that do not improve with antibiotic treatment. It is important for clinicians to understand that *C. neoformans* can cause inexplicable skin lesions in immunocompetent individuals as well. An oral antifungal is advised to achieve full recovery, the duration of which may be case based.

Consent

Informed consent was taken from the patient.

Ethical Approval

The study was approved by the Institutional Ethical Committee.

Funding

This case report did not receive funding from third parties.

Conflicts Of Interest

The authors declare no conflict of interest.

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