



# Disseminated Cryptococcosis in an Immunocompetent Patient: A Case Study

Jemima Islam<sup>a++\*</sup>, Mir Wasim Ali<sup>a++</sup>,  
Sabyasachi Chowdhury<sup>a++</sup>, Soumyadip Rakshit<sup>a++</sup>,  
Md. Karimulla Mondal<sup>a#</sup>, Anup Kumar Datta<sup>a†</sup>,  
Kokila Banerjee<sup>b‡</sup> and Soumitra Ghosh<sup>a‡</sup>

<sup>a</sup> Department of Internal Medicine, IPGMER & SSKM Hospital, Kolkata - 700020, India.  
<sup>b</sup> Department of Microbiology, Drs Trivedi and Roy Diagnostic Laboratory, Kolkata, India.

## 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 Study**

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## ABSTRACT

Cryptococcosis is the fungal infection caused by the yeast that belongs to the cryptococcus species which is divided into two broad categories, Cryptococcus neoformans and Cryptococcus gattii. Cryptococcosis is the opportunistic infection in the immunocompromised individual, particularly in HIV infected individual. In immunocompetent individuals, there may be serological evidence of cryptococcal infection, but cryptococcal disease is very rare in the absence of impaired immunity.

<sup>++</sup> Junior Resident;

<sup>#</sup> Senior Resident;

<sup>†</sup> Assistant Professor;

<sup>‡</sup> Professor;

\*Corresponding author: E-mail: jemimaislam12370@gmail.com;

Here we are reporting a case of disseminated cryptococcosis (multiple cold abscesses, sacroiliitis and asymptomatic pulmonary nodules) in an immunocompetent patient, which was initially thought to be mycobacterium tuberculosis infection.

**Keywords:** *Cryptococcosis; immunocompetent; cold abscess.*

## 1. INTRODUCTION

Cryptococcal infection is acquired from the environment. *Cryptococcus neoformans* is frequently found in the soil, infected with pigeon excreta [1]. In contrast, *Cryptococcus gattii* inhabits a variety of arboreal species, including several types of eucalyptus tree. In immunocompromised patients, the majority of the infections are caused by *Cryptococcus neoformans*, where *Cryptococcus gattii* more commonly affects HIV negative individual [2]. HIV infected individuals with CD4 count less than 100cells/mm<sup>3</sup> are at highest risk of infection [2]. The annual incidence of cryptococcosis in HIV negative patients is approximately 0.2 to 0.9 per 100,000, depending on the geographical area studied [3]. The spectrum of the disease caused by cryptococcus species consist predominantly of meningoencephalitis and pneumonia but skin and soft tissue infection also occur, in fact it can affect any organ and tissue. Cryptococcosis can present with wide variety of skin manifestations, including papule, plaque, purpura, vesicles, nodule, abscess, granuloma, pustule, draining sinus, cellulitis, tumour like lesion, rash [4].

## 2. CASE REPORT

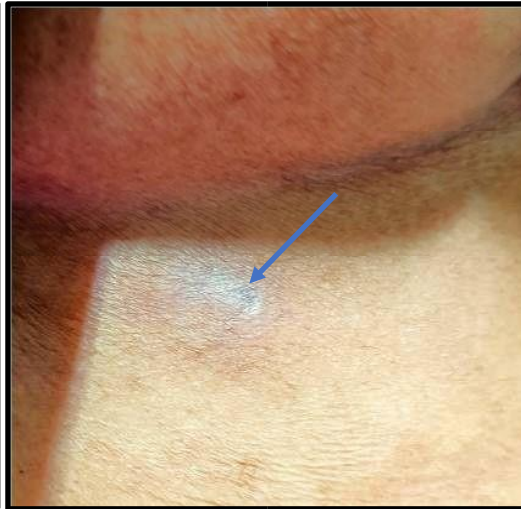
A 55-year-old female without any comorbidity presented with complaints of swelling over the left elbow, followed by left sided lower back region and behind the left ear for the last 3 months, pain in the right buttock for similar duration. She also complained of discharge from right inframammary area for the last 1 month. On clinical examination, she had mild pallor with unremarkable systemic examination. On the left elbow she had papulopustular lesion (Fig. 1), In inframammary region, there was discharging sinus with an underlying swelling (Fig. 2) and a nodular lesion behind the ear (Fig. 3). On the left infrascapular area there was a soft tissue swelling without overlying sinus formation (Fig. 4). Sacroiliac (SI) joint tenderness was present in right side with positive Patrick test. Central nervous system examination was unremarkable.

On evaluation, complete hemogram showed normocytic and normochromic anaemia

(Haemoglobin 10.8gm/dl, TLC 4500/ $\mu$ l, Platelet count 3.5 Lac) with raised inflammatory markers (ESR 110mm/hour, CRP 6.45 mg/L) revealed. Liver and renal function tests were normal. Chest imaging (HRCT thorax) revealed broncho centric nodules with lymphocytic interstitial pneumonia (Fig. 5a&b). Lymphocytic cellularity was found in the BAL fluid study without any evidence of infection. Ultrasonogram of the whole abdomen and pelvis showed no pelvic collection or psoas abscess. USG of bilateral breast showed 22x15 mm sized thick wall collection in the anterior chest wall below the inframammary fold on the right side, in the subcutaneous plane (volume 0.5 cc) (Fig. 6). MRI of the back revealed altered signal intensity peripherally enhancing septated collection in left posterior abdominal wall in intermuscular plain and intramuscular plane of left latissimus dorsi muscle extending into subcutaneous plane with partial to complete thick enhancing septation (Fig. 7a and 7b). MRI of the pelvis showed altered signal intensity enhancing areas noted in right sacrum involving right sacroiliac (SI) joint (Fig. 8). MRI of the left elbow joint showed asymmetrical bone destruction with marrow oedema of olecranon process, surrounding soft tissue swelling with oedema around tricepsanconaeus (Fig. 9a, b, c, d). The contrast MRI of the brain revealed no evidence of central nervous system involvement. CSF study was unremarkable. USG guided aspiration was done from back swelling and aspirate fluid ZN stain, modified ZN stain, gram stain as well as CBNAAT were negative. Rapid culture for mycobacterium tuberculosis from aspirate fluid was negative. Special stain like Grocott stain and Alcian blue stain of pus material revealed budding yeast cells (Fig. 10a&b). India ink stain showed round budding yeast with small capsule (Fig. 11). Antigen testing for cryptococcus was positive (Titre 1:126) by Cryptococcal Antigen Latex Agglutination System (CALAS) in the pus material (Fig. 11). Culture growth from pus revealed no fungal growth. She had negative result of HIV serological test. Her CD4 T cell count was normal and the level of serum immunoglobulin including IgG, IgA, IgM, and total IgE were within normal range.



**Fig. 1. Papulopustular lesion over left elbow (Red Arrow)**



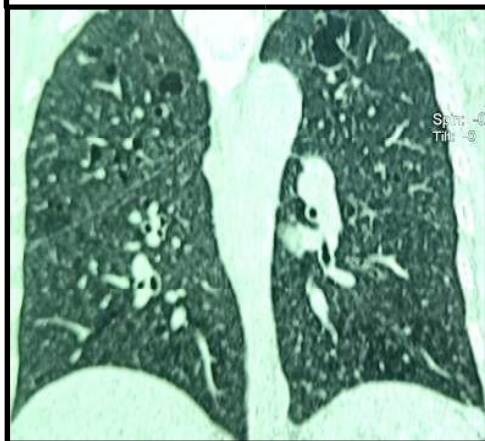
**Fig. 2. Discharging sinus in right inframammary region (Blue Arrow)**



**Fig. 3. Nodule behind the ear (Red Arrow)**



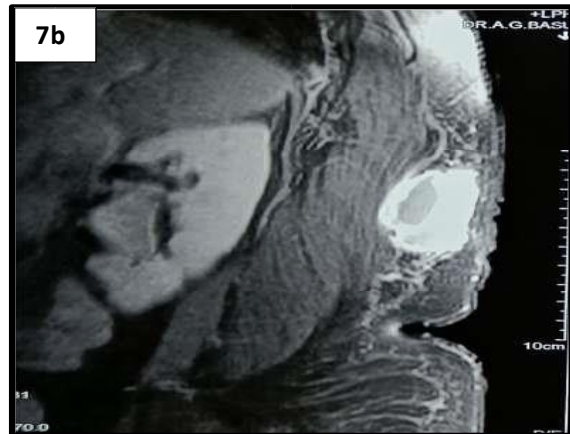
**Fig. 4. Soft tissue swelling in infrascapular area (Blue Arrow)**



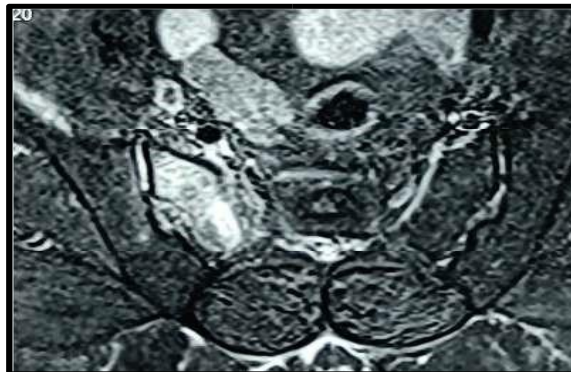
**Fig. 5a &b: (HRCT thorax): Bronchocentric nodule with lymphocytic interstitial pneumonia**



**Fig. 6. Superficial collection in anterior chest wall in right inframammary area**



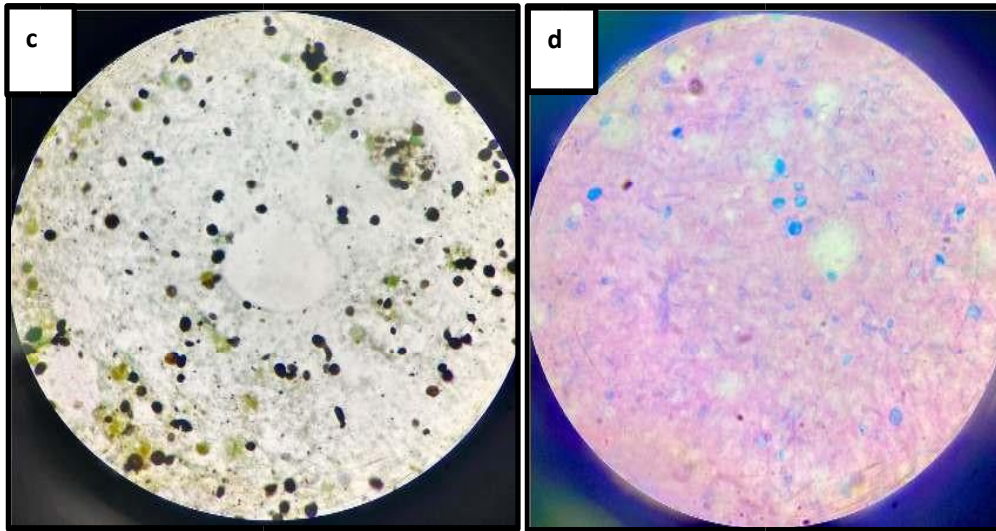
**Fig. 7a & 7b. Collection in left posterior abdominal wall and left latissimus dorsi muscle**



**Fig. 8. Altered signal intensity changes in right sacrum involving right sacroiliac joint**



**Fig. 9a & b. Asymmetrical bone destruction with marrow oedema of olecranon process**



**Fig. 9c. (Grocott Stain), 9d. (Alcian Blue Stain): Capsule Negative Budding Yeast Cells**



**Fig. 10. Round budding yeast with small capsule**



**Fig. 11. Antigen testing for positive (Titre 1:126) by CALAS**

### 3. DISCUSSION

Cryptococcosis is an opportunistic infectious disease caused by basidiomycetous, yeast like fungus that exist as yeast in both environment and tissue [5]. Primary focus of the infection is the lung by respiratory droplets with dissemination through hematogenous route in the meninges, skin, bone, prostate, and other organs. Disseminated cryptococcosis in immunocompetent population is very rare and usually involves central nervous system. Most of the cutaneous infections occur as a sign of disseminated cryptococcal infection, which can be seen in 10 to 15% of the cases [6]. In tuberculosis endemic countries, cryptococcosis

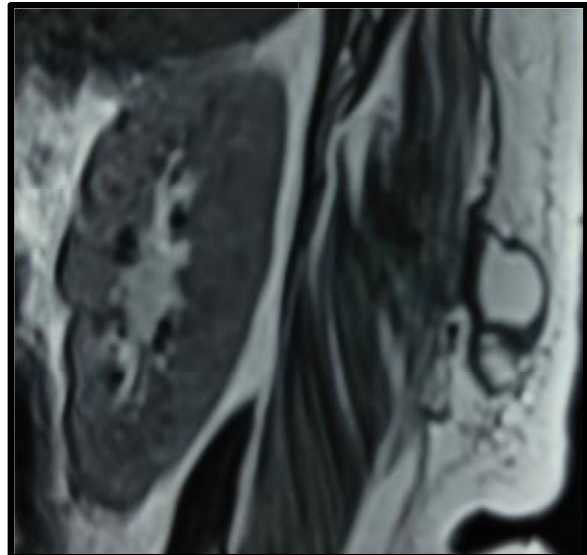
can be easily misdiagnosed as tuberculosis as there is a high degree of overlap in clinical, laboratory, and radiographic presentations. In high tuberculosis burden area disseminated tuberculosis should be ruled out carefully when cryptococcosis is complicated with tuberculosis [7]. Disseminated cryptococcosis is confirmed by positive culture or pathological results. Cryptococcus from biological samples can easily grow on routine fungal and bacterial culture media [8]. However, our patient was negative for fungal culture, which may be due to insensitivity of culture at early stage of infection. In addition, less fungemia is seen in immunocompetent patient compared with immunocompromised host. CLAT detect the capsular polysaccharide

antigens, which has been established as a reliable diagnostic tool with overall sensitivities of 93 to 100% [9,10]. The capsule is composed of glucuronoxylomannan and galactoxylomannan polysaccharide. It is the one of the classical virulent factors for neoformans and mutant without capsule are less virulent [11]. Several genes that synthesize capsules have been identified and site directed gene mutants result in hypo capsular or acapsular strains. The CrAg test is approximately 95% sensitive and specific [12,13]. False negative results are reported due

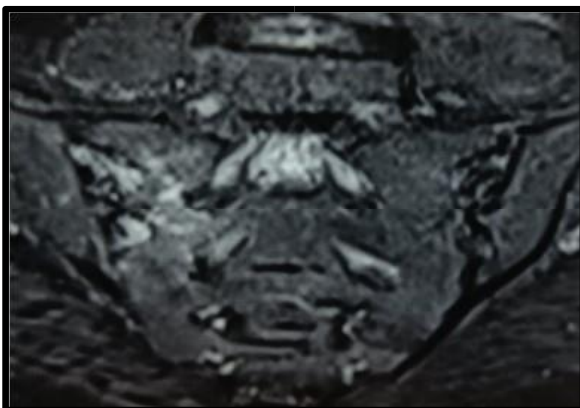
to poorly encapsulated strain. Our patient was treated with liposomal amphotericin B (3mg/kg) along with oral Flucytosine (100mg/kg/day) for 14 days. Now the patient is on consolidation phase with oral fluconazole (800 mg/day). After 14 days of induction therapy, swellings have been reduced in size (Fig. 12); buttock pain has been improved. Repeat MRI of the back was done which revealed decreased size of the collection with less signal intensity (Fig. 13). Repeat MRI of sacroiliac (SI) joint also showed decreased signal intensity of right sacroiliac (SI) joint (Fig. 14).



**Fig. 12. Back swelling has reduced in size after 14 days of induction therapy**



**Fig. 13. (MRI Back): Decreased collection size**



**Fig. 14. MRI of SI joint showed decreased signal intensity compared to before therapy**

#### 4. CONCLUSION

In developing countries like India where there is a high incidence of tuberculosis, fungal infection like cryptococcosis is likely to be missed; if high index of clinical suspicion is not there. From this case, we want to highlight that disseminated cryptococcosis should be kept in mind, where clinical picture is like tuberculosis but relevant investigation does not define tuberculosis.

#### CONSENT

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### ETHICAL APPROVAL

As per international standard or university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

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#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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