

Disseminated Cryptococcosis presenting as community acquired pneumonia in a patient with acquired immunodeficiency syndrome

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Abstract

Disseminated Cryptococcosis is an important cause of morbidity and mortality in immunocompromised patients. The respiratory tract is the primary site of infection from where it disseminates hematogenously to the central nervous system and skin. Timely diagnosis is essential to initiate appropriate antifungal treatment. We describe a case of disseminated Cryptococcosis in a patient with acquired immunodeficiency syndrome (AIDS) who presented with pneumonia and a solitary skin lesion.

Keywords: Disseminated Cryptococcosis; skin lesion; pneumonia.

1. Introduction

Cryptococcus neoformans is an opportunistic fungus with worldwide prevalence. It can cause life threatening infections in immunocompromised individuals. In most cases, the respiratory system is the primary site of infection and dissemination occurs to other organ systems like the central nervous system (CNS) and skin. In the human immunodeficiency virus (HIV) infected, primary Cryptococcosis and its dissemination presents with varied manifestations. Case fatality is high if it is not recognized early and if treatment is not initiated promptly. [1-3] We describe a case of disseminated Cryptococcosis in a patient with Acquired Immunodeficiency Syndrome (AIDS) who presented with pneumonia and a solitary skin lesion

revealed a massive splenomegaly with mild hepatomegaly. There were no focal neurological deficits. During examination, an ulcer was observed on the facial skin over the right temporal region. On further examination, the patient admitted to having had the ulcer for the preceding one month. It had started as a papule and progressed to a non-healing ulcer. In view of the progressive respiratory distress, the patient was intubated.

Laboratory parameters were as follows: Hemoglobin -10.3 gms/dl, total leucocyte count- 9700 cells/cu.mm. , ESR- 78mm/ hour. Sputum examination was negative for acid fast bacilli. Computed tomography (CT) thorax revealed the presence of diffuse randomly scattered miliary nodules involving bilateral lung fields, minimal bilateral pleural effusion, consolidation of right lower lobe and multiple paraaortic lymph nodes. CT abdomen indicated the presence of multiple para-aortic, aortocaval, mesenteric and bilateral iliac lymphadenopathy and splenomegaly. CT brain had no abnormalities. Paired blood samples were sent for culture. A provisional diagnosis of miliary tuberculosis or community acquired bacterial pneumonia was thought of and treatment with anti-tuberculous regimen, ceftriaxone and azithromycin was started.

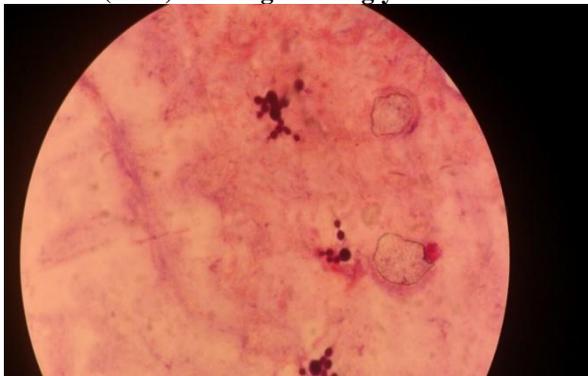
2. Case Report

A 42 year old male was brought to the emergency room of the hospital with complaints of breathlessness for 4 days and intermittent low grade fever for one month. He also had cough with expectoration, loss of appetite and loss of weight for one month. On examination he was conscious, oriented and febrile (Temperature: 39°C). Bilateral cervical, axillary and inguinal lymph nodes were enlarged and palpable. On auscultation, crepitations were present in the infrascapular region on both sides. Abdominal examination

In view of the multiple lymphadenopathies, fine needle aspiration cytology (FNAC) of bilateral cervical nodes was performed. This revealed the presence of necrotizing inflammation with fungal yeasts resembling *Cryptococcus*. Subsequently, serological testing for HIV was requested. The patient was found to be seropositive for HIV antibodies. The CD4 count was 450 cells/ cu mm. In the light of HIV status, endotracheal aspirate (ETA), urine, swab from the ulcer were submitted for culture. Gram's stain examination carried out on all samples revealed the presence of yeasts cells with budding (figure-1). Both blood cultures, cultures of ETA, swab from the ulcer and urine yielded the growth of *Cryptococcus neoformans*. They were identified as *Cryptococcus neoformans* using the VITEK 2 system yeast identification card YST -21343 and antifungal susceptibility was determined using Vitek-2 AST-YS07 card (BioMérieux, Marcy L'Etoile, France). The isolates were susceptible to amphotericin B, fluconazole, voriconazole, caspofungin and flucytocine. A lumbar puncture was done under aseptic precautions to rule out CNS involvement. A visibly clear Cerebrospinal fluid (CSF) was obtained which had 2 polymorphonuclear leucocytes / cu mm, sugar of 65 mgs/dl and protein of 57mgs/dl. Gram stained smear and India ink smear examination of the centrifuged deposit of CSF specimen showed occasional polymorphs and encapsulated budding yeast cells. Cryptococcal antigen was detected in the CSF by latex agglutination (titre-1:64) (Cryptococcal Antigen Latex Agglutination System (CALAS®), Meridian Biosciences, Inc, Cincinnati, United States). CSF culture also yielded the growth of *Cryptococcus neoformans*.

Eventually, a diagnosis of disseminated Cryptococcosis was made and therapy with Amphotericin B and fluconazole was initiated. Despite the administration of intensive treatment, the patient died after two days.

Figure 1: Gram stained smear of endotracheal aspirate (ETA) showing budding yeast cells



3. Discussion

Cryptococcus neoformans is encapsulated yeast present in the environment worldwide. It has been recovered from avian excreta, especially pigeon droppings, soil and from decaying wood. The main portal of entry of the aerosolized infectious yeast is the respiratory tract and clinical evidences indicate that cryptococcosis is most often a

reactivation of a dormant infection.[4] Patients usually present with pneumonia. The frequent sites of involvement following hematogenous dissemination from the lungs are the central nervous system and the skin. [1,5] The predisposing factors for Cryptococcosis include immunocompromised states such as HIV infection, immunosuppressive therapy, malignancy and post organ transplantation [6]. Dissemination and meningoencephalitis due to *Cryptococcus neoformans* represents the most common clinical manifestation in patients with AIDS and carries a high degree of mortality and morbidity.[1,2] A positive culture from at least two different sites along with a positive blood culture is considered to be a disseminated Cryptococcosis. The clinical manifestations of dissemination are variable and depend on the organ system involved. *Cryptococcus neoformans* has been isolated from specimens such as blood, CSF, sputum, ascitic fluid, urine, prostatic fluid, bone marrow and skin. [6,7]

An important diagnostic clue indicating disseminated disease may be the presence of diffuse maculopapular rash. [6] Skin involvement in Cryptococcal infection may also be non-specific. Cutaneous lesions affect the face and neck with different presentations including papules, pustules, plaques, ulcers, granulomata, cellulitis, subcutaneous nodules, herpetiform, molluscum contagiosum like, or acniform lesions.[1,4,8] The literature states that primary cutaneous Cryptococcosis usually presents as solitary lesion whereas disseminated disease with skin involvement presents as multiple skin lesions. The former is associated with a history of trauma and minor injuries or exposure of the skin to contaminated environment and usually occurs in the exposed parts of the body. [4,8] In this patient the skin lesion started as a papule which then became an ulcer over a period of one month. He developed respiratory symptoms only 3 days prior to admission. This patient hailed from a rural area but did not have contact with soil and avian droppings and his daily activities or occupation did not suggest predisposition to skin injuries. Though the skin involvement was a solitary lesion, it is unlikely that this was primary cutaneous Cryptococcosis. The primary site of infection in this patient is probably the lungs which had been dormant and asymptomatic with subsequent dissemination to skin and CNS

The FNAC examination of the lymph nodes was helpful in the diagnosis of Cryptococcosis. Subsequently, cultures from all the sites sampled yielded the growth of *Cryptococcus neoformans* thus fulfilling the diagnostic criteria for dissemination.

The diagnosis of cryptococcal pneumonia in its early stages is difficult due to fact that, in HIV patients the initial clinical symptoms and radiological findings are indistinguishable from other causes of pneumonia namely military tuberculosis, bacterial pneumonia, atypical pneumonia, histoplasmosis and *Pneumocystis jirovecii* pneumonia. [3] In this patient the radiological findings were

suggestive of miliary tuberculosis and treatment was initiated for the same. Since the immunocompromised status of the patient was not known at the time of admission, a differential diagnosis of community acquired bacterial pneumonia was also considered and empirical antibiotics were initiated. In this patient it can be assumed that the primary foci of infection was the lung and dissemination to CNS, skin and lymph nodes followed. The patient died as a result of progressive pneumonia with respiratory insufficiency although he was initiated on treatment with amphotericin B and fluconazole.

4. Conclusion

This case highlights the importance of considering cryptococcal pneumonia in immunocompromised patients even if the chest radiograph show the presence of miliary nodules suggestive of tuberculosis. FNAC is a useful diagnostic tool when lymphadenopathy is present. Skin lesions should be looked for when disseminated Cryptococcosis is considered.

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