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RESEARCH ARTICLE

MASSIVE THORACIC AND CERVICAL LYMPHADENITIS OF CRYPTOCOCCAL AETIOLOGY IN AN IMMUNOCOMPETENT ADULT A rare case report

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Abstract

Introduction: Cryptococcus infection is the second most common life-threatening; opportunistic infection in human immunodeficiency virus (HIV) infected individuals after *Mycobacterium tuberculosis*. Most cryptococcal infections start in the respiratory tract and secondarily involve the central nervous system, skin and bone marrow but rarely disseminate to lymph nodes and chest wall.

Case presentation: Cases of multiple cryptococcal lymphadenitis with or without meningitis is very rarely reported in immunocompetent individuals. Here, we report a rare case of multiple (cervical, axillary, supraclavicular and mediastinal) cryptococcal lymphadenitis extending to the chest wall without meningitis in an immunocompetent patient diagnosed by fine-needle aspiration cytology (FNAC) of the involved lymph nodes.

Conclusion: To conclude one should have a cautious approach towards the diagnosis and treatment of granulomatous lymphadenitis and should not be biased towards TB. Even if caseous necrosis is present, we should look for other causes of granulomatous diseases. Absence of immune suppression should not be a reason to exclude cryptococcosis from the differential diagnosis

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INTRODUCTION

Cryptococcosis is a chronic, sub acute or (rarely) acute pulmonary, systemic or meningeal infection caused by the yeast *Cryptococcus neoformans*⁽¹⁾. Cryptococcal infection is the second most common life-threatening, opportunistic infection in human immunodeficiency virus (HIV) infected individuals after *Mycobacterium tuberculosis*^(2,3,4), and in immunocompromised hosts the yeast is disseminated to almost all organs of the body⁽³⁾. Cryptococcal infections have a special predilection for the central nervous system, and meningitis is the commonest presentation^(1,4). Lymph node involvement is rarely found in cryptococcal infection in either HIV-infected or HIV-negative individuals,⁽⁵⁾ although some cases of disseminated cryptococcal lymphadenitis with or without meningitis have been reported.^(6,7,8,9)

We present a rare case of multiple (cervical, axillary, supraclavicular and mediastinal) cryptococcal lymphadenitis extending to the chest wall without meningitis in an immunocompetent adult person. FNAC is an inexpensive, easily available, simple, reliable and rapid method of diagnosing cryptococcal lymphadenitis.⁽³⁾

Case report:-

A relatively healthy adult male aged 35 years, without any established co-morbidities presented with following complaints, Swelling on right side of the neck, loss of appetite and significant weight loss followed by dry cough and Shortness of breath for the last 2 months of duration. He is non smoker, non alcoholic but gutkha chewer (10 packets/day). After 1 week of admission he developed new multiple, enlarged, non-tender, discrete swellings both

sides of infraclavicular area of anterior chest wall. No other abnormality detected on examination of the respiratory, cardiovascular and CNS. On physical examination, swelling on right supra clavicular region is largest measuring 4 x 3cm in size, tender. Visible vessels seen on right side of his chest. Facial puffiness present. Vitals stable, blood counts normal. CNS involvement was excluded by cerebrospinal fluid (CSF) analysis, which was negative for cryptococcal antigen and fungal culture.

A standard chest radiograph showing paratracheal opacity. CT chest suggestive of ill defined inhomogenously enhancing mass lesion in right Paramediastinal region extending to the anterior Pleural surface which is suggestive of carcinoma lung with superior venacaval obstruction and also mediastinal and bilateral supraclavicular lymphadenopathy, large in homogenously enhancing mass lesion in right deep axilla and upper infraclavicular chest wall. Ultrasound chest suggestive of cold abscess. Aspiration of pus from right supraclavicular lymph node sent for AFB stain which was negative but revealed fungal elements with yeast like bodies showing narrow based budding. Smear stained with Haematoxylin & Eosin, PAS (periodic acid-Schiff), Methenamine silver stain, Grams stain and India ink preparation. These findings conclude cryptococcal abscess. In culture cryptococcal grown on SDA within 24 hours of incubation. Diagnostic bronchoscopy and bronchoalveolar lavage (BAL) negative for cryptococcus. He was initially put on tablet flucanazole for two weeks as there was no improvement noted clinically and in view of massive mediastinal adenopathy with SVCO features, we switched over to injection Amphotericin 2 gr. Over 6wks I.V in 5% dextrose. He tolerated well with treatment without any side effects.

Discussion:-

Cryptococcosis is a systemic infectious disease caused by inhalation of yeast like fungus, *C. neoformans*. It is frequently found in soil contaminated with bird droppings particularly those of pigeons. Though it is classified as a primary pathogen, it is often encountered as a cause of opportunistic infection more often in AIDS. It may cause an asymptomatic pulmonary infection, sometimes followed by meningitis, pneumonia, pulmonary nodules, or mass lesions. Generally it starts as a primary pulmonary lymph node complex. Cryptococcal meningitis and disseminated cryptococcosis have gained importance recently because of rapid rise in the worldwide incidence of HIV infection. In our case, multiple lymphnodal involvement by cryptococcosis is very unusual. Cryptococcosis is one of the AIDS defining criteria according to the Center for Disease Control and Prevention guidelines.^[15] The purpose of presenting this case is to highlight the importance of careful evaluation of granulomatous lymphadenitis particularly in tuberculous endemic regions. Pulmonary cryptococcosis is rare in immunocompetent patients [1]. In a study by Aberg et al. [1], only 18 (35%) of 52 patients with pulmonary cryptococcosis were immunocompetent. Pulmonary cryptococcosis most commonly occurs in HIV patients, those undergoing cytotoxic chemotherapy, those receiving other immunomodulating agents such as corticosteroids, transplant recipients, or patients with hematologic malignancy. CNS is more commonly affected. According to the severity of cryptococcal infection, and patient's health status, a wide range of clinical manifestations may be resulted including cough, fever, pneumonia, meningoencephalopathy, disseminated disease, or even death. In immunocompetent hosts, the pulmonary infection has a tendency toward spontaneous resolution and is frequently asymptomatic. If the immune system fails to overcome the infection at this point, organisms will spread, through blood to the brain and other tissues.⁽⁹⁾ Pulmonary cryptococcosis is caused by inhalation of cryptococcal particles of the infecting organism *C. neoformans* variant *gattii* or variant *neoformans* which is an encapsulated, unimorphic fungus that is ubiquitous in soil and particularly abundant in pigeon excreta and decayed wood.^[10,12] The *neoformans* variant tends to cause extensive pulmonary involvement associated with disseminated disease, especially in immunocompromised patients^[10]. *Cryptococcus* variant *neoformans* and *Cryptococcus* variant *gattii* occur mainly in tropical and subtropical regions, thought to be due to its association with the Eucalyptus tree, and tend to cause more focal pulmonary and cerebral disease, mainly in immunocompetent patients^[10].

cryptococcal nodule or mass may simulate lung cancer^[12]. Fox and Müller^[13] reported that CT manifestations and the clinical presentation are influenced by patient age. In that series, six patients who were older than the median age of 44 years present with only one or two peripheral nodules and were asymptomatic. An additional six patients with multiple nodules, consolidation, or cavitation, they were younger than the median age, and of these, five were symptomatic and one was asymptomatic. Miliary dissemination, cavitation, lymphadenopathy, and pleural effusions are rare in immunocompetent patients and frequently seen in immunocompromised patients^[10,12], but our case multiple lymphadenopathy in immunocompetent person. Sputum cultures are not reliable and serum titers are usually not elevated except in disseminated disease^[12]. Therefore, the diagnosis depends on pathologic confirmation of the mucinous yeast capsule that stains strongly positive, bright red with India ink. A methenamine silver stain reveals yeast forms with narrow based budding. On PAS (periodic acid-Schiff) stains, the organism appears as a pale round structure^[11].

Here, we have reported a case of multiple lymphnodal involvement with *Cryptococcus* in an immunocompetent patient without meningitis. Multiple cryptococcal lymphadenitis is an uncommon form of cryptococcosis and is considered to be an AIDS-defining criterion according to the Centers for Disease Control and Prevention guidelines⁽³⁾. However, the fact that HIV-non-infected individuals may also be present with cryptococcal lymphadenitis has been proven by this study as well as by previous studies^(7,9). In developing countries like India, tubercular lymphadenitis is more common than cryptococcal lymphadenitis or may be coexistent^(10,11). Tuberculosis is ruled out by AFB staining of pus from lymphnode. *Cryptococcus neoformans* was identified as the fungal agent in this case with the characteristic narrow based budding. This finding is in contrast to most studies where *Cryptococcus neoformans* var. *neoformans* was found to be associated with immunocompromised individuals, whilst *Cryptococcus gattii* was the fungal agent implicated in HIV-negative immunocompetent patients^(1,9,12). Clinical acumen and a high index of suspicion are the key factors for early diagnosis and initiation of treatment, which leads to a favourable outcome by preventing dissemination of infection. Mortality in untreated cases of disseminated cryptococcosis can be as high as 80%⁽¹⁴⁾.

To conclude one should have a cautious approach towards the diagnosis and treatment of granulomatous lymphadenitis and should not be biased towards TB. Caseation should be looked for and if absent, other causes of granulomas are to be considered. Absence of immunosuppression should not be a reason to exclude cryptococcosis from the differential diagnosis.

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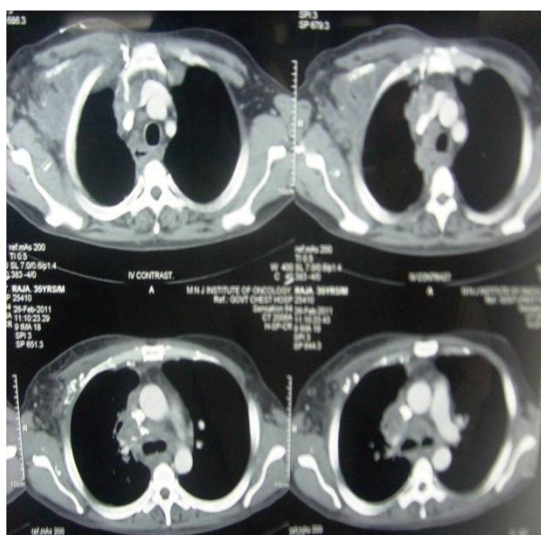
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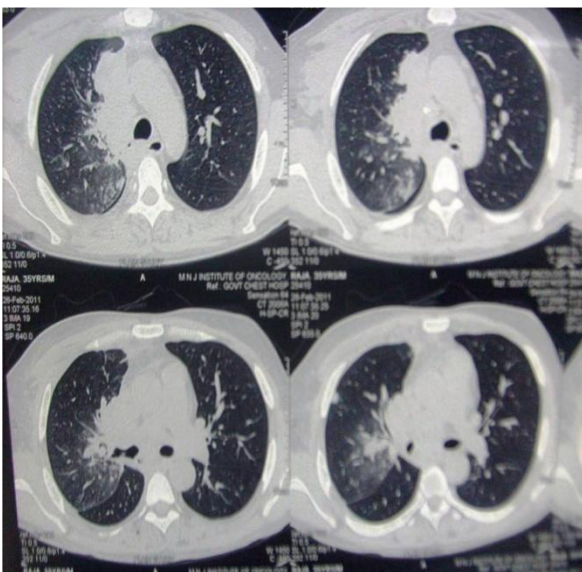
Picture 1:- Swelling in the right supraclavicular and infraclavicular region.



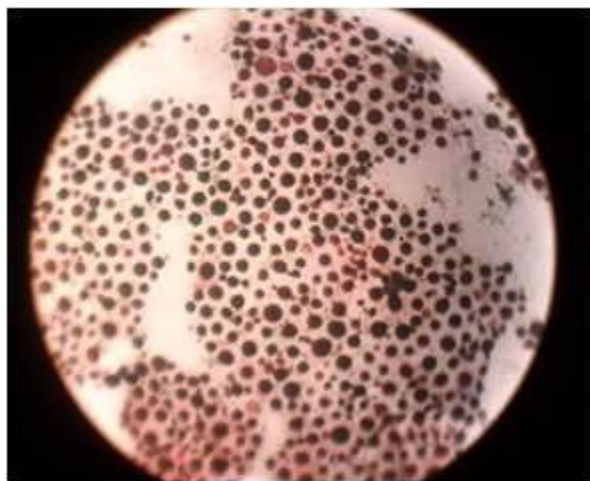
Picture 2:- Chest X-ray PA view showing upper mediastinal widening and right paratracheal adenopathy.

Picture 3:- CT scan chest mediastinal window showing upper mediastinal adenopathy





Picture 4:- CT scan chest lung window showing upper mediastinal widening.



Picture 5:- GMS stain showing fungal elements with yeast like bodies showing narrow based budding suggestive of Cryptococcus.



Picture 6:- India ink preparation confirming the Cryptococcus growth.