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CLINICAL VIGNETTE

Glenohumeral *Cryptococcus neoformans* septic arthritis: A Case Report

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Introduction

Cryptococcus neoformans is an encapsulated yeast-like fungus and a human pathogen throughout the world. Ubiquitous in soil and commonly present in bird excreta, *Cryptococcus* primarily enters the body through inhalation[1]. Although cryptococcosis can occur in immunocompetent hosts, it is much more commonly found in patients with deficits in immunity such as HIV/AIDS, those with hematologic malignancies or those undergoing treatment with systemic corticosteroids[2,3]. Infection can result in a primary pulmonary process with a variable presentation from asymptomatic to fulminant pneumonia. More commonly, cryptococcosis results in CNS infection secondary to hematogenous and lymphatic dissemination from the initial pulmonary site of entry and can produce a life-threatening meningoencephalitis[1-4]. Dissemination can also result in a localized or widespread cutaneous and mucocutaneous infection. Rarely, musculoskeletal infection produces a septic arthritis or osteomyelitis, with bony involvement occurring in about 10% of systemic cryptococcosis[2,3]. There have been 24 cases of arthritis caused by *Cryptococcus* described in the English language literature[5-7]. To our knowledge, this is the first reported case of glenohumoral joint septic arthritis due to *Cryptococcus*, and the second reported occurrence of *Cryptococcus* arthritis associated with systemic lupus erythemtosis (SLE).

Case Report

The patient is a 44 year-old African American female who presented with one month of right shoulder pain. The patient complained of chills, subjective fevers, and nausea. Medical history includes idiopathic thrombic purpura (ITP) for which she underwent splenectomy, and recurrent contralateral *Mycobacterium tuberculosis* axillary lymphadenitis for which she was being treated with rifampin, ethambutol, isoniazid, pyridoxine and pyrazinamide. The patient carried a diagnosis of systemic lupus erythematosis, but was not taking any rheumatologic medications at that time.

Pertinent exam findings were a fever of 101.3F, right shoulder pain with passive and active range of motion, and tenderness and swelling about the shoulder.

Laboratory studies revealed a mildly elevated white blood cell count of 15,900, C-reactive protein of 10.7, and a erythrocyte sedimentation rate of 40.0.

X-ray of the shoulder showed inferior humeral head subluxation and a joint effusion (Figure 1). MRI showed glenohumeral effusion and humeral head changes consistent with septic glenohumeral arthritis and humeral head osteomyelitis (Figure 2). Glenohumeral aspiration revealed gross purulence. Gram's stain revealed yeast forms and aerobic cultures ultimately grew *Cryptococcus neoformans*. Mycobacterial stains and culture, routine cultures and serologic testing for coccidioidiomycosis were negative.

In surgery, glenohumeral arthroscopic incision and debridement with open humeral head curettage was performed. Operative findings were consistent with septic arthritis and humeral osteomyelitis.

Infectious disease consultation was obtained and fluconazole 800mg qday was started. HIV testing was negative. Serum cryptococcal antigen was 1 to greater than 2,275. Given the high risk for CNS involvement, a lumbar puncture was performed and was negative for CNS infection. The patient's hospital course was complicated by a right upper extremity deep venous thrombosis and Herpes simplex lesions on her back, both of which resolved with medical treatment. The patient was discharged on fluconazole 800mg daily as well as rifabutin, INH, and pyridoxine for her preexisting tuberculous lymphadenitis.

At 3 months follow-up, she was clinically free from infection and her shoulder tenderness and range of motion had improved significantly.

Discussion

Septic arthritis is a rare complication of cryptococcal infection with only 24 previously reported cases in the literature[5-7]. The majority of the reported cases involved isolated infections of the knee joint (9), or were polyarticular (7) of which 6 included infections of the knee, making it by far the most commonly afflicted site. There have been several cases involving joints of the upper extremity, including elbow, acromio-clavicular, sternoclavicular and wrist joints, however to our knowledge, there have been no previously reported cases involving the glenohumoral joint.

Defects in cell-mediated immunity especially predispose to *Cryptococcus* infection. Of the previous 24 cases, 6 were solid organ transplant recipients, 2 had AIDS, and 3 with sarcoidosis. 9 of 24 patients were on immunosuppressive therapy, most commonly prednisone and azathioprine. Only 4 of 24 patients had no known underlying disease prior to development of cryptococcal arthritis. There has only been one patient previously reported to have SLE as their only predisposing risk factor[3].

Although no specific guidelines exist for managing cryptococcal arthritis, adhering to the recommendations for management of cryptococcemia appear to be reasonable in treating joint involvement[5]. Patients with cryptococcal arthritis should be evaluated carefully for disseminated disease and involvement of the central nervous system. Successful management of isolated cryptococcal arthritis involves initial administration of either amphotericin B or oral fluconazole with or without oral flucytosine for 6-12 months[8] and often requires surgical intervention (9/24 previous cases refs). Depending on the severity of immunosupression and persistent or recurrent disease, chronic suppressive azole administration, as is suggested for HIV patients may be considered[9].

The vast majority of septic arthritis continues to be bacterial. However, atypical pathogens such as *Cryptococcus neoformans* should be considered in the differential, particularly in patients with compromised cellular immunity.

FIGURE LEGENDS

Image 1 – Anteroposterior(AP) Xray of right shoulder demonstrating inferior subluxation of humeral head consistent with joint effusion

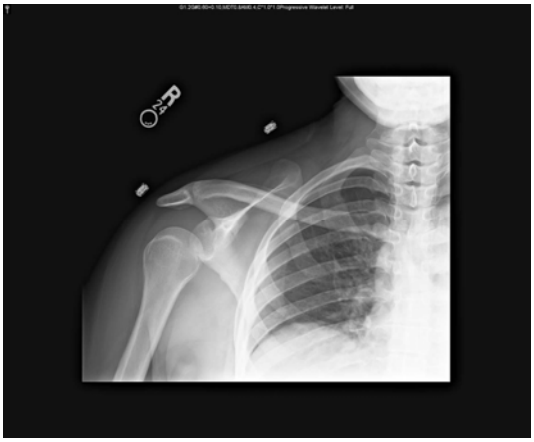
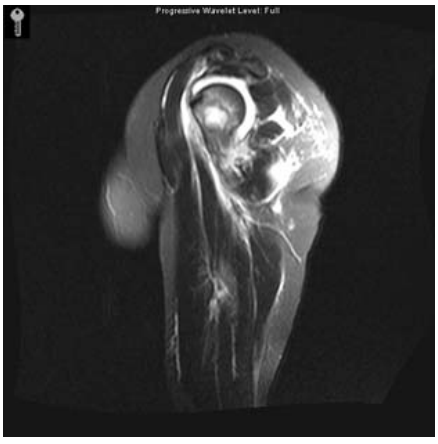


Image 2 -- Sagittal T2 Weighted MR demonstrating diffuse soft tissue infiltration and proximal humeral fluid collection consistent with osteomyelitis



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