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Case Report

Pyrexia of unknown origin in a healthy adult: a case report

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ABSTRACT

A 23-year-old male, with no known co-morbid illnesses, presented with a history of chronic fever and left hip pain of 6-months duration. The persistence of the fever with the progressive worsening of pain despite outpatient management prompted him to seek further evaluation. He was evaluated outside on multiple occasions and was diagnosed with a left sacroiliitis with left gluteal and paraspinal fluid collection 2 months prior, for which he was initiated on empirical anti tubercular treatment (ATT). In view of worsening of symptoms, he presented to our centre where he underwent a curettage and bone grafting of the left SI joint following repeat imaging. Tissue culture grew *Cryptococcus neoformans* and he was started on liposomal Amphoterecin B with Flucytosine. Patient clinically improved and was discharged on the same regimen. This case report aims shed light on the evidence of primary skeletal cryptococcal infection in an immunocompetent individual.

Keywords: Skeletal cryptococcosis, PUO, IFI

INTRODUCTION

Cryptococcus is a yeast associated with invasive fungal infections in humans. It consists of two species: *Cryptococcus neoformans* and *Cryptococcus gatii*.[1] Immunocompromised individuals are typically at risk for invasive disease with a high prevalence of cryptococcal meningitis among non-virally suppressed HIV positive individuals.[2] Skeletal cryptococcal infections are rare and the estimated prevalence is less than 10% persons with disseminated disease.[3,4] Very few cases of isolated bone and joint space infections have been reported in literature. Immunocompetent individuals have also been reported to have cryptococcal infections with lesser prevalence.[5]

CASE REPORT

Our patient was a 23-year-old male, with no known comorbid illnesses, who presented with a history of fever and left hip pain for 6 months. The fever was insidious in onset, high grade, intermittent, associated with chills without diurnal variations. The hip pain was insidious in onset, intermittent to begin with and was severe in intensity with radiation to the entire left leg. The pain gradually progressed and was soon continuously present even at rest. He had difficulty in moving his leg with worsening on postural change. There was no other significant history.

He was diagnosed with left sacroiliitis, left gluteal and left paraspinal collections and was started on ATT empirically elsewhere based on imaging. In view of worsening of symptoms, a repeat magnetic resonance imaging (MRI) done 2 months after ATT initiation revealed radiological worsening following which he presented to us. On presentation, he was febrile. His vitals and general examination were normal. Local examination of the left hip revealed severe tenderness on movement with restricted range of all hip movements and tenderness over the gluteal region. Examination of other systems were normal.

His clinical syndrome was suggestive of a septic arthritis of the sacroiliac joint with adjoining soft tissue abscesses.

In view of the high prevalence of tuberculosis in India, tuberculosis of the hip or sacroiliac joint with soft tissue involvement was considered as a diagnosis. Another differential diagnosis considered was a chronic osteomyelitis of the hip or sacroiliac joint with adjoining soft tissue abscesses secondary to a bacterial infection. A fungal aetiology was much lower down in the list as the patient had no known immunocompromising conditions. Patient had no history suggestive of an ongoing malignant process. Sacroiliitis secondary to an autoimmune or rheumatologic disease such as ankylosing spondylosis was a possibility but the characteristics of the pain was not suggestive of an inflammatory arthritis.

He was started on broad spectrum antibacterial agents. His baseline investigations (Table 1) showed a neutrophilic leucocytosis with elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Repeat MRI showed cortical destruction of the left SI joint with gluteal and paraspinal collection. Patient subsequently underwent curettage with bone grafting of his left sacroiliac joint under GA. Tissue gram stain showed budding yeast cells and tissue culture grew *Cryptococcus neoformans*. He underwent a detailed workup to look for another source of infection and an underlying immunodeficient state, which was negative (Table 1).

His HIV antibody and antigen testing was negative. He was started on IV liposomal Amphoterecin B and flucytosine. Patient clinically improved and was discharged on the same regimen. At follow up, patient was pain free and clinically stable. His back pain resolved and he had no problem with weight bearing.

Surgical wound was clean and patient was continued on the same regimen for 6 weeks and was switched to tablet Fluconazole 800 mg/day for a period of 12 months. He is currently doing well.

Table 1: Laboratory investigations.

Investigations	Values
Hb	8.7 g/dl
TLC	13.60 thou/ul
Plt	608 thou/ul
Creatinine	0.7 mg/dl
BUN	6.27 mg/dl
Na	137 mmol/l
K	3.9 mmol/l
Bilirubin-total/direct	0.3/0.3 mg/dl
AST/ALT	31/32 IU/l
ALP/GGT	100/135 IU/l
Chest X-ray	Normal
2 D ECHO	Normal
Pus culture	*Cryptococcus neoformans*
Serum Cryptola antigen	Negative
NCCT chest and brain	Normal

DISCUSSION

Cryptococcal skeletal infections are rare and are more often seen in disseminated cryptococcosis seeding from another source. Isolated skeletal infections and soft tissue abscesses is a rare occurrence. A systematic review of 85 cases of cryptococcal bone infections between 1987 and 2013 found that 57.7% had isolated infections.[7] It is also prudent to note that 36 % occurred in immunocompetent individuals. *Cryptococcus gatii* is known to affect immunocompetent individuals as opposed to *C. neoformans*. 17 cases have been reported from 2013-2022 which were isolated infections of which 11 were seen with immunocompetent individuals.[8-10] All these infections were proven to have been caused by Neoformans species. The management of joint/bone infections is less studied and single drug therapy with fluconazole is recommended for non-CNS cryptococcosis. Specific guidelines for bone, joint or soft tissue infections do not exist at present. Successful treatment with multidrug regimens has been well documented.[11] In our case, we administrated a combination regimen with Amphotericin and Flucytosine, followed by fluconazole. Patient showed significant improvement in clinical symptoms.

CONCLUSION

It is essential to have a high index of suspicion in patients with prolonged fever and unresolving soft tissue or joint collections despite an empirical therapy aimed at covering common organisms based on local prevalence. It is also to be stressed upon that tissue diagnosis is crucial in determining the etiology in such infections. Empirical ATT should be used with great caution especially when no attempt has been made to obtain tissue for sampling. We hereby add to the existing evidence on cryptococcal joint and soft tissue infections which is largely becoming a known entity requiring specific guidelines on approach and management.

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