CLINICAL VIGNETTE

A Case of Septic Arthritis with Cryptococcus Neoformans in a Patient with Lupus and TB lymphadenitis

Christine Lau, M.D., and David Taylor, M.D.

Introduction

Septic arthritis is a medical emergency with an increasing frequency and a high associated mortality[1]. Although the classic microbiologic presentation still represents the majority of cases[2], the increasing population of immunocompromised patients is changing the presentation[3]. In particular, these patients are at increased risk for fungal causes, which may present with a more indolent course and atypical picture[4]. Here we present a case of cryptococcal arthritis in an asplenic patient with systemic lupus erythematosis.

Case Description

A 44-year-old African-American woman with a medical history significant for systemic lupus erythematosis, idiopathic thrombocytopenia purpura requiring splenectomy, recurrent tuberculous lymphadenitis on therapy, and obsessive-compulsive disorder presented to the emergency department with one month of right upper extremity pain. The pain was worse with movement and was progressive in severity. She had been evaluated by her primary medical doctor with X-rays and an ultrasound of right upper extremity which were unrevealing. Physical exam revealed limited range of motion of right shoulder and elbow secondary to pain; this matched tenderness on palpation over the posterior mid-humerus. She was febrile to 101.3F and laboratory studies were remarkable for mild leukocytosis, anemia, and an elevated erythrocyte sedimentation rate (ESR) of 50 millimeters per hour (mm/hr). Repeat films of the right shoulder showed inferior subluxation of the humeral head with joint effusion. Magnetic resonance imaging (MRI) of shoulder showed a large joint effusion with marked edematous changes of the rotator cuff muscles, consistent with septic arthritis. Arthrocentesis revealed RBC 3900 and WBC 195,000 with a differential of neutrophils 95%, lymphocytes 2%, and monocytes 3%. Gram stain was negative for bacteria. Orthopedic surgery debrided the shoulder, and cultures from both the aspiration and debridement grew yeast, subsequently identified as Cryptococcus neoformans. She was started on high-dose oral fluconazole. Lumbar puncture was performed and showed no evidence of cerebrospinal fluid (CSF) involvement.

Case Discussion

Recent studies show septic arthritis to be increasing in incidence with a frequency as high as 10 per 100,000 patients per year[1]. This is thought to be primarily related to increased prevalence of risk factors such as immunocompromised state, diabetes, and prosthetic joints[1]. Among culture positive cases, staphylococcus aureus or streptococci continue to represent the majority of cases; these pathogens have been the identified etiology in up to 91% in case series[2]. Regardless of the organism, joint involvement results from direct inoculation from an exogenous source, hematogenous dissemination, or direct extension from an adjacent focus[3]. In this patient, her history of obsessive-compulsive disorder with dermatillomania with multiple associated skin excoriations led us to suspect that S. aureus and Streptococci were the most likely causative organisms of the septic arthritis. She was started on vancomycin and ceftriaxone empirically until culture results returned. Ultimately, when the cultures grew Cryptococcus neoformans, she was treated with a course of fluconazole with subsequent improvement.

Fungal arthritis is a rare condition that usually presents in an indolent fashion and is found typically in immunocompromised patients[4]. Diagnosis may be delayed as inflammation is

often less severe and because of the slow progression of disease[4]. Recognition of underlying medical problems that predispose to this condition is key in establishing an appropriate level of suspicion to make the diagnosis. This patient presented with a relative immunocompromised state with her history of SLE. In addition, her history of splenectomy predisposed her to opportunistic infection with encapsulated organisms, including Streptococcus, Neisseria, Haemophilus, and Klebsiella. Cryptococcus neoformans, an encapsulated yeast is also an opportunistic pathogen that can target splenectomized patients[5]. Splenectomy has been identified as a risk factor for Cryptococcal infection in 3% of cases[6]. Primary infection usually results in pulmonary disease[4]. In immunocompromised hosts and immunocompetent patients with CNS involvement, recommended induction therapy is with amphotericin-B and 5-flurocytosine and fluconazole during consolidation[7]. In immunocompetent hosts, isolated pulmonary Cryptoccocus may be carefully observed[7]. Symptomatic patients with non-CNS-isolated Cryptococcus can be treated with fluconazole for 3-6 months[7]. More severe disease requires amphotericin[7]. There is no established standard of care for the treatment of cryptococcal septic arthritis.

This case is more unusual because the patient also had concomitant TB lymphadenitis that was actively being treated. Literature search produced another case of Cryptococcus arthritis and TB lymphadenitis in the same patient[8]. Cryptococcus inhibits production of TNF alpha, IL-12, IL-18, and interferon gamma but stimulates production of IL-10. TNF alpha is known to play a role in the inhibition of pulmonary TB. This patient may have had inhibition of TNF alpha from the Cryptococcal infection, which reactivated the TB lymphadenitis. This patient is currently undergoing immunologic work-up to further evaluate the underlying etiology of her multiple infections.

Although rare, the diagnosis of cryptococcal septic arthritis should not have been surprising based on key elements from her history: signs and symptoms suggestive of an infected joint; an immunocompromised state; a particular predisposition to encapsulated organisms; and the possible biological link between active cryptococcal infection and active tuberculosis. This case is an excellent example of the importance of tying apparent disparate elements from the history and physical exam into a unifying diagnosis.

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