Coccidioidomycosis in Chennai


Abstract
Coccidioidomycosis is a deep mycosis caused by the fungus *Coccidioides immitis*. Disseminated disease can affect any part of the body. Coccidioidal synovitis is a rare manifestation of musculoskeletal coccidioidomycosis requiring aggressive treatment. We report a case of a 65 year old man who presented to our centre in Chennai with pain and restriction of movement of the elbow of 4 months duration. After being investigated, he was subjected to a synovectomy following which he was diagnosed to have coccidioidal synovitis of the elbow joint by histology and culture. He was treated with itraconazole. He was doing well on the most recent follow up. The case is presented for its rarity in India.

Introduction
Coccidioidomycosis (commonly known as Valley fever or San Joaquin fever) is caused by the dimorphic soil dwelling fungus *Coccidioides*. Genetic analysis has documented the existence of two different species *C. immitis* and *C. posadaii*. The species are indistinguishable with regard to clinical disease, though most human infections are caused by *Coccidioides immititis*. Coccidioidomycosis may vary from a clinically inapparent infection to a severe or fatal mycosis. We hereby report a case of coccidioidal synovitis in a 65 year old man.

Case Report
A 65 year old man presented to another centre with breathlessness in October 2008. His chest X-ray at that time had shown right sided pleural effusion and upper lobe infiltrates. He had been started on empiric anti-tuberculous therapy with rifampicin, isoniazid and gemifloxacin. He responded to the treatment which was evidenced by resolution of pulmonary symptoms and weight gain.

In February 2009, he presented to our centre with pain and restriction of the right elbow joint, which had started 4 months ago. The pain was relieved by NSAIDs. The patient did not smoke or abuse alcohol. He is not a known hypertensive or diabetic. On specific questioning it was elicited that he had been visiting his son in Phoenix, Arizona in USA every year. He spends six months of a year in Phoenix.

On examination the elbow joint was found to be in 20 degrees of flexion and movement was painful in all directions. There was a diffuse swelling around the joint. Synovial fluid aspiration was negative for acid fast bacilli on smear and showed no growth on bacterial and mycobacterial cultures. All investigations were normal. Chest X-ray at our centre showed no abnormalities.

A subtotal synovectomy was done and tissue was sent for culture and histopathological examination. Multiple fragments of synovial tissue were received and on histology showed sub acute to chronic inflammation seen amidst fibrinous exudates and supplicative granulomatous inflammation. (Figures 1 and 2). In some multinucleate giant cells, thick walled large round structures were seen, which on PAS stain showed globular sporangia with some of them possessing sporangiospores suggestive of Coccidioidomycosis. (Figures 1 and 2). The fungal culture of the synovial tissue on Sabouraud Dextrose Agar (SDA) and Brain Heart Infusion Agar (BHIA) at 25 to 30°C yielded gray white colonies that showed abundant floccose, aerial mycelium after 6 to 7 days (Figure 3). The fungal colonies were identified as *Coccidioides* species from an LPCB (lactophenol cotton blue) mount that showed the typical arthroconidia with alternating dysjunctors cells (ghost cells) (Figure 4) confirming the diagnosis of synovial coccidioidomycosis.

Discussion
Coccidioidomycosis is caused by the dimorphic soil dwelling fungus *Coccidioides immitis*. The fungus is endemic to a geographically delineated area within the United States known as the Lower Sonoran Life Zone. The reason for the disease not being prevalent in India might be attributed to the lack of optimum conditions such as the semi arid climate and the flora for the fungus to thrive. Consequently, most cases of coccidioidomycosis in the literature occurring in parts of the world other than the Western hemisphere are imported.

As the soil becomes dry and nutrients become limited, the fungus disarticulates its hyphal form and gets transformed into small environmentally resistant arthroconidia. Upon fragmentation of the hyphae, the infectious arthroconidia become airborne spores measuring 2-6 micrometers in diameter and are easily aerosolized. It is the inhalation of these arthroconidia that leads to disease in both humans and animals. Exposure to the soil containing spores is the only risk factor for acquiring the disease. High inoculum exposures during windstorms, digging, farming and construction are more likely to result in symptomatic disease. Our patient denied a history of any such activity. Human to human transmission is extremely rare.

In tissue, pus and sputum, *C. immitis* is identified by large globular sporangia, which contain sporangiospores or endospores. The spores enlarge to form spherules that are round double-walled structures which undergo internal division until they are filled with hundreds to thousands of endospores. Rupture of the spherules leads to the release of endospores which elicit a supplicative reaction as evidenced in our case. Sporangia are usually readily identified on H & E stains, but sporangiospores or hyphae are best seen with fungal stains. Intact sporangia usually elicit a granulomatous reaction of histiocytes, epithelioid cells and giant cells of the foreign body or of Langhan’s type.

After being exposed to the infecting agent, about 60% of the individuals remain asymptomatic with nothing other than a
positive reaction to coccidioidin skin test. The remaining 40% of the people develop "valley fever" which is a self limiting flu like illness. Only about 5% of the people develop evidence of granulomatous pulmonary disease. Desert rheumatism, a self limited migratory sterile polyarthritis occurs in some patients. Only 0.5% people develop a disseminated disease. The skin is the most common site of extrapulmonary disease. Coccidioidomycosis is also a bio-hazard and poses a serious problem to people especially in areas that are not endemic to coccidioidomycosis.¹

In our patient, the chronic nature of the disease, absence of bone erosions and a synovial effusion suggested a mycotic or tuberculous synovitis. The diagnosis was confirmed by synovial biopsy and culture. Primary coccidioidal synovitis is an uncommon but a well recognized feature of musculoskeletal coccidiomycosis, which results in chronic synovial proliferation without osseous involvement.² At this point we cannot be sure whether he had pulmonary disease due to tuberculosis or coccidioidomycosis, especially because coccidioidomycosis is known to cause pneumonia and pleural effusion which resolve on their own.¹

Primary coccidioidal synovitis is extremely difficult to cure. The guidelines suggest amputation, arthrodesis along with systemic chemotherapy as the treatment of choice. Although
total synovectomy with systemic chemotherapy have shown promising results in some cases, the chance of recurrence is more. The drugs used to treat coccidioidomycosis are fluconazole, itraconazole and in severe cases amphotericin B.⁴

Our patient was put on itraconazole 200 mg twice a day and he was also asked to continue his ATT (without rifampicin) till he finished his course of 6 months. The interaction between anti-tubercular and anti-fungal drugs requires special mention. Rifampicin is an enzyme inducer and is not recommended for use concomitantly with itraconazole because rifampicin shortens the half life of itraconazole and reduces its efficacy. To date our patient remains well on itraconazole on most recent follow up after 2 months.

Coccidioidomycosis is extremely rare in India with only a handful of reported cases earlier, in which one of them was from our centre.² In recent times with an increase in international travel some travelers acquire infection indigenous to the regions traveled and on their return pose baffling clinical problems. This case report emphasizes the importance of a proper travel history to detect unusual and exotic infections.

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References


