Case Report

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Internal Medicine Section

Disseminated Cryptococcosis with Adrenal and Lung Involvement in an Immunocompetent Patient

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ABSTRACT

Disseminated cryptococcosis usually occurs in immunocompromised patients. Occasionally, it affects immunocompetent persons and mimics tuberculosis in clinical presentation and radiological findings. Usually, it affects lungs and central nervous system. Rarely, it may affect adrenal glands. We present a case of 65-year-old gentleman with prolonged pyrexia. Computed Tomography (CT) scan of chest and abdomen showed miliary pattern in the chest with bilateral adrenal masses. On the basis of clinical and radiological findings, the case was initially diagnosed as disseminated tuberculosis and anti tubercular treatment was started. Subsequently, on histopathological examination, the diagnosis was confirmed as disseminated cryptococcosis. Even in a country with high prevalence of tuberculosis, other causes of miliary mottling should be considered and histopathological examination should be sought.

Keywords: Adrenal cryptococcosis, Adrenal Tuberculosis, Disseminated tuberculosis, Empirical ATT, Immunocompetent

CASE REPORT

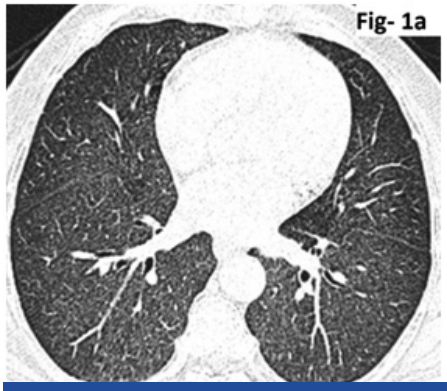
A 65-year-old retired government officer presented to Department of Medicine of All India Institute of Medical sciences, New Delhi, India, with the complaints of high grade fever and significant weight loss for the last five months. He was a known case of Type 2 diabetes mellitus with good glycemic control on oral hypoglycemic agents (Tab Glimipiride 2 mg, Metformin 500 mg and Voglibose 0.3 mg daily). Patient denied any exposure to bird droppings or excessive dust from nearby civil construction or high risk behaviour. Besides, there was no past history of tuberculosis or contact with a patient with pulmonary tuberculosis.

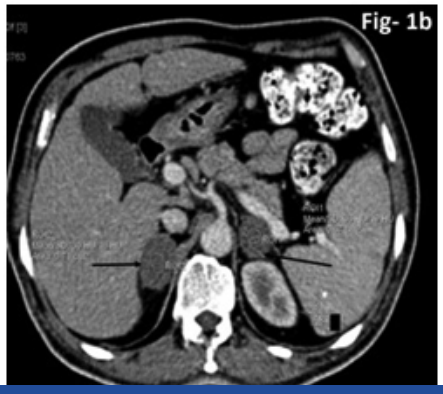
At the time of presentation, patient had fever and tachycardia. His body weight was 51 kg. Other general physical examination was unremarkable. Abdominal examination revealed mild hepatosplenomegaly with no free fluid. Other systems examination was non contributory. Hematological and biochemical investigation revealed an elevated ESR of 103 mm in first hour, deranged hepatic and renal function tests (serum creatinine 1.2 mg/dl, urea 53 mg/dl, uric acid 8.9 mg/dl, AST 89 IU/L, ALT 49 IU/L, and Alkaline phosphatase 1022 IU/L). His fasting blood sugar was 153 mg/dl and HbA1c was 6.5%.

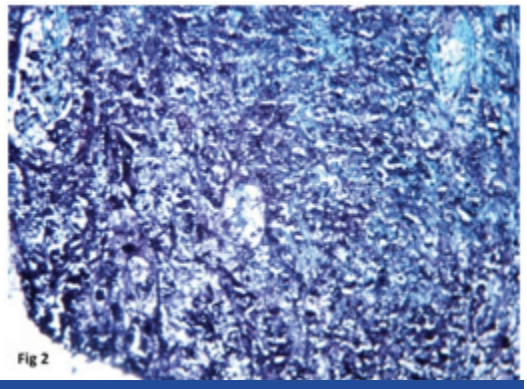
Urine and blood cultures were sterile and peripheral smear for malaria was also negative. Chest radiograph was normal. Ultrasound abdomen revealed mild hepatosplenomegaly with bilateral adrenal masses. CECT of chest and abdomen showed fine miliary mottling of bilateral lung fields and bilateral adrenal involvement [Table/Fig-1a,b].

Serum levels of adrenal hormones revealed adrenal insufficiency-Serum cortisol - 11.05 ug/dl (Normal 6.2-19.4 ug/dl), ACTH-90.98 pg/ml (Normal 7.2-63.3 pg/ml). Based upon the radiological findings, a presumptive diagnosis of disseminated tuberculosis was made and patient was started on antitubercular therapy (ATT) with replacement doses of steroid (prednisone 2.5 mg OD). The patient developed contrast induced nephropathy after three days of CECT examination and one day of starting ATT. FNAC of adrenal was planned to establish microbiological diagnosis once renal function normalized. Adrenal cytology revealed PAS positive, silver methamine stained capsulated budding organisms morphologically suggestive of cryptococcosis [Table/Fig-2] which was again later confirmed by adrenal biopsy. AFB staining and gene XPERT MTB/RIF was negative for *Mycobacterium Tuberculosis*. Hence, the final diagnosis of the case was disseminated Cryptococcosis with Type II Diabetes Mellitus and Essential Hypertension. Disseminated Tuberculosis was the differential diagnosis considered.

CSF examination was performed which ruled out meningeal involvement. Immunological workup revealed normal HIV serology, normal immunoglobulin levels and CD4 counts. ATT was stopped and liposomal Amphotericin B in a dose of 3 mg/ kg was started. It was given for three weeks. The patient improved symptomatically and fever subsided after one week of the treatment. Patient tolerated

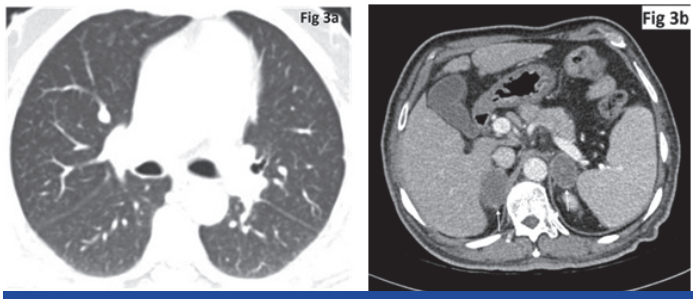






[Table/Fig-1a]: Axial HRCT chest reveals miliary nodules scattered in bilateral lung fields **[Table/Fig-1b]:** Axial CECT abdomen reveals enlarged bilateral low density adrenal glands (arrows) without any evidence of calcification **[Table/Fig-2]:** Methenamine silver stain shows the yeast, some of which demonstrate budding (40x)

the drug and there was no major adverse effect. Amphotericin B was stopped after three weeks of the treatment and patient was discharged on tab fluconazole 400 mg OD for consolidation therapy. CECT chest and abdomen was repeated after two months to look for the effect of the treatment. It showed resolution of miliary mottling and reduction in the size of adrenal masses with appearance of specks of calcification (healed lesions) in both adrenals [Table/Fig-3a,b]. Currently, after one and half years of the discharge, patient is asymptomatic and has gained eight kg of weight.



[Table/Fig-3a]: Axial CT chest lung window obtained two months after starting treatment reveals resolution of the miliary nodules
[Table/Fig-3b]: Axial CECT abdomen (post-treatment) shows slight decrease in the size of adrenals with appearance of specks of calcification (arrows)

DISCUSSION

Cryptococcosis is an opportunistic fungal infection that spreads by inhalation of dust particles contaminated with the droppings of the bird or dust from an area where civil construction is going on [1]. Disseminated Cryptococcus infection in immunocompetent individuals are rare and only a few cases have been reported previously [2].

In the present case, disseminated cryptococcosis involved lungs and adrenals without affecting CNS or other viscera. The patient had no features to suggest immunodeficiency. The findings of CECT chest and abdomen closely mimicked tuberculosis and the diagnosis could be established only after histopathological examination. The patient responded to antifungal agents without requiring adrenalectomy. In a similar case, an immunocompetent adult male had bilateral adrenal involvement along with liver involvement. The patient presented with adrenal insufficiency and was managed by adrenalectomy and antifungal agents [3]. In another case report, a young immunocompetent patient had disseminated cryptococcosis presenting as primary adrenal insufficiency. MRI revealed bilaterally enlarged adrenals. The patient was treated successfully by oral anti-fungal drugs [4].

Certain studies have highlighted that adrenal cryptococcosis presenting with adrenal insufficiency is usually refractory to antifungal chemotherapy. In cases which do not respond to anti-fungals, bilateral adrenalectomy was effective for controlling the disease [4,5]. The present patient has adequately responded to Injection Amphotericin B and Tablet Fluconazole.

In countries with limited resources and high prevalence, the diagnosis of tuberculosis on the basis of suggestive clinical features and radiological evidence is not uncommon. Invariably these patients are started on empirical anti tubercular treatment. In present case also, the patient was initially started on anti-tubercular treatment on the basis of clinical presentation and imaging findings. In a similar case, disseminated Cryptococcosis in an immunocompetent child presenting as pyrexia of unknown origin, was initially diagnosed as tuberculosis, patient and ATT was started. The case, however, was later treated successfully by antifungal agents [6]. In another case report of disseminated cryptococcosis in a young immunocompetent female, ATT was started on empirical basis. The patient however succumbed to her illness [7].

CONCLUSION

Tuberculosis is the commonest cause of miliary mottling on chest imaging and in the presence of other suggestive features; patients are often started on anti tubercular treatment, particularly in countries with limited resources and high prevalence of the disease. As disseminated histoplasmosis and cryptococcosis can mimic this condition, they should be considered in the differential diagnosis and confirmatory pathological and / or microbiological confirmation should be sought.

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