Case Report

A Case of Adrenal Histoplasmosis

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Abstract

Histoplasmosis is a fungal disease that may present as chronic pulmonary infection or in disseminated form. Disseminated histoplasmosis frequently affects the adrenal gland; sometimes adrenal gland may be the only site of demonstrable disease. Unilateral involvement in immunosuppressed patients is the usual presentation but bilateral involvement may be also there. Early diagnosis and treatment may save the patient from catastrophic adrenal insufficiency. Considering the risk of morbidity following adrenal insufficiency and the wide availability of effective treatments, adrenal histoplasmosis must be considered in adults who had adrenal masses. Though asymptomatic adrenal involvement has been described in patients with disseminated histoplasmosis; isolated adrenal involvement with or without adrenal insufficiency as the presenting feature of the disease is rare. In this report, a 42 years male presenting with history of weight loss, fever and later revealed bilateral adrenal mass, who was successfully treated with antifungal drug is described.

Keyword : *Adrenal histoplasmosis, Adrenal mass, fever, weight loss.*

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Introduction

Histoplasmosis is an infectious disease caused by the fungus *Histoplasma capsulatum*.[1,2] The endemic areas include the central and eastern states of the United States, South America, Africa and Asia.[1, 2] In nature, it exists as a mycelium in soil contaminated with excrement of birds and bats.[1, 2] When inhaled by humans or animals, it produces the yeast phase, which has an affinity for the macrophages that comprise the reticuloendothelial system.[1,2] Inhalation of *H. capsulatum* produces a lung infection with widely varying symptoms.[1,2] In most people, it produces asymptomatic lung involvement that resolves without treatment. In some susceptible individuals it may cause chronic pulmonary disease or disseminated disease.[1,2]

Cases of disseminated and extrapulmonary histoplasmosis are uncommun. Nevertheless, they have been reported from endemic areas, particularly among immune-compromised individuals and in those at the extreme of age.[2-4] There is high incidence of liver, spleen, lymph node, bone marrow and adrenal involvement.[2] The clinical presentation of the disseminated disease includes pyrexia, anorexia, nausea, vomiting, weight loss and fatigue. These symptoms are nonspecific and resemble other chronic infections and malignancies.[2,4] Adrenal involvement is usually sequelae of previous infection. Though very rare, cases of disseminated histoplasmosis have been reported. In this rare subset, involvement of the adrenal gland, either unilaterally or bilaterally, is not uncommon. In fact, the adrenal gland is the most common organ involved in disseminated *H capsulation* infections and adrenal involvement may serve as the only demonstrable site of active fungal disease in these patients.[5,6] Furthermore, adrenal histoplasmosis must be treated meticulously due to the possibility of advancement to adrenal insufficiency – the most common cause of death in patients with disseminated h*istoplasmosis*.[7,8]

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Case Report

A 42-year-male with diabetes presented with fever for 4 months along with fatigue, weight loss and generalized pigmentation for 1 month. For last 4 months he was advised several investigations including evaluation for tuberculosis which all revealed normal. He had past history of tuberculosis contact with his father who was a case of smear positive tuberculosis. He took several courses of antibiotic but which did not help to fever subsidence. His general and systemic examination was normal except fever and general pigmentation. Preliminary investigation revealed bilateral adrenal mass Table II.

As the adrenal mass was found nonfunctional, CT guided FNAC done which revealed granulomatous inflammation suggestive of adrenal histoplasmosis. After confirmation of diagnosis, systemic antifungal – Inj. Liposomal amphoterecin B was given for 14 days followed by oral itraconazole 200 mg daily with a plan to continue for next 18 months. The patient's fever subsided and general condition improved. In his follow up after 3 months patient's general well being improved, he was back to his job and able to do his regular daily activities. In his follow up at 6 months after diagnosis repeat imaging of adrenal mass was done. CT Scan of abdomen revealed Rt adrenal 6.1×3.1 cm ,Lt adrenal 6.1×3.5 cm and there is no biochemical evidence of adrenocortical insufficiency revealed by repeat normal short synacthen test[Basal cortisol-232nmol/l,at 30 min-714 nmol/l, at 60 min-865.8 nmol/l.

Table I. Preliminary Investigation reports of the patient

Investigation	Patient value
CBC	Hb 12.4 gm/dl, TC-8300 N-71 %. L-20%, M-6%, E-3%, ESR-40 mm in 1st hr, Platelet -426000
Renal function	B. urea-17 mg/dl, S.creat-0.8 mg/dlurine R/E- normal
Liver function	SGPT-95 u/l, SGOT-82 u/l,TP-73.1 gm/l , Alb 33.3 gm/dl
S. Electrolyte	Na-133, K-4.0, Cl-101, TCO2-21, S. Ca-8.9mg/dl, S. Mg-0.6 mmol/l
Glycemic status	F-6.4 mmol/l, ABF 8.2 mmol/l, HbA1C-6.6%
Mantoux test	0 mm
Blood C/S, Urine C/S	No growth, no growth
Imaging	Chest X-Ray- Normal, USG of whole abdomen-Bilateral adrenal mass

As USG of whole abdomen revealed adrenal mass evaluation of adrenal functions and CT scan of abdomen was done to see the details of anatomy and physiology of adrenal gland (Table II).

Table II. Anatomy and physiology of adrenal gland

Investigation	Patient value	Remark
CT Scan of abdomen	Bilateral adrenal mass measuring right-5.6cm×2.4cm, left-6.6 cm ×2.4 cm	Figure 1
Hormone evaluation	B. Cortisol-665.94 nmol/l,ACTH-23.5 pg/ml 24 hr. Urinary Metanephrine-1236 nmol/l, S. Epinephrine 88.57 pg/ml, S.norepinephrine-219 pg/ml	Normal

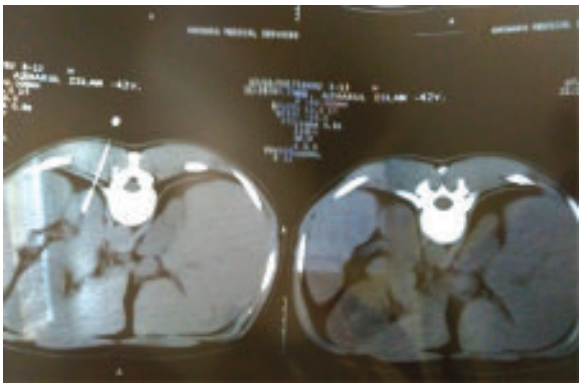

Figure 1. CT Scan of adrenal gland at Diagnosis

Discussion

This case of a young man complaining of weight loss, fever, fatigue and pigmentation at first drawn the attention for tuberculosis. Because abdominal ultrasound revealed bilateral adrenal enlargement, the differential diagnosis included benign or malignant adrenal tumors, metastatic tumors, sub-acute adrenal hemorrhage and disseminated infections such as tuberculosis, sarcoidosis and histoplasmosis. In a Brazilian series of 131,466 post-mortem examinations, there were 254 cases of adrenalitis, of which 43.7% were caused by tuberculosis, 33.8% by paracoccidioidomycosis and 1.2% by histoplasmosis.[9] Percutaneous biopsy or fine-needle aspiration using either CT or ultrasound guidance is the mainstay for evaluating adrenal mass after excluding pheochromocytoma as a cause of adrenal mass. Additional diagnostic tests for diagnosing histoplasmosis, such as tissue sample culture, antigen detection, serology and molecular diagnosis by polymerase chain reaction[1,2] are not available in all the centres. Most of the bilateral adrenal histoplasmosis cases are associated with adrenal insufficiency but in this case the patient had good adrenal reserve.

The recommended first treatment of histoplasmosis is amphotericin B for critically ill hospitalized patients.[1] For moderate to severe disseminated infections, the Infectious Disease Society of America recommends liposomal amphotericin B followed by itraconazole, although itraconazole therapy alone is often sufficient for milder cases.[1,10] In spite of high cost, our patient managed to get the total 18 doses of Inj. Liposomal Ampoterecin B at a dose of 1 mg/kg/day followed by oral Itraconazole 200 mg/day with a plan to continue for 18 months.

This case emphasizes the fact that adrenal histoplasmosis does occur in patients with bilateral adrenal mass. Adrenal insufficiency has to be monitored and in rare situation and possibly if diagnosed at early stage of the disease the patient may not have any feature of adrenal insufficiency . It is widely recognized that a prolonged treatment of at least 1 year is necessary due to *Histoplasma*'s adeptness at persisting latently within the human body.[11] For this reason in this case the duration of antifungal therapy is planned to be maintained for at least 12-18 months according to patient's response. In this case though the patient showed slow regression of adrenal mass as evidenced by imaging but the patient had dramatic improvement of the symptoms, body weight and wellbeing. The most noticeable thing is that in this case the patient has good adrenal cortisol reserve at diagnosis and 6 months follow up.

As there is the risk of severe patient decompensation due to adrenal insufficiency the wide availability of effective treatments for this infection, adrenal histoplasmosis must be considered even in all patients having constitutional symptoms with unilateral or bilateral adrenal masses.

Conclusion

The diagnosis of adrenal histoplasmosis should be considered in patients presenting with constitutional symptoms and unilateral or bilateral adrenal mass with or without Adrenal insufficiency.

Conflict of interest: Nothing to declare.

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