Bilateral Adrenal Enlargement Due to Disseminated Histoplasmosis in a Bangladeshi Patient

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Abstract:

Human infection with Histoplasma capsulatum is largely asymptomatic but disseminated disease is fatal if left untreated. We report a case of bilateral adrenal enlargement due to disseminated histoplasmosis in a Bangladeshi male who was successfully treated.

Key words: Histoplasmosis, disseminated, adrenal gland.

Introduction:

Human infection with the soil fungus Histoplasma capsulatum is largely asymptomatic and benign. Rarely it may cause serious and fatal illness. Both acute and chronic disseminated disease present diagnostic challenges to the clinician. The prominent clinical features are non-specific and include fever and weight loss(1). One useful clue in the diagnosis of disseminated histoplasmosis is bilateral enlargement of the adrenal gland (2). A microbiological diagnosis can be made with CT guided fine needle aspiration of the adrenal glands. Histoplasmosis is endemic in certain areas of North and Latin America(2). In this paper we report a case of disseminated histoplasmosis in a diabetic Bangladeshi patient who presented with prolonged fever and bilateral adrenal enlargement

Case Report:

A 40-year-old Bangladeshi male was admitted to Hamad General Hospital in November 2000. He presented with a two months history of fever associated with night sweating. He had been seen in the emergency room six weeks before admission because of fever and was found to have a palpable spleen and high blood sugar. Glibenclamide was prescribed for him.

He had been working in a supermarket in Doha, Qatar, for the last twenty years and visited his home country every two years. He had returned from leave only a few weeks before his admission.

Physical examination revealed an average built young man, fully alert, orientated, not pale or jaundiced and not in any distress; temperature 39.8°C, pulse rate 110 /min, BP 140/80 mm Hg, no lymphadenopathy, no mouth or oropharyngeal lesion; respiratory and cardiovascular systems were normal. Abdominal examination revealed a soft abdomen with a palpable spleen 3 cm below the costal margin.

Laboratory investigations reported WBC 5.8 000/mm³, Hb 13.8 gm/dL, platelets 265,000/mm³, blood sugar 12 mmol/L; electrolytes and liver function tests were normal. ELISA test for HIV, Hepatitis B and C serology, brucella, and Leishmania antibodies were negative. CD+4 cell count 448 cells/mm³. Urine and blood cultures were negative. Serum protein electrophoresis was normal. Cortisol 429 nmol/L (ref. range 0-276). 24 hr urine for VMA 28 umol/L (normal up to 40), 24 hr urine for metanephrines 2 umol/L (normal up to 5). Chest x-ray was normal. Ultrasound of the abdomen showed splenomegaly, bilateral adrenal enlargement and a left ureteric stone with mild hydronephrotic changes. Computerized tomographic (CT) scan of the abdomen showed markedly enlarged adrenals and a stone in the left ureter (Figure 1). Bone marrow examination showed no evidence of lymphoma or malignancy, and culture for Mycobacterium tuberculosis was negative. Fine needle aspiration of the adrenal gland showed necrotizing granulomatous inflammation, with multiple intra-histiocytic organisms showing morphological features of histoplasmosis (Figure 2). Treatment with itraconazole was started, the fever subsided after five days and the patient was discharged to continue treatment for nine months.

Discussion:

Histoplasma capsulatum is one of several dimorphic fungi capable of producing human disease. The fungus grows as a mycelium in soil contaminated by bird and bat excretions and in decayed wood. Microconidia are inhaled when sites are disturbed. Haematogenous spread from initial pulmonary infection may occur before development of a cell-mediated immunity(1). Disseminated histoplasmosis is a systemic illness that usually presents in a non-specific manner with persistent fever and constitutional symptoms. Although disseminated disease
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usually occurs in immunosuppressed patients, 20–30% have no demonstrable immunologic defect and often have no evidence of pulmonary involvement\(^1\).

Our patient was previously healthy and when he presented for the first time to the emergency room with fever, he was discovered to have diabetes mellitus. It is not clear whether diabetics are more prone to disseminated histoplasmosis but, in a study of 43 adults with disseminated histoplasmosis, four were diabetic\(^2\).

As our patient showed fever a few days after his return from leave in Bangladesh, we assume that he contracted the infection there. Reports of disseminated histoplasmosis from that region are rare. Goswami reported five cases diagnosed at the School of Tropical Medicine, Calcutta between February 1996 and September 1997\(^3\) and a total of 38 cases reported from India over 42 years from 1954 to 1996 \(^3\). The authors believed that histoplasmosis is not uncommon in India and that cases are misdiagnosed as visceral and mucocutaneous leishmaniasis. The problem is further aggravated by the fact that the antifungal agent amphotericin B is also highly effective against Leishmania donovani\(^3\).

Bilateral adrenal gland involvement occurs frequently in disseminated histoplasmosis\(^4,5\). In the series of Goodwin, 82% of an autopsy series of patients with disseminated histoplasmosis had bilateral adrenal enlargement\(^2\), while bilateral adrenal enlargement was seen in one patient out of 38 Indian cases and in three of 13 cases of Indian origin reported from UK\(^3\). The rarity of adrenal enlargement might add to the difficulties in the diagnosis of disseminated histoplasmosis inpatients from the Indian subcontinent.

Our patient presented with fever for two months but physical examination did not reveal the oropharyngeal lesions which are present in two thirds of chronic histoplasmosis cases\(^2\). Splenomegaly, which was present in our patient, was seen in most of the cases reported by Goodwin\(^2\). Laboratory findings did not show abnormality in the blood film. The chest x-ray was normal whereas two-thirds of chest x-rays in the Goodwin series were abnormal.

Diagnosis of disseminated histoplasmosis depends on demonstrating the fungus in an extra-pulmonary location in a patient with a progressive illness either by culture of body fluids or infected tissue or by microscopic examination of histopathologic materials obtained at biopsy\(^6\). Bone marrow examination was negative for histoplasmosis in our patient; this is uncommon and, in a series of 22 cases of disseminated histoplasmosis, bone marrow was positive for the organism in 15 cases \(^6\). Our case was diagnosed by CT guided fine needle aspiration and biopsy of adrenal glands. It is particularly important to rule out adrenal insufficiency if a diagnostic or therapeutic procedure that could induce an Addisonian crisis is anticipated, and also it is essential to rule out an occult pheochromocytoma before performing an adrenal biopsy because paroxysmal hypertension has been reported to occur during needle biopsy of an unsuspected pheochromocytoma\(^7\).

The mortality without treatment of disseminated histoplasmosis is 80% but can be reduced to < 25% with antifungal therapy\(^8\). Amphotericin B was effective in 68–92% of patients. Our patient responded to itraconazole and became afebrile after five days of treatment. Adrenal insufficiency is the most frequent cause of death when this disease is untreated\(^4\) and adrenal function should be assessed in every patient with disseminated histoplasmosis. The time of the appearance of Addisons disease cannot be predicted satisfactorily. Continued vigilance is necessary even in those who do not show evidence of adrenal insufficiency. The time interval of symptoms to diagnosis and starting effective treatment may determine which patient will develop adrenal hypofunction. The longer the disease can progress unchecked the greater the likelihood of adrenal gland destruction\(^9\).
References: