Adrenal insufficiency resulting from Histoplasmosis infiltration in an immunocompetent patient

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ABSTRACT
Histoplasmosis usually affects immunocompromised patients. Histoplasmosis infiltration to the adrenal in an immunocompetent host is rare, more so those who presented with adrenal insufficiency. We report a case of 54-year-old previously fit and healthy man who presented with chronic headache of two months duration that was associated with loss of appetite and weight-loss. He had hypotension, hyponatremia, relative hyperkalemia with morning cortisol of 160 nmol/L. Computed tomography of the adrenals showed bilateral enlarged adrenal glands and biopsy confirmed histoplasmosis infiltration. Treatment successfully ameliorate symptoms of hypocortisolism. This case illustrates that immunocompetent patient is still susceptible to adrenal histoplasmosis resulting in adrenal insufficiency.

Keywords: Adrenal insufficiency, histoplasmosis, immunocompetent, adrenal masses

INTRODUCTION
Histoplasmosis infection is due to inhalation of the spores of the *Histoplasmosis capsulatum*, mainly in contaminated soils by bird or bat’s droppings. Asia is one of the endemic areas for the disease in the world. 1 Disseminated histoplasmosis is rare and frequently affects adrenal gland up to 80%. 2 Bilateral adrenal involvement often present but only 7-20% of them results in hypoadrenalism. 3 Adrenal histoplasmosis commonly occurs in immunocompromised patient, but has been reported among immunocompetent patient. 4 Here, we report an immunocompetent patient who presented with adrenal insufficiency secondary to adrenal histoplasmosis.

CASE REPORT
A 54-year-old, previously fit and healthy man presented with chronic headache which worsens in the afternoon for the past two months. It was associated with lethargy, loss of appetite and weight. Close questioning revealed a compelling history of contact with an owl and its droppings since two months ago. The pa-
Patient actually found an injured owl in his courtyard, which he nursed, took care, fed and clean its cage for two months. He denied intake of traditional medication or history of high risk behaviour. He loss approximately 10kg of weight and his body mass index prior to illness was 25.3kg/m². There was no history to suggestive acute coronary syndrome, bleeding or volume loss. He did not have any other comorbidity such as diabetes mellitus, hypertension, dyslipidemia or heart disease. Clinically he was dehydrated. His body mass index was 22kg/m², blood pressure of 80/55 mmHg with significant postural hypotension. Systemic examination was unremarkable.

Initial investigation revealed sodium of 120 mmol/L (normal range 135-150), potassium 4.2 mmol/L (3.5-5.0), urea 8 mmol/L (2.5-6.4), creatinine 204 mmol/L (44-80), albumin 35g/L (35-50) and random blood sugar of 5.1 mmol/L (4-7.8). Despite of rehydration with normal saline, he remained hypotensive with persistent hyponatremia leading us to work on hypocortisolism as the provisional diagnosis. Indeed, his blood pressure improved and normalised a few hours after a stat dose of intravenous 100 mg hydrocortisone. This was followed with 100 mg 8-hourly. The hyponatremia improved to 130 mmol/L within less than 72-hour and normalised to 138 mmol/L 3 days later. Along with biochemical improvement, the headache and lethargy resolved. His morning serum cortisol was 160 nmol/L (68-469). Other laboratory investigations showed normal full blood count, serum calcium and ESR. Serology for retroviral, hepatitis A, B and C were negative. Electrocardiogram was normal.

Computed tomography (CT) of the abdomen showed bilateral well-marginated suprarenal masses (4.9 x 4.1 x 6.2 cm and 3.3 x 5.0 x 4.8 cm on the right and left, respectively) conforming to adrenal gland configuration and normal adrenal glands were not visualised (Figure 1). This was consistent with bilateral, diffuse adrenal gland enlargement.

Histopathology examination of adrenal biopsy revealed a necrotic tissue with fungal bodies consistent with histoplasmosis infiltration (Figures 2).

Figs. 1: a) Axial computed tomography (CT) view showing bilateral adrenal masses, and b) Sagittal view showing the masses (Asterisks).
He was treated with oral itraconazole 200mg 12-hourly and to be continued for at least 6 months. He also was started with oral hydrocortisone 10mg am/5mg noon and oral fludrocortisone 0.1mg daily. During follow-up, he remained well without any symptomatic, has gained weight and tolerated the treatment well.

DISCUSSION

Our immunocompetent patient presented with symptoms of hypocortisolism, loss of weight and appetite. In his circumstances of hypotension and hyponatremia, the morning cortisol was considered relatively low. His abdominal-CT scan showed bilateral well-circumscribed adrenal mass and adrenal biopsy confirmed histoplasmosis infiltration of the adrenals. The likely culpable source is his owl’s droppings. Another case of adrenal histoplasmosis has been reported in Malaysia, however it was in an immunocompromised host and the patient did not manifest hypoadrenalism. 5

Traditionally disseminated histoplasmosis is a disease of the immunocompromised and the extreme-age. 4, 6 In immunocompetent people, most of histoplasmosis infection resolved and only few of them becomes symptomatic. 4 So far thirteen cases of bilateral adrenal histoplasmosis have been reported in immunocompetent hosts. 6,7 To the best of our knowledge from English-medium literature search, the total reported number of immunocompetent patient with bilateral adrenal histoplasmosis resulting in adrenal insufficiency thus far, is less than 10 cases. 3, 6-8

Adrenal insufficiency in adrenal histoplasmosis is uncommon. 4 Kauffman reported that among 58 patients, 12 had adrenal involvement but none of them had adrenal insufficiency. 9 While Koene RJ et al reported 48.3% from 230 patients with adrenal (uni- or bilateral) involvement developed adrenal insufficiency based on literature review from 1971 to 2012 either in a form of case reports or case series. 4 However, these are generally immunocompromised host. 4 Most of immunocompetent host are asymptomatic. Similar finding showed by Wheat et al. in which only one out of 2200 infected immunocompetent people are symptomatic of hypoadrenalism. 10

Typical CT findings in adrenal histoplasmosis are bilateral adrenal enlargement with peripheral enhancement and central hypodensities due to central necrosis. However these findings are not
specific to histoplasmosis. Among other differential diagnoses which may present with similar findings include adrenal hemorrhage, lymphoma, metastatic or disseminated infections such as tuberculosis, cryptococcosis, blastomycosis or aspergilosis. Hence fine needle aspiration cytology or a percutaneous biopsy is mandatory for a definitive diagnosis.

The recommended treatment for critically ill adrenal histoplasmosis patients is using amphotericin B, followed by itraconazole once patients’ condition improved. In stable patients, itraconazole alone is effective. The recurrence of disease has been reported up to nine years after cessation of therapy, hence to reduce it the treatment should be prolonged to one or two years. Unfortunately in spite of eradication of the organism, hypoadrenalism may persist as showed in previous report.

In conclusion, in immunocompetent patient with bilateral adrenal masses or enlargement, a suspicion of adrenal histoplasmosis should not be dismissed particularly in endemic area. Adrenal biopsy is necessary for confirmatory diagnosis.

REFERENCES
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