

A rare case of Adrenal histoplasmosis presenting as adrenal insufficiency and hypogonadism .

Gideon Mlawa, Mahesh Deore, Saiji Nageshwaran,
St Georges Hospital, Darent Valley Hospital.

BACKGROUND:

Histoplasmosis is an opportunistic fungal infection that commonly affects immunocompromised individuals. Histoplasmosis may be asymptomatic or may present with progressive systemic manifestations (pulmonary or disseminated).

CASE:

A 76 year old immunocompetent man presented to hospital with 8 weeks history of general malaise and lethargy, intermittent night sweats, a productive cough, weight loss of 2.5 stones in two months and low grade fever. He had completed two courses of antibiotics prescribed by his general practitioner, with no resolution of his symptoms. He reported no history of tuberculosis contacts. Significant history was of travel to Malaysia and a visit to bat caves two years prior to the onset of symptoms. His past medical history includes BPH, Malaria, typhoid, and hepatitis. His medications included finasteride 5mg od, Xenical 120mg tds. On admission, he was haemodynamically stable BP 139/81, temp 36.4, so2 100% RA. Blood test showed potassium 4.5 mmol/L, sodium 139 mmol/L, urea 6.2 mmol/L, Creatinine 81µmol/L, chloride 101mmol/L, bicarbonate 28 mmol/L, bilirubin 12µmol/L, alanine transaminase 18U/L, Alkaline phosphatase 89U/L, albumin 31g/L, gamma GT 97U/L, phosphate 1.31mmol/L, calcium 2.32 mmol/L, C-reactive protein 80.2mg/L, WBC 6.2, neutrophils 4.4, platelets 224, MCV 86 fl, HIV negative.

CXR was normal. CT chest, abdomen and pelvis revealed large bilateral adrenal heterogeneous masses measuring 6.1cmx4.5cmx3.7cm on the right, and 6.4cmx6.2cmx4.3cm on the left (image 1&2). Adrenal biopsy showed fungal spores on microscopy. Ultrasound scrotum showed bilateral hydrocoele and changes in the right epididymis in keeping with infective process. **Histoplasma complement fixation antibodies test** from the adrenal biopsy was negative and culture was negative but the diagnosis of adrenal histoplasmosis was most likely as the history was suggestive.

He was started on itraconazole then posaconazole for likely adrenal histoplasmosis and discharged home.

He was readmitted 2 months later with a GCS of 6/15, Temperature 38°C, and hypotensive episodes. He had normal CT and MRI brain results, negative blood cultures and unremarkable CSF studies. Echocardiogram excluded the vegetations. He was treated with intravenous empirical antibiotics and hydrocortisone. He was continued on his antifungal therapy.

Initial short synacthen test showed normal response, however he became more tired and hyperpigmented with a subsequent short synacthen test showing a suboptimal response T0=333nmol/L, T 30=378nmol/L. ACTH 98ng/L, rennin<0.2, aldosterone<75pmol/L

It was suggested at this stage that the patient was developing adrenal insufficiency due to healing with fibrosis of adrenal gland. He also developed primary hypogonadism (table 1) subsequently, thought to be due to effect of antifungals or due to histoplasmosis itself.

Posaconazole was stopped a few months later following improvement of inflammatory markers. The patient is currently on a replacement dose of hydrocortisone 15mg morning, 5mg at midday and 5mg in the evening and fludrocortisone 50microgram o.d, as well as tamsulosin 400mcg OD and xenical 120mg tds, tesogel 50mg OD. His most recent blood tests showed a CRP of 2 and testosterone 11.4nmol/L.



Image1-Axial view of bilateral adrenal masses

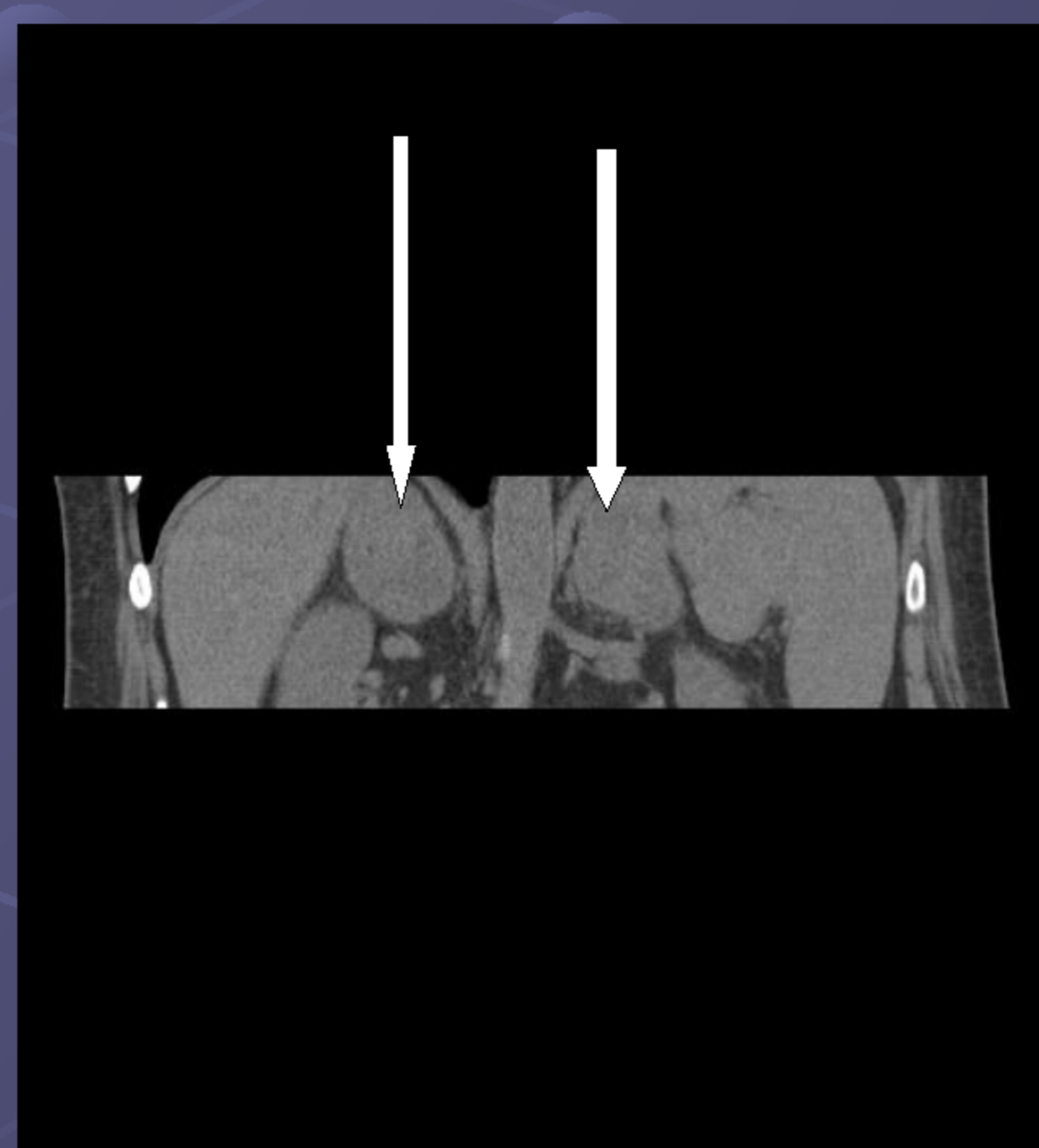


Image2-Coronal view of bilateral adrenal masses

Date	Testosterone	LH	FSH	SHBG
24/06/2008	8.6nmol/L	10	10.4	46nmol/L
05/08/2008	7.2nmol/L	10.4	12.7	47nmol/L
17/09/2008	7.3nmol/L	8	12.9	48nmol/L
04/11/2008	7.6nmol/L	9.8	12.9	44nmol/L
18/02/2009	6.8nmol/L			24nmol/L
16/06/2009	7.7nmol/L	8.0	12.9	30nmol/L

Table 1-Hormonal profile

DISCUSSION:

Histoplasmosis is caused by *Histoplasma Capsulatum*, a thermally dimorphic fungus, existing as a mould in the environment at a temperature below 35°C and as yeast (small oval buds 2-4µm) at temperatures above 35°C.

Infection with *Histoplasma Capsulatum* usually occurs after inhalation of the micronidia spores. There is no person to person transmission except through an infected organ in transplant patients. The primary reservoir is **nitrogen rich soil. Both bird and bat droppings** increase the levels of nitrogen in the soil and can therefore increase the likelihood of contamination with *Histoplasma Capsulatum*. Infection with *Histoplasma Capsulatum* can present as asymptomatic, pulmonary (acute or chronic) or disseminated (acute or chronic) infection.

Incubation period is 1-3 weeks after initial infection. Symptoms include fevers, chills, headaches, myalgia, arthralgia, loss of appetite, weight loss, fatigue, chest pain and non-productive cough.

Adrenal involvement may be unilateral or bilateral and may lead to adrenal insufficiency, presenting with bilateral adrenal masses. The differential for this presentation includes metastatic disease, adrenal haemorrhage, bilateral adrenal pheochromocytoma, sarcoidosis and infection such as tuberculosis and histoplasmosis. In our patient adrenal failure was due to healing with fibrosis following antifungal therapy as well as histoplasmosis itself. Hypogonadism was probably caused by antifungal therapy. Both Itraconazole and Posaconazole are potent inhibitors of CYP3A4, a member of cytochrome P450 super-family of enzymes involved in the synthesis of cholesterol, lipids and steroids including sex steroids.

CONCLUSION:

Adrenal histoplasmosis is rare, especially in immunocompetent individuals but should be considered as a differential diagnosis in any patient presenting with bilateral adrenal masses, constitutional symptoms and suggestive history.

Adrenal failure is common in disseminated form of histoplasmosis, and hypogonadism secondary to antifungal therapy is not uncommon, as demonstrated in this case report.

References:

- Assi, M. A., M. S. Sandid, et al. (2007). "Systemic histoplasmosis: a 15-year retrospective institutional review of 111 patients." *Medicine (Baltimore)* 86(3): 162-9.
- Nagappan, V. and S. Deresinski (2007). "Reviews of anti-infective agents: posaconazole: a broad-spectrum triazole antifungal agent." *Clin Infect Dis* 45(12): 1610-7.
- Sathapatayavongs, B., B. E. Batteiger, et al. (1983). "Clinical and laboratory features of disseminated histoplasmosis during two large urban outbreaks." *Medicine (Baltimore)* 62(5): 263-70
- Goodwin, R. A., Jr., J. L. Shapiro, et al. (1980). "Disseminated histoplasmosis: clinical and pathologic correlations." *Medicine (Baltimore)* 59(1): 1-33
- Murray, P. R. and E. J. Baron (2007). *Manual of clinical microbiology*. Washington, D.C., ASM Press
- Kauffman, C. A. (2007). "Histoplasmosis: a clinical and laboratory update." *Clin Microbiol Rev* 20(1): 115-32

