Adrenal histoplasmosis presenting as life-threatening adrenal insufficiency

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DESCRIPTION

In endemic areas, histoplasmosis should always be considered as a differential diagnosis in a patient presenting with fever of unknown origin, chronic fatigue, adrenomegaly and hyperpigmentation. Early diagnosis and prompt institution of antifungal therapy is imperative to prevent mortality as significant majority of patients with adrenal histoplasmosis develop life-threatening adrenal insufficiency.1

A 57-year-old male security guard by occupation presented with 6-month history of fatigue, abdominal pain, dizziness on standing, low appetite and significant weight loss. His history was significant for type 2 diabetes mellitus for 8 years which appeared controlled with glycosylated haemoglobin of 7.1%. Examination revealed body mass index of 18.2 kg/m2. His supine blood pressure (BP) was 100/60 mm Hg and his BP on standing erect was 70/50 mm Hg, with development of presyncope. He had hyperpigmentation of tongue and buccal mucosa for approximately 4 months’ duration (figure 1A). There was no palpable lymphadenopathy. Baseline laboratory parameters revealed serum sodium of 120 mmol/L (135–145 mmol/L), potassium of 6 mmol/L (3.5–5.5 mmol/L), random cortisol level of 93 nmol/L (133–537 nmol/L) with an adrenocorticotropic hormone (ACTH) of 110 pg/mL (7.2–63 pg/mL), consistent with a diagnosis of primary adrenal insufficiency. ACTH stimulation test was not performed as hydrocortisone treatment had already been started. Contrast-enhanced CT of chest and abdomen showed bilateral symmetrical hypodense adrenal masses with smooth borders and preserved contour with no evidence of lymphadenopathy, hepatosplenomegaly or chest parenchymal abnormality (figure 1B). Our diagnostic considerations included infections such as tuberculosis and histoplasmosis, metastasis from unknown primary, amyloidosis, lymphoma and neoplasia such as bilateral adrenocortical carcinoma. CT-guided biopsy from right adrenal mass revealed areas of necrosis with numerous fungal spores of Histoplasma capsulatum Light and electron microscopy showed absence of microorganisms. Histopathological examination with periodic acid–Schiff (PAS) stain highlights the fungal spores (figure 2A–D). Fungal culture confirmed growth of Histoplasma capsulatum.

Apart from diabetes mellitus, the patient had no other risk factor for histoplasmosis. Other immunodeficiency workup including HIV ELISA, dihydrorhodamine assay, Mantoux test, tissue GeneXpert for tuberculosis were negative. His CD4 count was 625 cells/mm3, thus ruling out underlying immunodeficiency. A diagnosis of bilateral adrenal histoplasmosis causing primary adrenal insufficiency was made and the patient was initiated on physiological doses of glucocorticoid and mineralocorticoid. Antifungal therapy with oral itraconazole 200 mg twice per day was started and is planned to continue for a duration of 1 year.

Histoplasmosis usually leads to self-limiting pulmonary infection that can rarely cause disseminated disease in immunosuppressed individuals. Although it can involve any organ system in disseminated disease, adrenal involvement is common and primary adrenal histoplasmosis has also been documented as in our case. The glucocorticoid-rich adrenal cells and the relative scarcity of reticuloendothelial cells contribute to the tropism...
of Histoplasma for the adrenal gland. Common risk factors include immunosuppressed state such as diabetes, primary immunodeficiency, HIV infection, solid organ transplant recipients, extreme age and patients receiving immunosuppressive drugs. The differential diagnosis of bilateral adrenomegaly with Primary adrenal insufficiency (PAI) includes lymphomas, tuberculosis, fungal infections and metastatic cancer. The gold standard for diagnosis remains demonstration of fungal spores with background inflammatory response and isolation of fungus from tissue sample by fungal culture. In endemic region, histoplasmosis should always be contemplated as a possibility in a patient presenting with hypoattenuating bilateral adrenomegaly. For mild to moderate disease, itraconazole 200 mg three times per day for 3 days followed by 200 mg two times per day for 1 year is recommended. Remission rates of 80%–100% have been reported with itraconazole therapy.

Contributors MG, JS: Manuscript writing, proofreading. SM, KG: Histopathological diagnosis and image acquisition.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES

Learning points
► Clinician should have high index of suspicion for adrenal histoplasmosis in a patient with primary adrenal insufficiency with adrenomegaly.
► Prompt institution of glucocorticoid and mineralocorticoid replacement therapy should be done once primary adrenal insufficiency is suspected.
► Adrenal histoplasmosis can present with life-threatening adrenal crisis.

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