



Persistent dizziness and recurrent syncope due to HIV-associated Addison's disease: Case report from a resource-limited setting

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Addison's disease or primary adrenal insufficiency is a well-recognised fatal endocrine condition among HIV-infected patients. HIV infection is associated with adrenal gland destruction and profound disruption of the hypothalamic-pituitary-adrenal axis. We describe a case of HIV-associated Addison's disease in a 58-year-old newly diagnosed HIV-seropositive male patient, highlighting its occurrence in this era of the HIV/AIDS pandemic.

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Addison's disease, or primary adrenal insufficiency, is a chronic disorder of the adrenal cortex resulting in inadequate production of glucocorticoids and mineralocorticoids. It is an often-missed and potentially lethal condition associated with increased mortality if untreated.¹ Addison's disease typically presents with nonspecific vague symptoms of an insidious onset, such as fatigue, malaise, abdominal pain, weight loss, nausea and vomiting. Physical signs include orthostatic hypotension or shock, and hyperpigmentation, while biochemical indicators include hyponatraemia, hyperkalaemia and hypoglycaemia.^{1,2} Causes of Addison's disease include: autoimmune adrenalitis; chronic infections such as tuberculosis (TB), cytomegalovirus (CMV) infection; adrenal haemorrhage or infiltration; and genetic and idiopathic causes.¹

Addison's disease has also been documented among HIV-infected patients.³ The potential pathophysiological mechanisms of adrenal dysfunction include direct destruction of the adrenal glands caused by HIV or opportunistic infections such as CMV or TB, neoplastic infiltration, and the effects of pro-inflammatory cytokines. The disease may also be drug-induced, e.g. by ketoconazole and rifampicin.^{3,4}

Case description

A 58-year-old newly diagnosed HIV-seropositive antiretroviral therapy (ART)-naive male patient presented with a 3-month history of progressive darkening of the palms of his hands, persistent postural dizziness, fatigability, profound general body weakness, syncope and recurrent episodes of fasting hypoglycaemia. He did not report a history suggestive of TB, fever, headaches, convulsions or chronic glucocorticoid use.

Physical examination revealed mild pallor of the mucous membranes, generalised hyperpigmentation involving the face, oral mucosa and the palmar creases, and absence of peripheral lymphadenopathy. Small volume tachycardia (110 beats/min) with postural hypotension (supine blood pressure 90/50 mmHg, sitting blood pressure 70/40 mmHg) was noted on cardiovascular examination. There were no signs of CMV retinitis or papilloedema on fundoscopy. An extensive clinical evaluation did not reveal any underlying neoplasm.

Laboratory tests revealed a mild normocytic normochromic anaemia (10.6 g/dl; range 12.0 - 16.0), a CD4 count of 17 cells/mm³, random blood sugar of 2.6 mmol/l (3.5 - 7.0), hyponatraemia (128 mmol/l; 135 - 150), mild hyperkalaemia (5.8 mmol/l; 3.5 - 5.5), raised creatinine (137 µmol/l; 0 - 106) and a low 8 am cortisol level (151.2 nmol/l). Results were normal for serum cryptococcal antigen (CRAG), liver function, serum albumin and corrected calcium level tests.

An electrocardiogram and echocardiography, performed to rule out any structural heart lesion, were normal. Results of a chest X-ray and abdominal ultrasound were also normal. Due to financial constraints, an 8 am serum adrenocorticotrophic hormone (ACTH) test, specific adrenal auto-antibody test and computed tomography (CT) scan of the adrenal gland were not performed.

A diagnosis of probable HIV-associated Addison's disease and severe immunosuppression was made. The patient received a slow bolus of intravenous 50% dextrose, intravenous fluids and hydrocortisone. He was later maintained on oral prednisolone (5 mg in the morning and 2.5 mg in the evening) and ART was initiated (emtrabine, tenofovir and efavirenz). Oral fludrocortisone and hydrocortisone were not used as they are not readily available in the country. The patient was discharged following remarkable improvement, and was fully counselled about his condition. No opportunistic infection has been discovered at subsequent follow-up visits.

Discussion

This case demonstrates that HIV-associated Addison's disease occurs especially with severe immunosuppression. An 8 am cortisol level <165 nmol/l (6 µg/dl) is highly suggestive of Addison's disease,¹ as demonstrated in our patient. However, most patients require further assessment with a synthetic ACTH test (250 µg Synacthen) for confirmation of the disease. Notably, this test is not readily available in most resource-limited settings. An increase in the serum cortisol level 1 hour after the Synacthen injection to >500 nmol/l (18 µg/dl) confirms the absence of the disease.^{1,2}

HIV has a direct independent destructive effect on the adrenal glands and disrupts the hypothalamic-pituitary-adrenal axis, producing subclinical to overt features of Addison's disease. Co-existing opportunistic infections, such as TB and CMV, among HIV-infected patients increase the risk of developing Addison's disease.^{3,4} Biochemical evidence of primary adrenal insufficiency is

more common in the late stages of HIV infection and with severe immunosuppression, as in this case.^{5,6}

European studies of hospitalised patients with advanced HIV infection reported a 17 - 22% prevalence of Addison's disease.^{6,7} However, a varying prevalence has been documented in Africa. Meya *et al.*⁸ reported a prevalence of 19% among 113 critically ill HIV-infected Ugandan patients. The majority of these patients had TB, Kaposi sarcoma and cryptococcal meningitis as the main underlying co-morbidities.⁸ None of the patients had advanced HIV infection as the sole clinical diagnosis. In contrast, studies by Soule⁹ and Ross *et al.*¹⁰ among South African patients reported no HIV/AIDS-related Addison's disease.

The management of Addison's disease is focused mainly on the correction of hypovolaemia and electrolyte imbalances with adequate amounts of intravenous fluids, the correction of hypoglycaemia, long-term glucocorticoid and mineralocorticoid replacement and the management of underlying causes.^{1,2} A CT scan of the adrenal glands is significant in cases secondary to infections such as TB, as well as in post-sepsis adrenal haemorrhage and neoplastic infiltration. In particular, TB of the adrenal glands revealed by CT imaging presents initially with bilateral adrenal enlargement; calcifications develop later in the disease.¹ CT imaging is costly, however, and not readily available in most resource-limited settings. In cases of HIV-associated Addison's disease, extensive screening for occult opportunistic infections prior to ART initiation and timely initiation of ART are highly recommended.

Conclusion

As demonstrated by this case, clinicians should have a high index of suspicion of Addison's disease in HIV-infected patients presenting with typical electrolyte abnormalities or unexplained hypotension. The disease should be managed instantly and appropriately to reduce the risk of mortality.

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