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A Rare Mechanism of Hyponatremia in HIV Disease

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Data Collection B
Statistical Analysis C
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Conflict of interest: None declared

Patient: Male, 25
Final Diagnosis: Corticosteroid resistance
Symptoms: Weakness
Medication: —
Clinical Procedure: Diagnosis
Specialty: Nephrology

Objective: Unusual clinical course





Background: Hyponatremia is the most common disorder of body fluid and electrolyte balance in clinical practice. It is associated with increased morbidity, mortality, and length of hospital stay. Little is known about the relationship between hyponatremia and HIV disease. It is thought that hyponatremia in HIV is associated with a syndrome of inappropriate ADH secretion (SIADH), volume depletion, and adrenal insufficiency. Another common association is with *Pneumocystis jirovecii* (PCP). In early 1990s, there were several reports linking hyponatremia and HIV disease. It was found that these patients with acquired immune deficiency syndrome (AIDS) had abnormal adrenal cortical function. Additionally, these patients showed an abnormally elevated baseline cortisol level and a blunted response to cosyntropin.

Case Report: Here, we present the case of an HIV patient presenting with hyponatremia and a physical examination suggestive of hypovolemia. Laboratory tests revealed urinary loss of sodium in the setting of normal serum cortisol level. The patient responded well to the administration of a mineralocorticoid hormone.

Conclusions: Glucocorticoid resistance is an unusual cause of hyponatremia, and needs to be identified and treated accordingly.

MeSH Keywords: AIDS-Associated Nephropathy • Hyponatremia • Receptors, Glucocorticoid

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/894299>

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Background

Hyponatremia is defined as a serum concentration below 135 meq/L [1]; it usually reflects an excess of total body water (TBW) relative to total body sodium. This clinical entity is very common and is extremely significant because it is found in 15–20% of emergency hospital admissions. It is associated with increased morbidity, mortality, and length of hospital stay [2]. There are several causes of hyponatremia, which could be due to true hyponatremia or pseudo hyponatremia. True hyponatremia occurs when the mechanisms for normal urinary dilution are affected, such as diminished glomerular filtration rate, increase in proximal tubular fluid and sodium reabsorption, defect in sodium chloride transport, and continued stimulation of vasopressin secretion by non-osmotic mechanisms [3]. The symptoms of true hyponatremia are primarily neurological and range from headache and lethargy to seizures and coma when serum sodium is less than 110–115 meq/L; this happens because as plasma osmolality falls, an osmolal gradient is created in the blood-brain barrier, resulting in intracellular water movement [4]. Treatment depends on the severity of hyponatremia and co-existing symptoms.

Adrenal insufficiency, due to diminished secretion of cortisol and aldosterone, is a less common cause of hyponatremia. Lack of these hormones contributes to increased release of antidiuretic hormone (ADH), which results in water retention and decrease in plasma sodium concentration [5]. Glucocorticoid resistance in HIV patients has been rarely reported in the literature; hence, we report this illustrative case, its management, and the pathophysiology.

Case Report

A young man presented to the emergency department with shortness of breath on exertion for 1 month, associated with mild chest pain, relieved by resting and accompanied by a cough productive of clear sputum. He also reported a 10-lb weight loss in the last few months prior to admission. Initial physical examination showed blood pressure of 128/73 mmHg, pulse 104 beats per minute, respirations 20 per minute, temperature 37.2°C, and BMI 23.7 kg/m². He was alert and oriented and was in mild respiratory distress. He had no cervical lymphadenopathy and no evidence of cyanosis or clubbing. Auscultation revealed tachycardia and decreased air entry at bases. The abdomen was benign as were the lower extremities. Given the tachycardia, hypoxia, and requirement of supplemental oxygen, a CT scan of the chest was obtained, which revealed no pulmonary embolism, but showed bibasilar ground glass opacities. With his history and clinical findings, there was high suspicion for possible infectious disease. He was tested for HIV 1 antibody by Western blot, which yielded a positive result.

In light of his pulmonary findings, *Pneumocystis pneumonia* was suspected, for which on day 1 of hospitalization he was started on Prednisone 40 mg p.o. twice daily for 5 days, tapered to 40 mg daily for 5 days, and finally 20 mg daily for 11 days. On day 3 Trimethoprim/ sulfamethoxazole was initiated. His kidney function remained at baseline (0.5–0.8 mg/dL) throughout.

His serum sodium on admission was 129 mmol/L; its improvement to 135 mmol/L coincided with administration of steroids and NSS (Figure 1). The measured serum osmolality was 258 mOsm/L. TSH was 0.588 uU/ml and cortisol was 21.4 ug/dL,

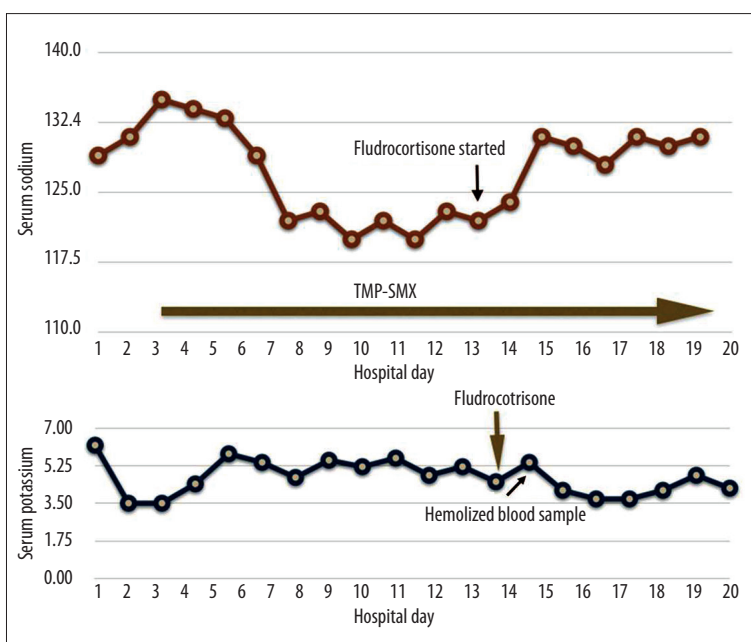


Figure 1. Changes in serum sodium and potassium. After prednisone taper was decreased on day 6, the patient's serum sodium dropped as well, suggesting that urine sodium reabsorption was dependent on steroids. He was started on Fludrocortisone due to its mineralocorticoid activity rather than Prednisone. From day 1 to day 5, Prednisone was contributing to correct the hyponatremia.

both within normal limits. On day 6, prednisone taper was implemented and his serum sodium significantly dropped (from 133 mmol/L to 120 mmol/L) and serum potassium remained unchanged. Salt tablets 2 g BID and fluid restriction were initiated on day 8, but serum sodium remained unchanged at 120 to 124 mmol/L. Blood pressure remained at the lower end of normal throughout the hospitalization.

At this point, given the fact that we ruled out all other possible causes of hyponatremia, the possibility of glucocorticoid resistance was considered. Fludrocortisone 0.1 mg PO twice daily was started and on the following day (Day 14) his serum sodium improved to 131 mmol/L and subsequently remained within normal range. The fludrocortisone dose was adjusted according to plasma renin activity, with a goal of 0.2–3.3 ng/ml/h. Of note, we have previously reported a case of hyponatremia due to steroid resistance in an HIV-positive patient [6] who was treated successfully with fludrocortisone.

Discussion

Hyponatremia in HIV disease and AIDS occur in 20–80% of hospitalized patients [7–9]. A syndrome of inappropriate ADH secretion, volume depletion, and adrenal insufficiency, as well as some drugs, are the most common causes of hyponatremia in HIV-infected patients. Glucocorticoid resistance refers to the inability of glucocorticoids to carry out their function in target tissues; it is divided into primary or familial and acquired. Glucocorticoid resistance in HIV patients is an entity that has not been well described.

HIV-infected patients who have glucocorticoid resistance can present with symptoms such as weakness, weight loss, hypertension, chronic fatigue, and intense mucocutaneous melanosis, resembling Addison's disease. In AIDS patients, this entity is asymptomatic [9]. The syndrome of glucocorticoid resistance was first described in 1990 when an AIDS patient in Italy was evaluated for adrenal insufficiency, but his serum and urinary cortisol levels were within normal limits. In 1994 Norbiato et al. reported a case series of 100 HIV patients with this syndrome [9]. A potential mechanism for glucocorticoid resistance has been postulated in HIV-positive patients. In these patients, glucocorticoid

affinity to its ligand is reduced and the glucocorticoid receptor number is increased, suggesting a partial glucocorticoid resistance state. This phenomenon might be due to altered cytokine action. A similar glucocorticoid resistance state is present in glucocorticoid-resistant asthma type 2 patients. These patients have a specific cytokine pattern consisting mainly of elevated Interleukin-2 and Interleukin-4 and also exhibit reduced glucocorticoid affinity to its ligand, closely resembling the glucocorticoid resistance state found in HIV-positive patients [10].

Menon et al. reported an AIDS patient with fever, diarrhea, weakness, dizziness, weight loss, and vague abdominal pain. Although the patient received volume expansion, he continued to be polyuric, with high urine sodium (resembling cerebral salt wasting) and elevated cortisol level. ACTH and renin activity were normal. He received supraphysiologic doses of glucocorticoids and mineralocorticoids, which resolved his hypotension and hyponatremia.

Despite the evidence of HIV infection of renal epithelial cells in susceptible individuals, which could cause collapsing glomerulonephritis and tubulointerstitial disease, these findings do not explain the cause of hyponatremia in HIV disease [11]. It has been reported that in patients with HIV, but not with AIDS, water handling is affected. This was proven by Musso et al. [12] in a small sample of patients, in which he excluded common causes of hyponatremia and found that these patients are unable to concentrate or dilute urine in the setting of water restriction and that this was independent of anti-retroviral therapy. Hence, these patients are at risk of dehydration if they undergo water deprivation.

Conclusions

This case illustrates the rare mechanism of hyponatremia and HIV caused by glucocorticoid resistance and the need to treat with high doses of steroids in order to correct it. Concomitant anti-retroviral therapy is also important, although sometimes kidney impairment is independent of viremia. Further studies are needed on the pathophysiology of glucocorticoid resistance in HIV patients and treatment in order to prevent fatal metabolic consequences of the disease.

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