Fatal persistent hyponatremia in an AIDS patient

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Abstract

Electrolyte disorders are frequently described in AIDS patients and can contribute to overall mortality in advanced disease. Hyponatremia is the most prevalent electrolyte abnormality occurring in 36% to 56% of patients hospitalized with AIDS. Many concomitant causes, including opportunistic infections, endocrine disorders and iatrogenic factors, need to be considered when investigating the etiopathogenesis of these disturbances, thus hindering early correct diagnosis and thereby delaying appropriate treatment for these patients.

Case Report

The patient, from the Ivory Coast, had resided in Italy for five months when neurological symptoms were noted, including left arm tonic-clonic seizures and syncope. His medical history was unremarkable, except for previous episodes of malaria. He was admitted to the Neurological Ward, where he underwent a cranial CT scan which revealed a nodular hypodense area with perilesional edema in the parietal right lobe with ring-like enhancement after contrast injection (3 cm² size) and a subsequent mass effect on the ventricular system, shifting from right to left. Mannitol, diazepam and sodium valproate were initiated. As the anti-HIV test was positive, he was transferred to the Infectious Disease Unit for a suspected opportunistic infection.

On admission to our Unit, the patient was confused, uncooperative and drowsy, without fever. Abnormal laboratory findings included ESR=58, Hb=9.5 g/dl, CD4+=6 (1%) cells/mmc and plasma HIV-RNA 2.230.600 copies/ml. Blood cultures were negative for aerobe/anaerobe bacteria; CMV, EBV, TOXO, HSV serology was IgG positive/IgM negative; CMV-DNA was negative. Intravenous anti-toxoplasmosis therapy with cotrimoxazole (5 mg/kg TMP and 25 mg/kg SMX) was initiated with rapid improvement of his neurological condition and consciousness after a few days.

Two days later, the patient presented hyperkostassies (plasma potassium concentration 5.8 mmol/L) and hyponatremia (plasma sodium concentration 127 mmol/L) with massive 24 hour natriuresis (470 mEq/L) and plasma osmolality of 245 mOsm/L. An endocrinological consultation was requested and the hypothesis of a cerebral salt-wasting syndrome was formulated. The patient was treated with an oral cation-exchange resin (sodium polystyrene sulfonate), glucose solution with insulin and NaCl, with a resulting improvement in the sodium level (131 mmol/L), even though it did not reach normality. In the following days the patient’s clinical condition improved and he was able to swallow and feed himself. Therefore, intravenous cotrimoxazole was replaced by oral sulfadiazine and pyrimethamine (pyrimethamine at 200 mg PO QD and then 75 mg daily plus sulfadiazine 1,500 mg QD). At the same time, a HAART regimen based on lopinavir/ritonavir, emtricitabina/tenofovir disoproxil was initiated. Due to the low level of CD4+ cells (1%), enfuvirtide was also included in the new regimen. However, after one week, the patient presented fever (38°C). An intravenous catheter infection was suspected and he was empirically treated with piperacillin (12 g/d)/tazobactam (1.5 g/d) and teicoplanin (800 mg/d for two days, thereafter 400 mg/d) with resolution of the fever after four days; blood cultures later resulted positive for S. aureus. Two days later there was a sudden deterioration of his clinical condition: fever and drowsiness recurrent. As a positive plasma CMV DNA was obtained (28,650 copies/ml) using a real-time polymerase chain reaction (Artus ® CMV RG PCR, Quigen...
Diagnostic, Hamburg, Germany), with a lower detection limit of 50 UI/mL (1 UI=1 cp/mL), therapy with foscarnet (90 mg/kg IV q12h) and intravenous anti-CMV immune globulin (50 mL - 2500 U - IV every week) were promptly added. Magnetic resonance imaging (MRI) of the brain showed a slight decrease of edema and gadolinium uptake by the right parietal lesion when compared to the CT scan. Throughout hospital admission, hyposodiemia persisted at levels ranging from 118 mmol/L to 131 mmol/L, not responding to therapy with saline solution. The patient died on the 57th day after admission.

Discussion

Hyponatremia, defined as serum sodium level less than 134 mmol/L, is a common disorder in patients with acute neurological symptoms, and contributes to worsening intracranial edema and hypertension by increasing the intracellular liquid volume. Other causes of electrolytic disorder, however, should be considered in AIDS patients. Firstly, the differential diagnosis of hyponatremia is based on the determination of plasma osmolarity. If its value is above 270 mOsm/L, a pseudo-hyponatremia might be suspected, which could be caused by many factors including hyperlipemia, hyperglycaemia and hyperproteinaemia. If, on the contrary, plasma osmolarity is less than 270 mOsm/L, as in the case of our patient, a dilutional hyponatremia could be hypothesized (caused by cirrhosis, heart failure, generalized edema, or polydipsia) or, alternatively, it could be determined by gastrointestinal vomiting and diarrhoea, acute renal failure, SIADH or use of diuretics (6).

Electrolyte imbalance abnormalities, however, may also be provoked by other less common causes; such as the cerebral salt-wasting syndrome (CSWS), CMV-induced adrenal insufficiency and renal drug toxicity. CSWS is defined by the development of excessive natriuresis in patients with intracranial lesions. It leads to hyponatremia and extracellular volume depletion. The mechanisms by which intracranial disease leads to renal salt-wasting remain unclear, though some hypotheses involve the release of natriuretic factors: atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), C-type natriuretic peptide and ouabain-like peptide, along with decreased sympathetic kidney input. These factors increase urinary sodium excretion and reduce effective arterial blood volume, thus stimulating the baroreceptors of ADH release.

Regarding the drug-induced electrolyte imbalance, Bevilacqua et al. (7) reported that high doses of trimethoprim act as an amiloride-like drug, inducing hyponatremia and hyperkalemia. Trimethoprim-sulfamethoxazole was believed to inhibit distal tubule sodium reabsorption and potassium secretion: our patient received TMP-SMX therapy for 14 days and this could have contributed to the persistent hyponatremia.

Lastly, adrenal infection by CMV is a common autopsy finding in patients with AIDS (8,9). Another case of CMV-induced adrenal insufficiency in an HIV patient with pneumocystis pneumonia treated with steroids and trimethoprim-sulfamethoxazole has been reported (10). In that patient the severe adrenal insufficiency was probably caused by the delay in CMV therapy and the treatment of pneumocystis pneumonia with steroids. In the present case, the first test for CMV-DNA was negative at time of hyponatremia occurrence, so the anti-CMV therapy was initiated as soon as the first CMV-DNA positive result was available, but the high level of CMV indicates a disseminated CMV infection which could also have colonized the adrenal glands. Therefore, CMV-related adrenal failure cannot be excluded.

In conclusion, it was not possible to establish the final cause of death. CSWS, disseminated CMV infection and CTX-related toxicity probably all contributed to the persistent electrolyte imbalance which led to cardiorespiratory arrest.

A complex differential diagnosis and management of hyponatremia is required in AIDS patients, for whom a multidisciplinary approach is necessary. The epidemiology of HIV-1 has changed in recent years in Italy, shifting from a prevalent HIV transmission in selected risk groups (intravenous drug users, homosexuals, hematological patients) who were targeted by and benefited from specific prevention strategies, to a larger heterosexual population with a low self-perceived HIV risk and subject to late HIV testing when immunological impairment is already evident (11). For this reason, even in the HAART era, the management of opportunistic infections in AIDS can be very challenging. Moreover, it is important to consider that the incidence of new HIV diagnoses in Italy is estimated to be eight times higher in foreign subjects than in the native population (12). Even if it is difficult to determine whether this increased risk depends on the higher prevalence of infection in the country of origin or on an increased risk of HIV acquisition in Italy, most likely due to social, cultural and economic reasons (13), immigrants should not only be offered easy access to HIV screening and treatment, but should also be the target of targetted measures for preventing HIV acquisition.

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REFERENCES