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Letter to the Editor

An unusual case of severe acute hyponatremia in patient with COVID-19 infection☆

Inusual caso de hiponatremia aguda grave en paciente con infección por COVID-19

Dear Director,

Hyponatremia is the most prevalent hydroelectrolytic disorder in clinical practice, and is linked to higher rates of morbidity and mortality. Coexistence of hyponatremia and COVID-19 infection (an emerging respiratory disease caused by the novel SARS-CoV-2 coronavirus) has been reported in recent studies, but without knowledge of the possible underlying pathophysiological mechanisms.[1,2] We present the case of a patient with severe hyponatremia and COVID-19 infection.

A 59-year-old man had a history of hypertension being managed with a combination of angiotensin-converting enzyme inhibitors and hydrochlorothiazide, which had been suspended four days before admission. He sought care due to signs and symptoms for 10 days consisting of a dry cough, slight difficulty breathing, and fever. Three days earlier, he also developed abdominal pain, nausea, and vomiting, and 24 h earlier he also experienced headache and drowsiness. During examination he showed confusion, bradypsychia, and clinical signs of mild dehydration of the skin and mucosae. Laboratory testing revealed severe hyponatremia (102 mEq/L) in the absence of azotemia as well as C-reactive protein 5.05 mg/dL (0.02–0.05 mg/dL), ferritin 252 ng/mL (30–400 ng/mL), D-dimer 174 ng/mL (0–500 ng/mL), and lymphocytes 1.35 × 10^3/μL. All other laboratory values are shown in Table 1. A chest X-ray showed a bilateral alveolar-interstitial pattern. PCR for SARS-CoV-2 yielded a positive result.

Treatment was started with hypertonic saline 3%, correcting the patient's natremia to 125 mEq/L, as well as azithromycin with hydroxychloroquine for the patient's COVID-19 infection. Initially, syndrome of inappropriate antidiuretic hormone secretion (SIADH) was suspected. Despite treatment with restriction of fluid, salt, and urea, on the fifth day, the patient had not yet achieved natremia values >125 mEq/L. The patient was found to have low levels of adrenocorticotropic hormone (ACTH) and cortisol (Table 1). Magnetic resonance imaging (MRI) showed a pituitary macroadenoma, with signs of intralesional bleeding (Fig. 1). On the sixth day, he was prescribed intravenous Actocortina [hydrocortisone] at an initial dose of 100 mg every/12 h and subsequently a maintenance dose of 100 mg/24 h. The three following days, his natremia was 139 mEq/L. Campimetry revealed the presence of bitemporal hemianopia. The final diagnosis was severe hyponatremia caused by adrenal insufficiency (AI) secondary to hypopituitarism (HPT) due to a pituitary macroadenoma with radiological signs of subacute pituitary apoplexy in a patient with COVID-19 infection. With this diagnosis, the patient underwent transsphenoidal surgical decompression of the lesion.

Our patient showed signs and symptoms of severe hyponatremia difficult to account for with only his vomiting and/or diuretic treatment, with a striking discrepancy between his clinical and laboratory findings, i.e. dehydration but no azotemia. Hyponatremia is a known form of presentation of HPT, having been reported in various clinical situations, but uncommonly as an initial sign of a pituitary tumor in the context of a respiratory infection due to COVID-19[3], which probably exacerbated its presentation. Lippi et al.[4], following an electronic search on MEDLINE (PubMed), Scopus, and Web of Science, using the keywords sodium, potassium, chlorine, and calcium in patients with COVID-19 disease, identified five studies with a total of 1,415 patients. Sodium was significantly lower in patients with severe disease compared to patients with mild disease due to COVID-19 (weighted mean difference: −0.91 mmol/L, 95% CI: −1.33–0.5 mmol/L). However, it is not yet known whether there is a greater risk of hyponatremia or other electrolyte abnormalities in patients with COVID-19, nor is the mechanism that would cause it understood.

Our patient met nearly all the criteria for SIADH, except for the presence of hormonal abnormalities in thyroid, adrenal, and pituitary function.[5] In the differential diagnosis, we ruled out cerebral salt-wasting syndrome (CSWS) given the absence of polyuria and the correction of natremia following vol-

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Table 1 – Course of laboratory values during admission and pituitary hormone testing.

	On admission	On the fifth day	On the eighth day	Normal values
Sodium (mEq/L)	102	125	139	135–145
Potassium (mEq/L)	4.3	4.1	4.1	3.5–4.5
Chlorine (mEq/L)	71	91	99	98–110
Bicarbonate (mEq/L)	20.6	22.7	28	22–28
Creatinine (mg/dL)	0.6	0.8	0.9	0.6–1.2
Calculated serum osmolality (mOsm/kg)	215	267	290	270–298
Urea (mg/dL)	21	18	31	17–60
Uric acid (mg/dL)	2.4	2.8	2.9	3.4–7
Diuresis (mL/h)	100 m L/h	80 mL/h	140 mL/h	–
Calculated urine osmolality (mOsm/kg)	990	660	330	80–1,200
Urine sodium (mEq/L)	157	82	52	20–200
Urine chlorine (mEq/L)	123	74	63	–
Urine potassium (mEq/L)	19	60	65	25–125
Cortisol (μg/dL)	N/A	3.1	N/A	4.8–19.5
Adrenocorticotropic hormone (ACTH) (pg/mL)	N/A	4.6	N/A	7–60
Prolactin (ng/mL)	N/A	8.7	N/A	4–15.2
Follicle stimulating hormone (FSH) (mU/mL)	N/A	2.5	N/A	1.5–12.4
Luteinizing hormone (LH) (mU/mL)	N/A	0.2	N/A	1.7–8.6
Growth hormone (ng/mL)	N/A	0.06	N/A	0.05–3
Somatomedin-C (IGF-1) (ng/mL)	N/A	36.6	N/A	36–200
Testosterone (ng/mL)	N/A	0.03	N/A	1.93–7.4
Thyroid-stimulating hormone (TSH) (μU/mL)	N/A	1.6	N/A	0.35–4
Thyroxine (T4) (ng/dL)	N/A	0.75–1.8	N/A	0.75–1.8

N/A: not applicable.

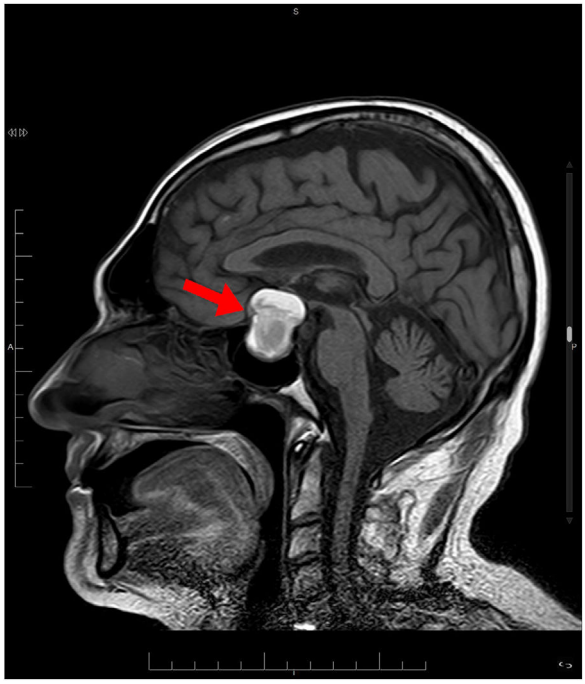

Fig. 1 – Sagittal MRI (T1). Pituitary macroadenoma with signs of subacute intralesional bleeding and pituitary apoplexy (red arrow).

ume and sodium replacement, which are fundamental factors in CSWS. By contrast, secondary AI is caused by insufficient hypothalamic-pituitary stimulation, with deficiencies in ACTH and glucocorticoids, but proper mineralocorticoid function and an intact renin–angiotensin–aldosterone axis.[6] This explains why our patient did not show classic AI symptoms, as mineralocorticoid deficiency is only present in primary AI.[7] Our patient's severe hyponatremia presented after he developed gastrointestinal signs and symptoms and respiratory infection. We do not know whether stress-induced glucocorticoid decompensation was triggered by this infectious condition.

Endogenous cortisol exerts a tonic inhibitory effect on ADH secretion. Glucocorticoid deficiency features ADH release that cannot be suppressed despite existing hyposmolality.[8] Glucocorticoids cause a negative feedback loop in both corticotropin release and ADH release.[9] This corrects the hydroelectrolytic abnormality (which would not occur in CSWS) and normalizes ADH levels and renal aquaporin-2 mRNA expression.[10]

In conclusion, in patients diagnosed with severe hyponatremia, unusual causes should be considered among the possible diagnoses. In our case, we believe that COVID-19 infection may have played a role in the severity of the patient's hyponatremia.

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Letter to the Editor

Crateriform plaques in a patient with end-stage renal disease. The case of an acquired reactive perforating collagenosis☆

Placas crateriformes en un paciente con enfermedad renal crónica. Un caso de colagenosis perforante reactiva adquirida

Dear Editor,

The skin conditions which can occur in chronic kidney disease patients are: xerosis, pruritus, calciphylaxis, pseudoporphyria, uraemic frost and acquired perforating skin disorders; the latter are characterised by presenting transepidermal elimination of material from the dermis, and consist of Kyrle disease, reactive perforating collagenosis and elastosis perforans serpiginosa.[1]

We present the case of a 78-year-old male with a history of type 2 diabetes mellitus, systemic hypertension, long-term hypothyroidism and chronic kidney disease on replacement therapy with peritoneal dialysis for the past five years, with adequate control. The patient was hospitalised due to healthcare-associated pneumonia. We were consulted due to a disseminated, bilateral and symmetrical dermatosis which affected the lateral side of both arms and the anterior side of the knees, made up of multiple plaques measuring 0.5–1 cm in diameter which were circular, erythematous, had a crateriform appearance with a haematic scab on their surface, were itchy and had first appeared six weeks previously (Fig. 1).

A biopsy of one of the lesions was performed which showed in the haematoxylin and eosin stain: epidermis with moderate acanthosis which surrounded a plug made up of the scab, keratinous detritus and inflammatory cells; in the base of this plug, flattened epidermis with introduction of collagen fibres running vertically from the dermis could be seen; with Masson's trichrome stain, the presence of transepidermal elimination of collagen fibres was confirmed (Fig. 2). With these findings, the diagnosis of acquired reactive perforating collagenosis (ARPC) was made. The patient was treated with fluocinolone acetonide cream 0.01% every 12 h plus levocetirizine tablets 2.5 mg/day, with an adequate response in treatment weeks, an interval during which his symptoms of pneumonia resolved and he was discharged. The patient remained under follow-up by our department.

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