

Severe Symptomatic Hypernatremia in a Patient with Panhypopituitarism after Short-Term Discontinuation of Desmopressin

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The pituitary gland is responsible for the production and secretion of several hormones, which have a major role in regulating the daily physiological processes of the human body. Panhypopituitarism is defined as an impairment in the secretion of all the pituitary hormones and was found to be associated with increased mortality, mostly due to cardiovascular and respiratory disease.

One of the hormones produced by the pituitary gland is antidiuretic hormone (ADH), which is also known as vasopressin. ADH plays a crucial role in maintaining serum osmolality (the concentration of dissolved particles such as salts and glucose) preserving the volume of water in the extracellular fluid. The clinical expression of ADH deficiency is the excretion of large volumes of dilute urine (polyuria). This condition is termed diabetes insipidus (DI), which results in increased thirst and hypernatremia [1].

There are two forms of DI with different causes for each. The main form is central DI (CDI), which is caused by impaired secretion of the hypothalamic hormone due to malignant or benign tumors, head trauma, surgeries, or idiopathic conditions. The other form is nephrogenic DI, in which there is sufficient ADH secretion but the kidneys do not respond appropriately to its stimulation.

The primary and widely used drug to treat CDI is desmopressin, a synthetic analog of vasopressin, with significant advantages compared to exogenous vasopressin. Some advantages include ease of administration and stability at room temperature. Exogenous vasopressin is used in intensive care patients with hemodynamic shock, who remain hypotensive despite fluids, and catecholaminergic vasopressors treatment. There are reported cases of transient DI and severe hypernatremia after discontinuation of this treatment in such patients [2]. Although this condition is becoming more common in the literature, with a rising number of case reports, it is still considered a rare condition with yet unknown incidence. However, severe hypernatremia after discontinuation of desmopressin in patients with panhypopituitarism is even less common, with limited reports to date.

We report on a case of severe hypernatremia in a patient with panhypopituitarism who was hospitalized with symptoms and signs of adrenal insufficiency combined with severe hypernatremia after inadvertently interrupting her hormone replacement therapy with both steroid and desmopressin for a few days. In a short period of only 2 days, she developed extremely severe life-threatening hypernatremia, necessitating transfer to the intensive care unit (ICU) for further treatment and follow-up.

PATIENT DESCRIPTION

Our patient was a 27-year-old female with a suprasellar craniopharyngioma after previous partial resection, which

left her with panhypopituitarism and blindness. Soon after the surgery, the tumor continued to grow. However, it was decided to continue with conservative treatment since the tumor was considered inoperable.

The patient was admitted to the emergency department with severe weakness, which started on the day of admission, and hypothermia (32°C). According to her relatives, she was given approximately half of her regular steroid dose on the days prior to her admission due to a lack of these medications at her home. At admission, she was somnolent, and other than hypothermia, vital signs and physical examination were within normal limits. Laboratory tests showed mild hyponatremia of 131 mmol/L and hypoglycemia of 3.1 mmol/L with marked oliguria. As secondary adrenal insufficiency was clinically suspected, the patient was treated with hydrocortisone with a rapid response and clinical improvement.

Due to the mild hyponatremia and oliguria, her chronic desmopressin treatment was stopped. During the next 24–48 hours, the patient developed worsening weakness and altered consciousness. She responded to questions with single-word answers and followed only simple commands. Blood tests revealed severe hypernatremia (plasma sodium > 196 mmol/L, normal range 135–145 mmol/L). Following a consultation with the endocrinology team, treatment with dextrose 5% infusion (200 ml/hour) and desmopressin was initiated.

Due to clinical deterioration, including decrease consciousness and additional neurological signs, the patient was

transferred to the ICU for tight sodium level titration and close monitoring. Sodium levels normalized within 2 days as well as rapid neurologic improvement. The patient was transferred from the ICU to the internal medicine department and was eventually discharged without new neurologic deficit. Following the initiation of treatment, with the clinical and Natrium plasma concentration improvements, urine osmolarity was maximally concentrated to 1016 mOsm/kg and urine natrium concentration was 204 mmol/L, indicating the exogenous ADH activity. The full course of her sodium levels is described in Figure 1A.

COMMENT

Panhypopituitarism is a complex condition that can be challenging to manage due to the delicate balance between the absent hormones replacement and the co-existence of other factors such as the presence of a growing inoperable brain tumor, as in our patient. Our case required an individual approach and specialized care. The patient arrived with mild hyponatremia, most probably due to a lack of appropriate steroid replacement. During hospitalization, our patient developed extreme iatrogenic hypernatremia to levels that are rarely reported in the medical literature.

We think there were two leading causes of the life-threatening deterioration in the patient's condition. First, the severe and rapid hypernatremia occurred due to the short 2-day interruption of regular desmopressin treatment, in addition to the patient's physical restraints (blindness) limiting her access to water and an altered thirst sensation. To the best of our knowledge, only one similar case report [3] has been described in the literature. However, in that case, the patient presented with a much lower sodium level. Second, we believe that the use of a glucocorticoid stress dose contributed to unmasking this situation as described previously in patients with hypopituitarism and CDI.

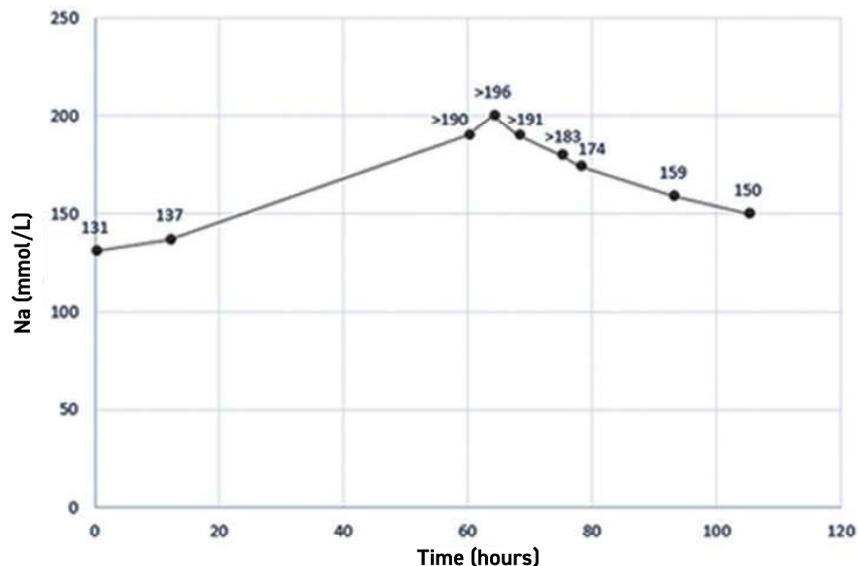
As the patient's clinical condition and sodium levels initially improved under steroid replacement. She did not receive fluids as part of her treatment, and a close monitoring the urine output was missing, which probably contributed to the rapid and extreme increase in the plasma sodium levels, the alteration in her consciousness, and her dramatic general deterioration.

In our case, we faced a few questions which had to be resolved. One of them was the extreme levels of so-

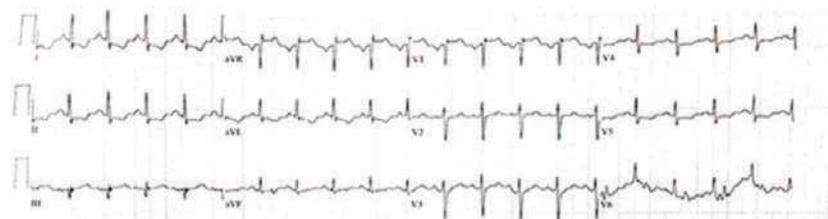
dium. Due to this rare situation, the information regarding its course and symptoms are scarce. There are reports of electrocardiographic changes, such as QT-segment prolongation and diffuse ST-segment depressions, as well fatal arrhythmias, like ventricular tachycardia, at such levels [4]. Our patient developed tachycardia and ST-segment depressions in the lateral wall leads with ST-segment elevation in AVR and V1 without elevated troponin levels. See the ECG in Figure 1B. Those

Figure 1. Sodium laboratory results during the patient hospitalization period and electrocardiogram results

[A] Sodium levels over time, measured in millimoles per liter (mmol/L), normal range 135–145. Time is listed in hours (h). Timepoint 0 is regarded as the first blood test that was taken during the admission to the emergency department



[B] Electrocardiogram was performed during the extreme hypernatremia (Na >196 mmol/L) time and showing sinus tachycardia rhythm approximately 150 beats per minute, ST-segment depressions in the lateral wall leads with ST-elevation in AVR and V



changes normalized with the decrease in sodium levels. Another concern was the correction speed of the hypernatremia.

Due to the rapid increase in sodium levels in less than 48 hours, as well as the substantial neurologic symptoms, it was decided to correct the hypernatremia as soon as possible with aggressive fluid infusion and hormone replacement. A retrospective cohort study evaluating the correction rate of severe hypernatremia (above 155 mmol/L) of 131 patients was previously performed. Those authors found that only 36% of the patients were corrected within 72 hours of onset [5]. A slower correction rate was found to be a significant predictor of 30-day patient mortality.

CONCLUSIONS

Severe hypernatremia due to desmopressin discontinuation in a patient with panhypopituitarism is a rare condition. The complexity of such patients mandates careful management with close monitoring of plasma and urine electrolyte levels and osmolarity, with strict clinical follow-ups to avoid dangerous swings.

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Capsule

High contagiousness and rapid spread of severe acute respiratory syndrome coronavirus 2

Severe acute respiratory syndrome coronavirus 2 is the causative agent of the 2019 novel coronavirus disease pandemic. Initial estimates of the early dynamics of the outbreak in Wuhan, China, suggested a doubling time of the number of infected persons of 6–7 days and a basic reproductive number (R0) of 2.2–2.7. Sanchez et al. collected extensive individual case reports across China and estimated key epidemiologic parameters, including the incubation period. The authors then designed two mathematical modeling approaches to infer the outbreak dynamics in Wuhan by using high-resolution domestic

travel and infection data. Results show that the doubling time early in the epidemic in Wuhan was 2.3–3.3 days. Assuming a serial interval of 6–9 days, the authors calculated a median R0 value of 5.7 (95% confidence interval 3.8–8.9). The authors further showed that active surveillance, contact tracing, quarantine, and early strong social distancing efforts are needed to stop transmission of the virus.

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Capsule

Salting neutrophils' game

Sodium chloride, commonly known as table salt, has been shown to invigorate immune responses in various contexts. However, Jobin and colleagues showed that salt can impair antibacterial responses in the neutrophils of mice. Animals on a high-salt diet experienced exacerbated *Escherichia coli* kidney or systemic *Listeria monocytogenes* infections due to a reduced capacity of neutrophils to kill ingested bacteria. The neutrophil deficiencies were not caused

directly by salt or urea, but instead were dependent on salt-induced hyperglucocorticoidism. Neutrophils from healthy human volunteers who had consumed additional salt in their diet were also less capable of controlling bacteria ex vivo. High-salt diets need further investigation as a factor in some types of infections.

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