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WHEN ISN'T EXTREME HYPERNATREMIA FOLLOWED BY CEREBRAL HEMORRHAGE? A CASE REPORT AND A REVIEW OF LITERATURE

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Abstract:

Background. *Hypernatremia is an electrolyte disturbance frequently encountered in patients in intensive care units (ICUs). On admission, 2-6% of patients have hypernatremia, and 7-26% develop hypernatremia during their stay. Hypernatremia was found to be an independent risk factor for mortality. While the underlying pathology of hypernatremia can be characterized as a net increase in total sodium or a net loss of free water, clinical diagnosis of the underlying pathology is not always clear. Tetraparetic patients are a special risk group for hypernatremia. They are immobilized for long periods and depend entirely on nursing.*

Case report. *We presented a challenging case of a 49-year-old patient with a history of subarachnoid hemorrhage, complicated with an episode of extreme hypernatremia accompanied by hydrocephalus.*

Conclusion. *Even though the most serious complication of hypernatremia is subarachnoid hemorrhage, the severe episode of hypernatremia did not result in re-bleeding. The patient's extreme serum sodium levels (197 mmol/L) mentioned in the literature as incompatible with life, together with the absence of re-bleeding, confers particularity to the current case.*

Keywords: *hypernatremia; subarachnoid hemorrhage; hydrocephalus.*

Rezumat

Introducere. *Hipernatremia este una dintre cele mai frecvent întâlnite disfuncții electrolitice la pacienții critici. La internare în terapie intensivă (TI), 2-6% dintre pacienți prezintă hipernatremie, iar 7-26% dezvoltă hipernatremie pe perioada internării, aceasta fiind un factor de risc independent pentru mortalitate. Mecanismul fiziopatologic al hipernatremiei este reprezentat de o creștere netă a sodiului total sau o pierdere netă de apă liberă, diagnosticul clinic al patologiei subiacente nefiind întotdeauna clar. Pacienții tetraparetici prezintă un risc crescut de apariție a hipernatremiei, fiind imobilizați pentru perioade lungi și dependenți de îngrijire permanentă.*



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Prezentare de caz. *Prezentăm cazul unui pacient de 49 de ani cu antecedente de hemoragie subarahnoidiană, tetraparetic, internat pentru un episod de hipernatremie extremă (197 mmol/L) și hidrocefalie. După corectarea disfuncției electrolitice pacientul a fost externat din TI*[3]*.*

Concluzie. *Cea mai gravă complicație a hipernatremiei este hemoragia subarahnoidiană. În cazul prezentat, valoarea extremă a sodiului seric nu a provocat resângerare. Particularitatea cazului este conferită de valorile extreme ale sodiu seric, menționate în literatură ca fiind incompatibile cu viața, și absența resângerării.*

Cuvinte cheie*: hipernatremie, hemoragie subarahnoidiană, hidrocefalie.*

Introduction

Hypernatremia is an electrolyte disturbance frequently encountered in patients in intensive care units (ICUs). It is mainly due to infusions of significant quantities of isotonic fluids, IV administration of medications, excessive insensible losses, reduced thirst response, and/or an inability to respond adequately to thirst[1]. On ICU admission, 2-6% of patients manifest hypernatremia, and 7-26% of patients develop hypernatremia during their ICU stay, most commonly in the first week of treatment. In both cases, hypernatremia has been proven to be an independent risk factor for mortality under various conditions[2,3]. The severity of hypernatremia, rather than its duration, has been linked to increased mortality and length of stay (increases of 40% and 28%, respectively)[4]. Even though hypernatremia is far less common than hyponatremia, it is associated with death rates of up to 40-60%[5]. Oude Lansink-Hartgring and collaborators saw a significant change from hyponatremia to hypernatremia in the last two decades. This clearly indicates therapy changes as underlying causes of hypernatremia. Infusions including sodium solution, diuretics, and hydrocortisone may be linked to this shift. Because ICU-acquired hypernatremia is mainly iatrogenic, it should be avoided, and its occurrence may be used to assess treatment quality[6].

While general causes of hypernatremia might be summarized as a net gain in total sodium or a net loss of free water, clinical diagnosis of the underlying pathology is not always straightforward. Sodium levels >160 mmol/l are considered severe hypernatremia, whereas sodium levels >190 mmol/l are considered extreme hypernatremia[2,3,7].

The symptoms of hypernatremia are directly related to its severity and time of installation. They vary from nausea, vomiting, muscle weakness, restlessness, and fatigue, to confusion, nystagmus, seizures, myoclonic jerks, and even mortality. The degree of hypernatremia is linked to the level of consciousness[8, 9]. Acute hypernatremia can cause fast transcellular redistribution of fluid, resulting in a decrease in brain water content and neurological impairment[10].

Chronic hypernatremia causes a reduction in brain volume, which might be reversed by cerebrospinal fluid migration into the brain, increasing interstitial volume[11]. Because of shrinkage of the brain parenchyma, ventriculomegaly commonly occurs in neurodegenerative disorders[12]. Patients from neuro-psycho-motor recovery centers are a special risk group for hypernatremia, Tetraparetic patients, who are immobilized for long periods and who depend on permanent nursing, frequently have comorbidities that affect water and electrolyte balances. Also, poor care, limited access to water, and inefficient monitoring are causes of dehydration in these patients[13, 14]. Decreased blood or CSF osmolality may cause neurological symptoms.

Disruption of bulk flow inside the parenchyma is likely to induce neuronal and glial dysfunction[14].

Hypernatremia's most severe complication is subarachnoid or subdural hemorrhage due to the rupture of bridging veins and dural sinus thrombosis. Nontraumatic subarachnoid hemorrhage (SAH) is a type of hemorrhagic stroke most commonly caused by the rupture of saccular aneurysms. It can cause permanent brain damage or even death. Rapid correction of chronic hypernatremia leads to cerebral edema, seizures, and permanent brain damage[15,1].

We present a case of extreme hypovolemic hypernatremia that occurred in an immobilized patient with a neurosurgical history.

Case report

We present the case of a 49-year-old patient, who presented in the emergency room for neurological deterioration with motor aphasia. The patient has a history of epilepsy, sequelae flaccid tetraparesis following a rupture of a saccular aneurysm of the anterior communicating artery (AcoA), which was surgically clipped 2 years earlier, hospitalized in a rehabilitation center (Figure 3 A and B). A complete medication list was provided by the patient's assisted living facility. It included: Carbamazepine 200 mg/day (LaborMed Pharma S.A. Romania), Omeprazole 40 mg/day (LaborMed Pharma S.A. Romania), Sertraline 50 mg/day (Arena Group S.A., Romania), Fraxiparine 4000 UI/day (Aspen Pharma Trading Limited, Ireland). By admission, the patient had precarious general status, cachectic appearance. The patient was dehydrated, but without signs of head trauma. At clinical examination he had a Glasgow Coma Score (GCS) of 9 points, a heart rate of 96 bpm, blood pressure of 110/70 mmHg, with effective spontaneous breathing. He was eupneic and oliguric (urine output <0.5 ml/kg/h). The neurological examination showed tetraparetic patient, with no signs of hyperreflexia, isochoric and light reflexive pupils with spontaneous eye opening, aphasia, and eye movement when commanded.

Laboratory analyses showed a profound hydro-electrolytic and metabolic imbalance: excessive hypernatremia (197 mmol/l) and hyperchloremia (161 mmol/l), serum creatinine of 3.19 mg/dL (glomerular filtration rate - GFR of 22.08 ml/min), serum



glucose of 134 mg/dL, serum urea 204.4 mg/dL, serum calculated osmolality of 474.4 mOsm/L and free water deficit of approximately 17 liters.

Cranial CT imaging showed moderate, communicating hydrocephalus (HCP) with signs of periventricular activity. There was severe, diffuse, bilateral cerebral atrophy and metal clip after aneurysmectomy. No hypothalamic infarct or other mass lesion or focal mass effect was seen (Figure 4 A, B and C). The patient was admitted to the intensive care unit (ICU), where we initiated supportive measures to correct the hydroelectrolytic imbalances. Following the neurosurgery examination, placement of the external ventricular drain was recommended under general anesthesia with orotracheal intubation. Post-operatively, the patient was transferred back to the ICU, orotracheal intubated and mechanically ventilated, and hemodynamically stable. The hydroelectrolytic imbalance was corrected with a decreasing rate of 8-12 mmol/L/24h. Serum sodium levels were checked at 4 hours, revealing a slow decrease of sodium to a minimum of 184 mmol/l in the first 24 hours (Figure 1). The cerebrospinal fluid (CSF) cell count was normal, the protein level was 430.7 mg/L, and the glucose level was 142.01 mg/dL. Postoperatively, the patient was successfully extubated on the second day. In the following days, the patient's condition improved, with serum sodium levels gradually decreasing to 140 mmol/L. On the seventh postoperative day, it was decided to suppress the external ventricular drainage. Neurological status was assessed daily, GCS after extubation was maintained at 14 points. Laboratory tests performed during ICU hospitalization revealed a high GFR, which may be associated with water rebalancing therapy (Table 1).

On day 11, after the suppression of external ventricular drainage, the patient's neurological condition degraded to GCS 11 points. A new CT scan was performed, which described HCP, so a new external ventricular drainage was placed (Figure 5 A and B). After surgery, the patient was transported to the ICU, and GCS was 14 points 2 hours after surgery.

Hydroelectrolytic therapy was continued, and the values were maintained within normal limits (Figure 2). The patient had a permanent urinary catheter. Urine culture revealed a urinary tract infection with Pseudomonas aeruginosa and later one with Providencia stuartii. They were treated according to the antibiogram. During the stay in intensive care, the patient also developed bronchopneumonia with Acinetobacter Baumannii, treated according to the antibiogram. Serum sodium levels returned to normal during the ICU stay. After 23 days, the ventricular drainage was suppressed, and the patient was sent to the recovery center. Renal function was recovered, and creatinine levels were within normal ranges.

Day	Na mmol/ L	K mmol /L	pH	HCO_3 mmol/L	Base excess mmol/ L	Cl mmol/ L	Lactate mmol/L	Blood glucose mg/dL	Creatinine mg/ dL	GFR milliliters /minute	Blood urea mg/ dL
1	197	3.8	7.4	18.7	-5.3	161	1.7	134	3.19	22.08	204.4
2	177	2.98	7.4	20	-5.0	141	1.5	366	2.63	27.58	169.5
3	176	3.84	7.34	19.5	-6.4	141	1.8	130	1.76	43.81	103.3
7	151	3.25	7.5	24.8	1.5	119.5	0.6	106	0.8	109.23	56
8	144.6	3.35	7.54	24.8	2.1	113.1	0.6	63.4	0.47	200	32.3
18	141	3.51	7.52	23.4	1.8	107.9	0.5	74.3	0.4	240.27	36.7
19	142	5.2	7.5	29	5.7	111	0.8	130	0.41	210	39.1
31	147	3.06	7.52	30.6	7.6	112	1.2	82.2	0.41	233.56	45.5

Table 1. *Laboratory analyzes performed at hospitalization and in the perioperative periods*

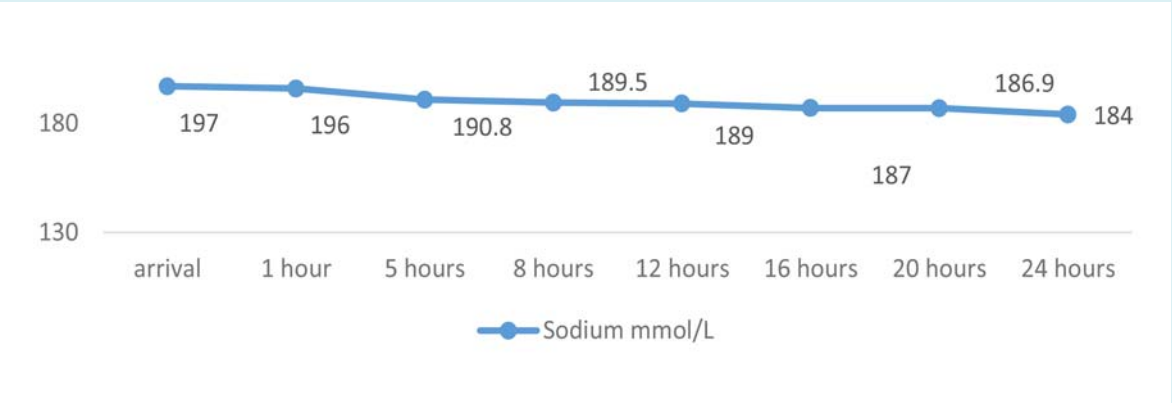


Figure 1. *Sodium levels in the first 24 hours*

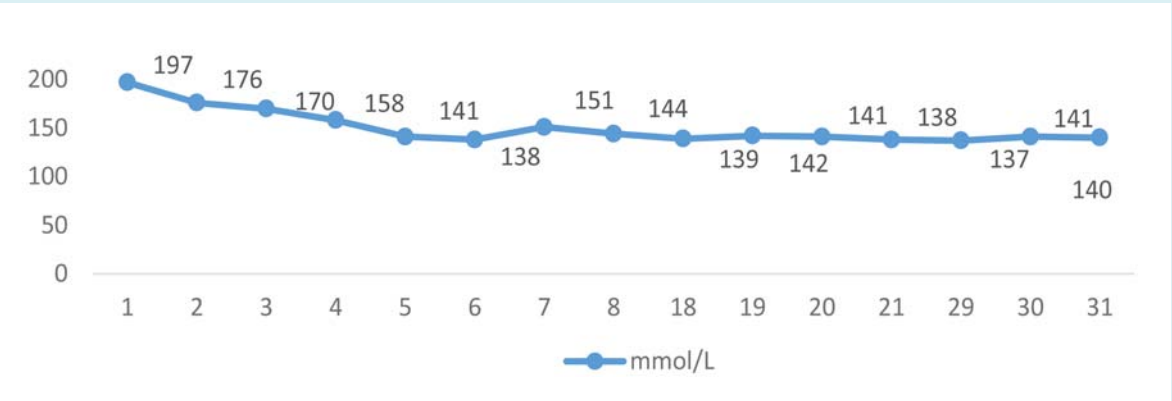


Figure 2. *Sodium values from admission to suppression of the second external ventricular drain*



Discussion

Acute elevations in plasma sodium levels or concentrations higher than 160 mmol/l are likely to cause severe symptoms, and they can lead to brain shrinkage and vascular rupture with intracranial bleeding[7,3]. This is the reason why, in emergency admissions, rapid evaluation of serum electrolytes and acid-base balance is indispensable. In cases of persistent hypernatremia (>48 hours), an osmotic adaptation occurs, limiting the degree of brain cellular dehydration and the resulting neurological symptoms[1, 16]. In our case, the initial analysis showed a hydroelectrolytic imbalance associated with hydrocephalus, which required hospitalization in ICU. Our case raises some questions: What caused hypernatremia? Why was it associated with HCP two years away from the AcoA aneurysm? What is the pathophysiological mechanism by which HCP appeared?

What caused the hypernatremia?

Exacerbated hypernatremia (197 mmol/L) in our patient was due to dehydration. Despite the patient's chronic medications (Sertraline and Carbamazepine), which may lower serum sodium levels through various mechanisms, it appeared from the heteroanamnesis performed later that the patient was with moderate hypernatremia on routine labs (137-170 mmol/L).

In patients with SAH, hypernatremia can occur as an extracranial complication[17]. Furthermore, hypernatremia can cause subarachnoid or subdural hemorrhage, creating a vicious cycle centered on hypernatremia, which can be both a complication and a cause of SAH[5]. In addition, diabetes insipidus might develop because of vasospasm-induced ischemia of the hypothalamus caused by an anterior communicating aneurysm.

Abnormalities in thirst and the release of arginine vasopressin can be linked to a range of infiltrative, neoplastic, vascular, congenital, and traumatic events in the circumventricular area. Despite hypertonicity, patients with hypodipsia show a lack of thirst, and this type of hypernatremia is known as “adipsic” or “essential”[18, 19]. Although conscious patients can become thirsty, neurologic patients may be cognitively compromised because of their primary pathology or the resulting electrolyte disruption, making thirst an inaccurate indicator[19]. To maintain plasma osmolality, the osmoreceptors in the anterior hypothalamus regulate vasopressin release and thirst perception. Vasopressin and thirst osmoreceptors are thought to be in the same area[20,21]. Small penetrating branches from the anterior cerebral or anterior communicating arteries deliver blood to this region. Damage to the thirst osmoreceptors in the anterior circumventricular organs of the hypothalamus may be caused by lesions affecting these regions. In the present case,

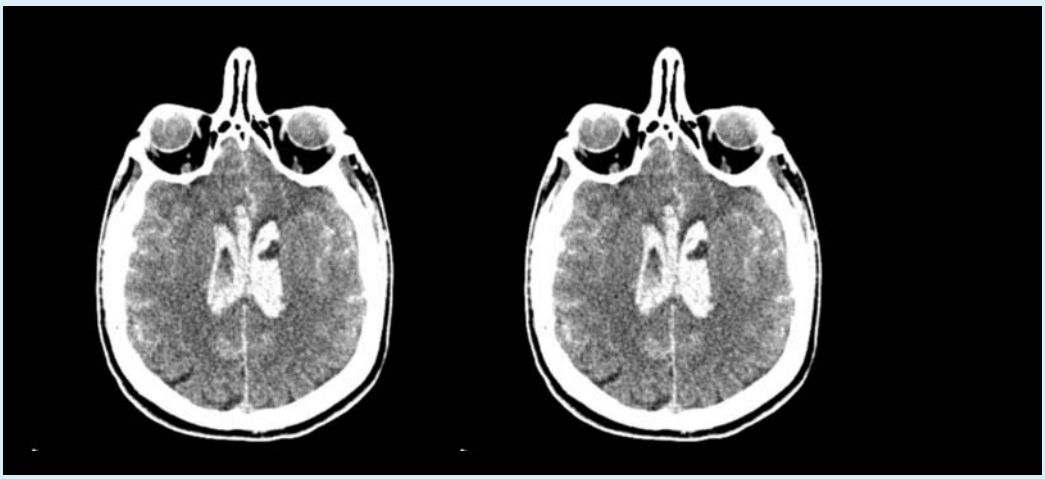


Figure 3 A and B. *CT images from the rupture of the saccular aneurysm of AcoA*

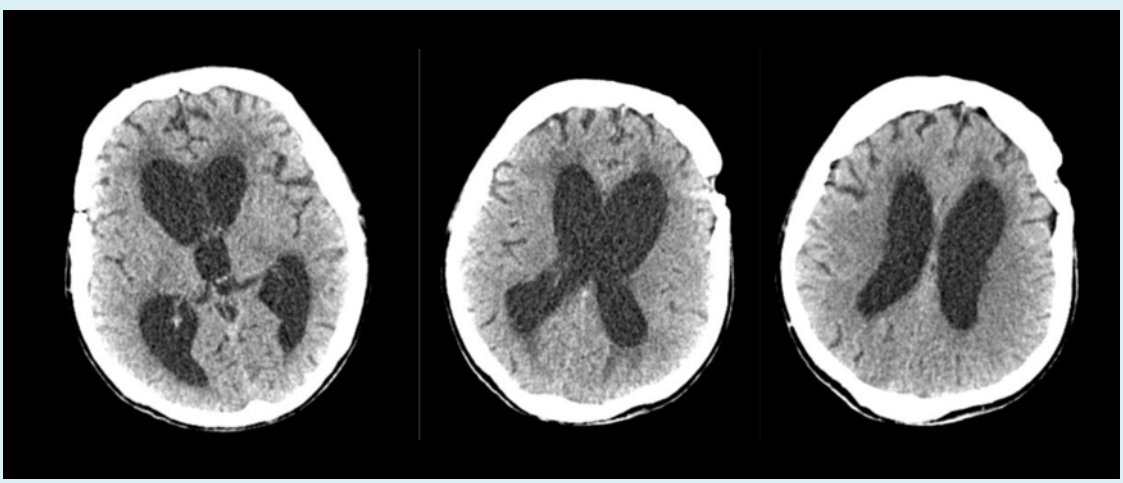


Figure 4 A, B and C. *CT image from presentation in emergency room, day 1*

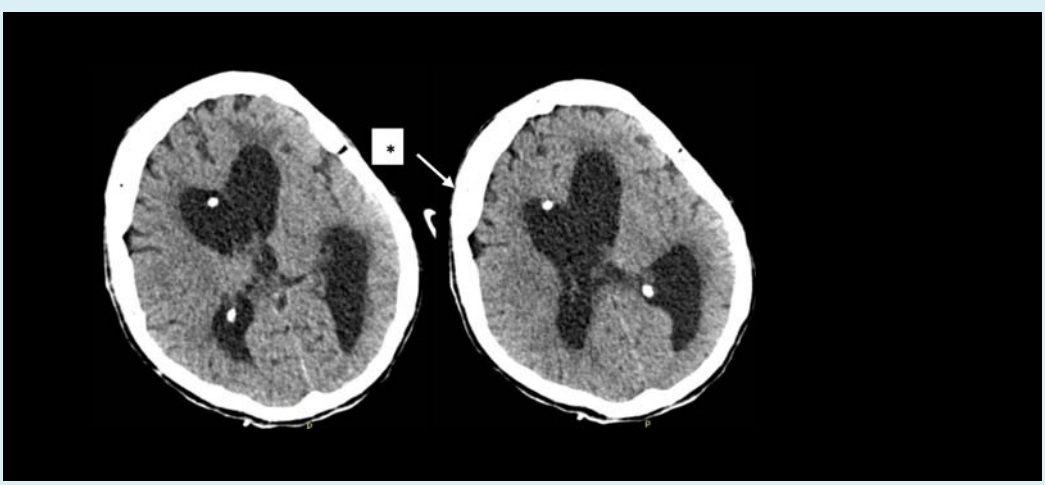


Figure 5. A. *CT scan after the first placement of external ventricular drain (ventricular drain). B. CT scan after the second placement of external ventricular drain*



an AcoA aneurysmal hemorrhage impaired the thirst arousal mechanism[21]. Hypodipsic hypernatremia is a pathological rise in serum sodium caused by a lack of thirst and osmoreceptor defects in the hypothalamus. Although vascular pathogenesis is found in 15% of hypodipsic hypernatremia patients, few cases have been reported[20, 21]. Therefore, in this case, due to the patient's neurological disorders (which also included elements of mutism), we can attribute the hyperosmolar state either to the disturbance of thirst regulation, poor care, or both.

Why was hypernatremia associated with HCP?

Hydrocephalus is a common complication of SAH in the acute phase[22]. If acute hydrocephalus develops within hours of SAH, delayed hydrocephalus might develop weeks to months after the initial occurrence. In individuals with neurological abnormalities caused by the initial SAH, symptoms such as headache, urine incontinence, gait difficulty, and cognitive deterioration may be modest or difficult to detect[23]. A significant number of patients with chronic HCP do not have increased intracranial pressure, as the chronic HCP is of the “communicating” type, attributed mainly to fibrosis and adhesions of the leptomeningeal and arachnoid granulations[24, 25]. On CT images, our patient presented severe cerebral atrophy after a rupturing of the aneurysm. In this case, HCP may be chronic, as a compensatory mechanism for cerebral atrophy, with which we can associate shrinkage of the brain parenchyma due to hypernatremia exacerbation. In the present case, the symptoms of HCP at admission were nonspecific, and they may be due to both hypernatremia and hydrocephalus.

In accordance with Starling's law of filtration, some claim that a hydrostatic pressure gradient between blood, choroid plexus epithelial cells, and the ventricles drives the production of CSF. Increased intracranial pressure in hydrocephalus, therefore, may reduce CSF secretion, while decreased pressure will increase it. We don't know in this case what role pressure gradients played in the secretion of CSF[21], but based on this statement, in our case, we can assume that HCP emerged as a compensatory mechanism for low intracerebral pressure. It has also been shown that changes in CSF osmolarity influence water flux across the choroid plexus and the blood-brain barrier[26,27].

The blood-CSF barrier comprises epithelial cells that surround the capillaries and selectively control the movement of solutes and water to regulate the composition of CSF. The net flow of Na^+, $HCO3^-$, and Cl^- into the epithelial cells of the choroid plexus is essential and driven by the Na gradient at the basolateral membrane[26,28,29].

Some older studies suggest a correlation between ventricular enlargement and

hypernatremia. Jernigan et al. presented a case report on episodic ventriculomegaly due to hypernatremia mimicking shunt malfunction, which improved once the osmolar imbalance was corrected. This condition can also be associated with the present case, the HCP appearing two years after the clipping of the aneurysm of the AcoA[30].

Conclusions

In this case, HCP was most likely chronic due to post-hemorrhagic cerebral atrophy, but the exacerbation of chronic hypernatremia caused deeper dehydration of brain cells, resulting in an increase in HCP volume and the appearance of the patient's symptoms. Even though the most serious complication of hypernatremia is subarachnoid hemorrhage, the severe episode of hypernatremia did not result in re-bleeding. The patient's extreme serum sodium levels (197 mmol/L) mentioned in the literature as incompatible with life, together with the absence of re-bleeding, confers particularity in the current case.

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Institutional Review Board Statement: *This was a purely observational case study that did not alter the patient's management and clinical outcomes. Thus, ethical approval was not required for this case report.* ***Informed Consent Statement:*** *Written informed consent has been obtained from the patient's first degree relatives to publish this paper.*

Data Availability Statement: *Data and material are available on request.*

Acknowledgments: *Not applicable.*

Conflicts of Interest: *The authors declare no conflict of interest.*

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