Acta Biomed 2024; Vol. 95, N. 2: e2024025 DOI: 10.23750/abm.v95i2.15308

Mini review

Hyponatraemia and head injury: Just a coincidence or a case of cerebral salt wasting syndrome?

Chiara Sciacovelli[1], Andrea Vercelli[2], Tommaso Sonnessa[1], Valentina Tinelli[2], Elvira Varrato[2], Erika Poggiali[2]

[1]Vita - Salute San Raffaele University and Emergency Department, San Raffaele IRCCS Hospital, Milan, Italy; [2]Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy

Abstract. We report the case of an 81-year-old woman who presented to our attention complaining of headache, dizziness, gear insecurity with muscle weakness, and vomiting after a forward fall down the stairs with a minor head injury 15 days earlier and investigated with a brain computed tomography, that excluded fractures and haemorrhage. Laboratory tests showed severe hyponatraemia, that we immediately investigated with a diagnostic workup, that included urine tests, point-of-care ultrasound, and orthostatic hypotension with "supine-to-standing test". Based on these results and the recent traumatic brain injury, cerebral salt wasting syndrome (CSWS) was diagnosed. The patient was treated with hypertonic saline infusion (3% NaCl), developing an initial osmotic demyelination syndrome due to the rapid correction of hyponatraemia, which completely solved stopping the infusion. CSWS is often misdiagnosed and commonly confused with inappropriate antidiuretic hormone secretion syndrome. CSWS can occur within the first 10 days following a neurosurgical procedure or acute neurological event (stroke, haemorrhage, and traumatic head injury). Since severe hyponatraemia is potentially life-threatening, emergency clinicians should always consider CSWS when evaluating hyponatraemic patients, particularly after a head injury. (www.actabiomedica.it)

Key words: hyponatraemia, cerebral salt wasting syndrome, head injury, sodium, orthostatic hypotension

Introduction

An 81-year-old woman presented to our attention with headache, dizziness, gear insecurity with muscle weakness, and a unique episode of vomiting after a forward fall down the stairs with a minor head injury 15 days earlier, that was investigated with a brain computed tomography (CT) excluding fractures and haemorrhage. Her medical history included hypertension treated with perindopril (8 mg daily) and bisoprolol (1.25 mg daily). At admission, she was in good clinical condition, apyretic, with a normal body mass index of 19. Her Glasgow Coma Scale (GCS) was 15, blood pressure 160/75 mmHg, heart rate 76 bpm, pulse oximetry 98% at room ambient, and respiratory rate 18/min. The neurological evaluation resulted in normal muscle tone and sensitivity in all four limbs. She was promptly investigated with a brain CT scan, that ruled out bleeding. Laboratory findings showed a severe hyponatraemia (109 mEq/L) with normal renal function (creatinine 0.48 mg/dL - normal value 0.6-1.2, blood urea nitrogen 26 mg/dL - normal value 10-50), transaminases, C-reactive protein, and glucose. The arterial blood gas analysis showed a metabolic alkalosis with a compensatory compensation with pH 7.42, pCO2 48 mmHg, pO2 67.8 mmHg, HCO3 29.3, and confirmed the severe hyponatremia (118 mEq/L) with normal potassium (3.5 mEq/L), calcium (4.41 mEq/L), and lactate (5 mg/dL, normal value 5-15), and reduced chloride (84 mEq/L).

She was admitted to our observation unit, and further investigations were done to identify the cause of hyponatremia. The spot urine sodium concentration was 46 mmol/L, and the urine osmolality was 218 mOsm/kg H2O. Urinary cortisol resulted in the normal range (221.5 µg/24 hrs, normal range 70-300). Other reasons for natriuresis, including polydipsia, alcohol abuse, thyroid dysfunction, antidepressants, proton pump inhibitors, non-steroidal anti-inflammatory drugs, and corticosteroids, were investigated and ruled out. In the past patient's laboratory exams, serum sodium was always in the normal range, and the patient had never experienced the symptoms before her head injury, excluding a role of perindopril in the pathogenesis of severe symptomatic hyponatremia.

To assess the patient's volume status, we used point-of-care ultrasound (POCUS), which showed a collapsed inferior vena cava and ruled out organ damage. We then investigated an orthostatic hypotension using a "supine-to-standing test", that documented a supine-to-standing systolic blood pressure drop ≥20 mmHg. These results were indicative of hypovolemia.

Neurological symptoms and vomiting were regarded as symptoms of severe hypotonic hyponatraemia, and given the recent head trauma, cerebral salt wasting syndrome (CSWS) was considered the cause of hyponatraemia. Perindopril was stopped and changed to a calcium antagonist (amlodipine 5 mg daily). A urinary catheter was placed to monitor the patient's urine output, and the patient was immediately treated with hypertonic saline infusion (3% NaCl, 35 mL/h), monitoring the sodium correction rate using a "point-of-care venous blood gas analysis". After 18 hours, the correction rate was 12 mEq/L, and the patient reported confusion, weakness in her legs, and altered vision with diplopia. These symptoms were completely solved within three hours after the hypertonic saline infusion was stopped, suggesting a diagnosis of initial osmotic demyelination syndrome (ODS) due to the rapid correction of hyponatraemia. Normal saline infusion (0.9% NaCl) was infused until normalization of sodium level, maintaining the correct targeted sodium correction rate (≤ 10 mEq/L in 24 hours). The patient was admitted to the Internal Medicine Ward and on day 7, she was discharged completely asymptomatic with a normal sodium value (138 mEq/L). At a subsequent laboratory control one month after her discharge, the sodium value was still in the normal range.

Discussion

Hyponatraemia (serum sodium < 135 mmol/L) is an electrolyte disorder that emergency clinicians often face. Understanding the aetiology of hyponatraemia can be difficult in the emergency setting. As recently proposed by Lindner *et al.*, the first step in the emergency department (ED) is to recognize acute or symptomatic hyponatraemia as it should be treated immediately (1). According to the European guidelines, hyponatraemia should be classified based on several parameters, including serum sodium values, onset, symptom severity, patient's volume status, and urine osmolality (2).

Hyponatraemia is mild if the serum sodium value is between 130 and 135 mmol/L, moderate between 125 and 129 mmol/L, and profound if less than 125 mmol/L. Acute and chronic hyponatraemia is distinguished by the onset: if it develops in 48 hours, it will be acute, otherwise, it will be chronic. This cut-off is based on the time it takes brain cells to adapt to the hypoosmolar condition by expelling water and electrolytes into the extracellular space (rapidly compensating pathway) (2,3). This mechanism can compensate for hyponatraemia to a limited extent and the decrease in serum sodium that occurs in less than 48 hours can lead to cerebral oedema and related symptoms (2).

Differentiating between acute and chronic hyponatraemia in the EDs is the most challenging task. Unless there are established factors that could produce acute hyponatraemia, such as iatrogenic causes, polydipsia, or thiazide prescription, hyponatraemia should be considered chronic if a decrease in serum sodium of 10 mmol/L within 48 hours cannot be documented (1,2). Acute hyponatraemia can present with moderate symptoms, including nausea without vomiting, confusion, and headache. Severe symptoms include cardiorespiratory distress, abnormal and deep somnolence, seizures, and coma caused by cerebral oedema (2). In these circumstances, patients should be treated

rapidly with infusion of 150 ml of 3% NaCl solution over 20 minutes, followed by a second measurement of serum sodium level 20 minutes later. The infusion can be repeated as long as the symptoms of brain oedema persist or until the serum sodium increases by 5 mmol/L (1,2).

The guidelines have limitations regarding the classification of the presenting symptoms and the stratification of the level of severity. Severe hyponatraemia (serum sodium < 125 mmol/L) is not always associated with neurological symptoms related to brain oedema (or pre-oedema). In a recent retrospective study to evaluate the impact of severe hyponatraemia in patients presenting to the EDs, only half of the 394 patients with serum sodium less than 116 mmol/L had neurological symptoms (4). Interestingly, only one patient was totally asymptomatic. According to European Guidelines (2), patients with hyponatraemia are never really asymptomatic.

When hyponatraemia develops more gradually (i.e., over 48 hours), brain cells respond to the hypoosmolar environment via the slow compensatory pathway by losing organic osmolytes, including neurotransmitters such as glutamate or GABA (3). The depletion of these neurotransmitters may be responsible for the mild neurological deficits observed in patients with chronic hyponatraemia (5).

In the case of asymptomatic or chronic hyponatraemia, ED clinicians should evaluate the patient's volume status before starting any therapy (1). Starting from the evidence that most of the cases are hypotonic hyponatraemia, it is preferable to classify them according to the volume status (1). Gastrointestinal fluid loss, transdermal loss, adrenal insufficiency, medications (thiazide diuretics and aldosterone antagonists), and cerebral/renal salt wasting syndrome are potential causes of hyponatraemia with reduced volume status. Instead, hyponatraemia with increased volume status can occur in conditions such as heart failure, cirrhosis, and nephrotic syndrome. Patients with the syndrome of inappropriate antidiuretic hormone secretion (SIADH), primary polydipsia, or hypothyroidism are typically euvolemic. Recognizing a hypervolemic patient is simple, as oedema, ascites, rales, and crackles on auscultation are common findings on physical examination. Detecting patients with hypovolemia is more insidious. Postural dizziness, dry mucous membranes, and the onset of orthostatic hypotension are clinical signs of hypovolemia. POCUS is a simple and easy method that is commonly used by emergency clinicians to assess the patient's volume status by measuring the diameter of the inferior vena cava and evaluating its collapsibility (6). Evaluating the patient's volume status is necessary and essential not only because the treatment obviously changes but also to identify forms of hyponatraemia that can be challenging to diagnose, particularly in the EDs, including CSWS.

Epidemiology

CSWS was first described in 1950 in a report of three patients with brain disease and concomitant hyponatraemia (7). Hyponatraemia is known to be a frequent finding in patients with acute neurological and neurosurgical diseases (8,9), particularly subarachnoid haemorrhage (SAH) (10). A retrospective study by Sherlock M. *et al*. examined 316 patients with SAH, demonstrating this population's high incidence of hyponatraemia (56.6%). In 62 patients with SAH and serum sodium levels < 130 mmol/L, CSWS was the cause of hyponatraemia in 6.5% of cases (11).

Hyponatraemia is a frequently encountered finding in the traumatic head injury population (12). In an attempt to determine the prevalence of CSWS among patients who have suffered head injuries, Leonard *et al.* reviewed the available literature from 1988 to 2010 (13). The study also aimed to define the timing of the onset of CSWS after trauma and evaluate biochemical changes in patients who developed the syndrome. The incidence of CSWS varied widely (0.8–34.6%) as the studies included in the review did not use the same diagnostic criteria for CSWS and different populations were examined in terms of age and type of traumatic injury. The incidence of CSWS after traumatic brain injury (TBI) was higher in patients with a GCS less than 9.

Volume studies with radioisotope determinations in neurosurgical patients have been the turning point in the evaluation of the incidence of CSWS (14-16). These studies revealed that CSWS is more prevalent

than SIADH in neurosurgical patients and showed that a significant percentage of patients with low serum sodium values also had hypovolaemia (the main clinical hallmark of CSWS).

Pathophysiology

The pathogenesis of CSWS is not universally defined and remains the subject of research today. Several pathogenetic pathways have been proposed, influenced by the type and location of the brain lesion and the patient's age (13).

The onset of CSWS can be explained by the serum increase of natriuretic factors, such as Atrial Natriuretic Peptide (ANP), Brain Natriuretic Peptide (BNP), C-type natriuretic peptide (CNP), Dendroaspis Natriuretic Peptide (DNP), which induce arteriolar vasodilatation and increase glomerular filtration, but also inhibit the renin-angiotensin-aldosterone system (RAAS) and sodium reabsorption in the distal tubule, causing hyponatraemia and increased natriuresis (17). Among the natriuretic factors, BNP seems to be the most frequently associated with the onset of the syndrome (18), although it is not yet known whether BNP is released from the brain, heart tissue, or both. Most of the studies were performed on patients who had aneurysmal subarachnoid haemorrhage. In these cases, BNP release may be determined by direct damage of SAH to the sympathetic projections of the hypothalamus (19). According to another theory, the increase in serum norepinephrine values, induced by stress, would lead to an increase in the release of BNP from cardiac cells (20). A direct correlation has also been proposed between intracranial pressure and natriuretic factors, which regulate brain water and sodium content and cerebrospinal fluid production. The onset of CSWS may be a protective measure to limit intracranial pressure rises that can occur due to SAH (18).

In the review by Leonard *et al.*, the authors reported that ANP and BNP are not increased in patients with TBI and CSWS (13). Only two patients had elevated BNP, but brain CT showed haemorrhage in both cases. This suggests that the increase in BNP could be caused by intracranial haemorrhage. Nevertheless, many studies have not demonstrated a direct correlation between increased natriuretic factors and the onset of CSWS (12, 21). According to Harrigan MR, an acute brain injury can cause a disruption of the sympathetic activity in the kidney, increasing blood flow and glomerular filtration rate, as well as inhibiting the RAAS, which reduces renal sodium reabsorption (12).

Maesaka *et al.* successfully isolated a protein with natriuretic activity from the serum of patients with neurosurgical diseases and Alzheimer's disease, identified as haptoglobin-related protein without signal peptide (HPRWSP). Their findings suggest that HPRWSP may be involved in the CSWS pathogenic pathway and may be the subject of further research (21).

Clinical features and differential diagnosis

Patients with CSWS have hyponatraemia with reduced serum osmolarity (hypotonic hyponatraemia), reduced volume status with onset of orthostatic hypotension and finding of low central venous pressure (10). Assessing the patient's fluid status can often be difficult and inaccurate. Therefore, POCUS, increased haematocrit, and plasma urea nitrogen (BUN) may help diagnose CSWS, reflecting low effective blood volume (1,10). Other typical findings include increased urinary sodium excretion with increased urine volume (polyuria) and negative fluid balance (10).

Other conditions that may lead to hypotonic hyponatraemia and/or renal salt wasting, such as adrenal insufficiency, hypothyroidism, and renal insufficiency, must be excluded.

CSWS tends to occur within the first ten days following a neurosurgical procedure or acute neurological event, such as SAH or stroke (22). In patients with TBI, the timing of the onset of CSWS varies widely and tends to occur from a few days to two months after the injury (13). This may suggest that different pathogenetic pathways can promote the development of CSWS in the TBI population (13). It has also been suggested that the onset of CSWS is earlier in paediatric patients than in adults (23).

The differential diagnosis is crucial when assessing a patient with hyponatraemia and a history of brain

injury (traumatic or otherwise). SIADH and CSWS share many diagnostic criteria, and both can occur as a result of brain diseases. It is essential to distinguish between these two forms, as the treatments are opposite. The patient's volume status is the clinical feature that makes it possible to distinguish between the two disorders immediately. Patients with CSWS are typically hypovolemic, whereas patients with SIADH may be in a state of euvolemia or hypervolemia (10).

The pathophysiological approach proposed by Maesaka *et al.* may be useful in the differential diagnosis between SIADH and CSWS (21). The infusion of isotonic saline results in the correction of hyponatraemia in patients with CSWS. Conversely, corrections of serum sodium values were not obtained in patients with SIADH. Fractional urate excretion is high in both groups, but decreases in SIADH when hyponatraemia is corrected, whereas it remains unchanged in CSWS.

Identifying HPRWSP as a natriuretic protein capable of causing CSWS could serve as a biomarker of this disease and simplify its diagnosis, as well as a potential therapeutic target (21).

Treatment and prognosis

The goal of treatment for CSWS is to restore volume status and achieve consensual correction of serum sodium (1,10). If extracellular volume decreases, baroreceptors are activated, and vasopressin is secreted to restore volume. This is more effective than the pathway regulated by serum hypoosmolarity (24). Thus, despite hypo-osmolality, patients with CSWS remain hyponatraemic. For this reason, saline infusion can remove the volumetric stimulus for antidiuretic hormone (ADH) secretion and allow hypo-osmolality to inhibit ADH secretion, increase free water excretion, and correct hyponatraemia.

Isotonic crystalloids (20 ml/kg/hour) with repeated measurement of serum sodium levels can be used for solving the problem. It is mandatory not to exceed the correction of 1.5-2 mmol in the first 2-3 hours and 8–10 mmol in 24 hours, due to the high risk of developing ODS, a demyelinating disorder of the central nervous system with irreversible consequences (4, 25). The case of patients with CSWS but symptomatic hyponatraemia is different. As already discussed, to lower the risk of the development of cerebral oedema, serum sodium levels must be corrected rapidly in these patients, always strictly monitoring the sodium correction rate with a recommended limit of ≤ 10 mEq/L in 24 hours to prevent ODS (26). To minimize the risk of ODS, some authors suggested limiting serum sodium correction to ≤ 8 mEq/L in those patients with severe hyponatraemia and high-risk features (i.e., alcohol use disorder, hypokalaemia, liver disease, and malnutrition) and supplementing patients with thiamine if their dietary intake has been poor (26).

The prognosis of CSWS is strictly related to the clinician's ability to recognize and diagnose it. A misdiagnosis could trigger inappropriate treatments and the development of life-threatening complications (27, 28). For instance, patients with SAH have long been diagnosed with SIADH as the aetiology of hyponatraemia and have been treated with fluid restriction. Subsequently, it was discovered that this practice promoted the development of cerebral ischemia and infarction, increasing SAH-related morbidity and mortality (29).

Concerning the TBI population, there is little evidence on prognosis in the literature. Only the case reports of CSWS reviewed provided information on clinical outcomes: of the 10 patients reported in the review, only one died (13). More data needs to be collected to estimate CSWS-related mortality correctly.

Conclusion

Hyponatraemia is the most common electrolyte disorder with significant morbidity and mortality. Severe hyponatraemia is infrequent but potentially life-threatening. Accurate diagnostic workup, using a step-by-step approach, and prompt treatment are mandatory to avoid fatal consequences, including ODS. Diagnostically, the initial step is to differentiate hypotonic from non-hypotonic hyponatraemia. Determining urine osmolality, urine sodium level and volume status are the following steps in differentiating hypotonic hyponatraemia. Emergency clinicians should

always consider CSWS in the differential diagnosis of hypotonic hyponatraemia in all the patients who presented to the ED for the occurrence of neurological symptoms, nausea, or vomiting within the first 10 days following a neurosurgical procedure or acute neurological event, such as traumatic brain injury, subarachnoid haemorrhage, or stroke.

Funding: This work was not supported by any grant.

Ethic Committee: As this was a descriptive case report and data was collected without patient identifiers, ethics approval was not required under our hospital's Institutional Review Board guidelines.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: CS, TS and VT collected details of the case. CS and AV drafted the manuscript. EV and EP critically revised the manuscript. All authors approved the final version and stated the integrity of the whole work.

References

1. Lindner G, Schwarz C, Haidinger M, Ravioli S. Hyponatraemia in the emergency department. Am J Emerg Med 2022;60:1-8. doi: 10.1016/j.ajem.2022.07.023.
2. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Nephrol Dial Transplant 2014;29 Suppl 2:i1-i39. doi: 10.1093/ndt/gfu040.
3. Gankam Kengne F, Decaux G. Hyponatraemia and the Brain. Kidney Int Rep 2018;3(1):24-35. doi: 10.1016/j.ekir.2017.08.015.
4. Mustajoki S. Severe hyponatraemia (P-Na < 116 mmol/l) in the emergency department: a series of 394 cases. Intern Emerg Med 2023;18(3):781-789. doi: 10.1007/s11739-023-03221-y.
5. Refardt J, Kling B, Krausert K, et al. Impact of chronic hyponatraemia on neurocognitive and neuromuscular function. Eur J Clin Invest 2018;48(11):e13022. doi: 10.1111/eci.13022.
6. Pourmand A, Pyle M, Yamane D, Sumon K, Frasure SE. The utility of point-of-care ultrasound in the assessment of volume status in acute and critically ill patients. World J Emerg Med 2019;10(4):232-238. doi: 10.5847/wjem.j.1920-8642.2019.04.007.
7. Peters JP, Welt LG, Sims EA, Orloff J, Needham J. A salt-wasting syndrome associated with cerebral disease. Trans Assoc Am Physicians 1950;63:57-64. PMID: 14855556.
8. Tisdall M, Crocker M, Watkiss J, Smith M. Disturbances of sodium in critically ill adult neurologic patients: a clinical review. J Neurosurg Anesthesiol 2006;18(1):57-63. doi: 10.1097/01.ana.0000191280.05170.0f.
9. Sherlock M, O'Sullivan E, Agha A, et al. Incidence and pathophysiology of severe hyponatraemia in neurosurgical patients. Postgrad Med J 2009;85(1002):171-5. doi: 10.1136/pgmj.2008.072819.
10. Cerda-Esteve M, Cuadrado-Godia E, Chillaron JJ, et al. Cerebral salt wasting syndrome: review. Eur J Intern Med 2008;19(4):249-54. doi: 10.1016/j.ejim.2007.06.019.
11. Sherlock M, O'Sullivan E, Agha A, et al. The incidence and pathophysiology of hyponatraemia after subarachnoid haemorrhage. Clin Endocrinol (Oxf) 2006;64(3):250-4. doi: 10.1111/j.1365-2265.2006.02432.x.
12. Harrigan MR. Cerebral salt wasting syndrome: a review. Neurosurgery 1996;38(1):152-60. doi: 10.1097/00006123-199601000-00035.
13. Leonard J, Garrett RE, Salottolo K, et al. Cerebral salt wasting after traumatic brain injury: a review of the literature. Scand J Trauma Resusc Emerg Med 2015;23:98. doi: 10.1186/s13049-015-0180-5.
14. Nelson PB, Seif SM, Maroon JC, Robinson AG. Hyponatraemia in intracranial disease: perhaps not the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). J Neurosurg 1981;55(6):938-41. doi: 10.3171/jns.1981.55.6.0938.
15. Wijdicks EF, Vermeulen M, ten Haaf JA, Hijdra A, Bakker WH, van Gijn J. Volume depletion and natriuresis in patients with a ruptured intracranial aneurysm. Ann Neurol 1985;18(2):211-6. doi: 10.1002/ana.410180208.
16. Sivakumar V, Rajshekhar V, Chandy MJ. Management of neurosurgical patients with hyponatraemia and natriuresis. Neurosurgery 1994;34(2):269-74; discussion 274. doi: 10.1227/00006123-199402000-00010.
17. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med 1998;339(5):321-8. doi: 10.1056/NEJM199807303390507.
18. Berendes E, Walter M, Cullen P, et al. Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid haemorrhage. Lancet 1997;349(9047):245-9. doi: 10.1016/s0140-6736(96)08093-2.
19. Takahashi K, Totsune K, Sone M, et al. Human brain natriuretic peptide-like immunoreactivity in human brain. Peptides 1992;13(1):121-3. doi: 10.1016/0196-9781(92)90149-w.
20. Tomida M, Muraki M, Uemura K, Yamasaki K. Plasma concentrations of brain natriuretic peptide in patients with subarachnoid hemorrhage. Stroke 1998;29(8):1584-7. doi: 10.1161/01.str.29.8.1584.
21. Maesaka JK, Imbriano LJ, Grant C, Miyawaki N. New Approach to Hyponatraemia: High Prevalence of Cerebral/

Renal Salt Wasting, Identification of Natriuretic Protein That Causes Salt Wasting. J Clin Med 2022;11(24). doi: 10.3390/jcm11247445.
22. Diringer MN, Zazulia AR. Hyponatraemia in neurologic patients: consequences and approaches to treatment. Neurologist 2006;12(3):117-26. doi: 10.1097/01.nrl.0000215741.01699.77.
23. Berkenbosch JW, Lentz CW, Jimenez DF, Tobias JD. Cerebral salt wasting syndrome following brain injury in three pediatric patients: suggestions for rapid diagnosis and therapy. Pediatr Neurosurg 2002;36(2):75-9. doi: 10.1159/000048356.
24. Baylis PH. Posterior pituitary function in health and disease. Clin Endocrinol Metab 1983;12(3):747-70. doi: 10.1016/s0300-595x(83)80063-2.
25. George JC, Zafar W, Bucaloiu ID, Chang AR. Risk Factors and Outcomes of Rapid Correction of Severe Hyponatraemia. Clin J Am Soc Nephrol 2018;13(7):984-992. doi: 10.2215/CJN.13061117.
26. Tandukar S, Sterns RH, Rondon-Berrios H. Osmotic Demyelination Syndrome following Correction of Hyponatraemia by </=10 mEq/L per Day. Kidney360 2021;2(9):1415-1423. doi: 10.34067/KID.0004402021.
27. Oh H, Seo W. An Integrative Review of Cerebral Salt Wasting Syndrome. J Neurosci Nurs. 2020 Dec;52(6):289-294. doi: 10.1097/JNN.0000000000000548.
28. Warren AM, Grossmann M, Christ-Crain M, Russell N. Syndrome of Inappropriate Antidiuresis: From Pathophysiology to Management. Endocr Rev. 2023 Mar 28:bnad010. doi: 10.1210/endrev/bnad010.
29. Wijdicks EF, Vermeulen M, Hijdra A, van Gijn J. Hyponatraemia and cerebral infarction in patients with ruptured intracranial aneurysms: is fluid restriction harmful? Ann Neurol 1985;17(2):137-40. doi: 10.1002/ana.410170206.

Correspondence:
Received: 15 October 2023
Accepted: 15 November 2023
Erika Poggiali, M.D.
Emergency Department, Guglielmo da Saliceto Hospital
Via Giuseppe Taverna 49, 29121, Piacenza, Italy
Tel.: +39 0523 303044.
E-mail: poggiali.erika@gmail.com