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Case report

Cerebral Salt Wasting Syndrome (CSW): An unusual cause of hypovolemia after spontaneous cerebral hemorrhage successfully treated with fludrocortisone ☆☆☆★

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ARTICLE INFO

Article history:

Received 3 August 2021

Revised 18 August 2021

Accepted 20 August 2021

Keywords:

Cerebral Salt Wasting Syndrome

Hyponatremia

Hypovolemic Shock

SIADH

Fludrocortisone-Serum Salin

ABSTRACT

Objective: Our objective is to demonstrate the interest of thinking about Cerebral salt wasting syndrome (CSW) in front of hyponatremia with severe hypovolemia after a brain injury, and at the same time the interest to differentiate between Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) and Cerebral salt wasting syndrome (CSW) as two etiologies to be evoked in front of a hyponatremia with brain injury.

Case report: We report the case of a 63-year-old patient with a recent history of hemorrhagic stroke admitted for severe hypovolemic shock in whom the investigations find a very deep hypotonic hyponatremia secondary to a cerebral salt wasting syndrome successfully treated with fludrocortisone.

Discussion: CWS is characterized by hypotonic hyponatremia associated with cerebral associated with hypovolemia, the difficulty of the diagnosis is explained by the points of convergences with SIADH which is also presented with hyponatremia. The treatment is based on filling with saline, if the symptoms are severe, hypertonic saline has its place. Fludrocortisone has proven its effectiveness in the correction of refractory hyponatremia in CWS.

Conclusion: It is essential to differentiate between hyponatremia in CWS and hyponatremia in SIADH because the medical care is categorically different.

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☆ Acknowledgments: We would like to thank the team of neurosurgery of university hospital for their management and availability.

☆☆ Competing interests: The authors declare no conflicts of interest

★ Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

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<https://doi.org/10.1016/j.radcr.2021.08.049>

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Introduction

CWS is a mysterious entity represented by hypotonic hyponatremia associated with an hypovolemia that can lead to hypovolemic shock. This renal sodium loss of cerebral origin can be secondary to any cerebral aggression but mainly the sub arachnoid hemorrhage (SAH), and neuro-meningeal tubercular infection. The diagnosis is not easy because there is another condition that can also explain the hyponatremia after a cerebral aggression, it is indeed the the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). The distinction between the two entities remains essential given the therapeutic difference between the two [1].

In this article, we report the case of a patient admitted with headache, asthenia and profound hypovolemia hypovolemia in whom the diagnosis of CWS was made secondary to spontaneous cerebral hemorrhage.

Case report

We report the case of a 63-year-old patient, with a history of arterial hypertension for 5 years, under a calcium channel blocker poorly treated and followed, hospitalized 10 days ago in the neurosurgery department for a spontaneous cerebral hemorrhage, not requiring surgical evacuation, The patient was discharged after 3 days of hospitalization with a very good clinical and analgesic treatment associated with an anti-convulsant treatment, admitted to the emergency room for a deep asthenia associated with a dyspnea installed 2 days ago and worsened the same day of his admission. On examination, the patient noted the notion of excessive polyuria during the last 3 days.

Initial evaluation: conscious patient GCS = 15/15, without sensory or motor deficit, hypotensive to 74/30mmhg, with tachycardia 135 bpm, generalized mottling, with coldness of the limbs, on the respiratory level the patient is polypneic with a SpO₂ very difficult to capture given the hemodynamic state. T° is 37.5. The weight is 65kg with a recent weight of 10 days at 71kg. The patient is oliguric with a diuresis of 0,3ml/kg/h.

The clinical examination found generalized dehydration folds, the cardiopulmonary auscultation was normal, there were no clinical signs in favor of an infection.

The electrocardiogram (EKG) revealed sinus tachycardia, transthoracic echocardiography showed collapse of the inferior vena cava during inspiration, preserved left ventricular ejection fraction (LVEF = 65%), and the right ventricle was of good systolic function with no signs of tamponade eliminating a cardiac cause of shock. Arterial gas analysis (Supplementary Table 1) revealed severe metabolic alkalosis with high serum lactate level (3.64mmol/l). Chest x-ray was otherwise normal.

The initial stabilization of the patient is ensured by oxygen therapy with glasses with a flow rate of 6l/min with a target of 96%, hemodynamically the patient did not respond to filling only by saline at 30ml/kg during the 1st hour requiring the introduction of norepheniphrine at 0.4ug/kg/min by a central venous femoral. The evolution was stable, and the patient was



Fig. 1 – Head CT -Scan Showing Spontaneous Hyperdensity in favour of an Intra-Parenchymal Cerebral Haematoma

hemodynamically stabilized with a BP=110/70mmhg and control Latates at 1.8mmol/l after 6 hours of admission, thus the patient renounced his diuresis again.

Biological workup (Table 1, Supplementary Table 2) was requested coming back in favor of a hemocentration, with hyponatremia (123mmol/l), hypochloremia (54mEq/l), hypokalemia (2.3mmol/l), glycemia at 1,03 g/l and a low effective plasma osmolarity (254,02 mmol/kg H₂O), normal infectious workup, elevated creatinine (120 umol/l), elevated urea (0,97g/l) in favor of functional acute renal failure.

The diagnosis of hypovolemic shock was made, with the origin of the loss most likely being the kidney. The urinary ionogram (Supplementary Table 3) showed very high natriuresis (62mmol/l) with urine chloride at (64mmol/l).

Given the Hypovolemic shock on admission, hypotonic hyponatremia as well as an increase in renal loss of Na⁺, without any notion of taking diuretics, and the notion of cerebral hemorrhage, the diagnosis of CWS is made. We completed the investigations with Brain Natriuretic Peptid (BNP) coming back very high (376pg/mL, normal <30pg/ml) which is in favor of the diagnosis.

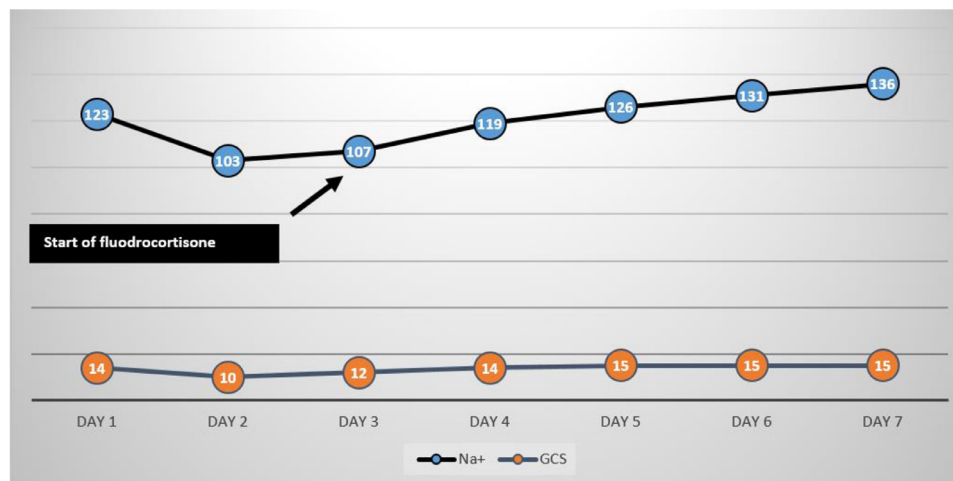
The treatment was based on correction of fluid and electrolyte disturbances using isotonic saline. correction of hypokalemia via a central line and monitoring secondary cerebral injury of systemic origin.

After 24 hours, the patient presented altered state of consciousness (GCS at 10/15), the head CT scan (Fig. 1) did not show any worsening of the cerebral hemorrhage, and the natriemia was 103mmol/l (Table 1) which required correction with 3% hypertonic saline, with good clinical improvement.

On the 3rd day of hospitalization, treatment with fludrocortisone was initiated with a marked improvement in his neuro-

Table 1 – Serum electrolyte.

Variable	Normal value	Day1	Day2	Day3	Day4	Day5	Day6	Day7
Na+ (mmol/l)	135-145	123	103	107	119	126	131	136
Cl- (mmol/l)	98-107	54	59	62	68,8	78	81	86
K+ (mmol/l)	3,5-5,5	2,3	2,9	3,1	3,0	3,0	3,5	3,8
Alcaline reserve (mmol/l)	20-30	57	58	51	43	45	39	31

**Fig. 2 – Evolution of Serum Sodium and GCS Before and After Fludrocortisone**

logical state and natriemia (Fig. 2), and his hemodynamic state remained stable with normal diuresis.

On the 7th day of hospitalization, the patient was discharged home with a very good clinical and biological evolution.

Discussion

In 1950, Peters et al. first put forward a new hypothesis to explain the mechanism of hyponatremia in patients with cerebral injury; this hypothesis was subsequently developed to explain the CSW. It is characterized by hypotonic hyponatremia associated with hypovolemia secondary to inappropriate loss of sodium by the kidney [1].

In 1957 the description of SIADH by Schwartz et al [1] created great confusion between the two syndromes. Indeed, after the identification of SIADH, the incidence of CSW cases decreased significantly given the difficulty in distinguishing the 2 entities. Over time, several studies have been carried out to explain their pathophysiology, their difference clinically and therapeutically [1]. It has been described that several brain etiologies could be responsible for CSW, but in the majority of cases it is a subarachnoid hemorrhage [2].

In a retrospective study by Hoffman et al. in 335 patients with hyponatremia after SAH, SIADH was the most common cause of hyponatremia, and the incidence of CSW was directly proportional to the Hunt and Hess grades of severity [1]. For cases of hyponatremia secondary to brain injury other than

SAH, CSW was more common in neuro-meningeal tuberculosis in adults [3], and brain tumors in the pediatric population [4].

The exact origin of the sodium loss during CSW remains unclear, but two hypotheses are proposed. The first is that of the decrease in sympathetic stimulation of the juxtaglomerular apparatus responsible for a decrease in the reabsorption of sodium and water as well as a decrease in the secretion of renin and aldosterone [2]. And the second hypothesis concerns the natriuretic peptides especially the brain natriuretic peptide (BNP) and the atrial natriuretic peptide (ANP) which are found in increased concentration in patients with SAH, explaining the renal loss of sodium [1].

Clinically, the symptomatology depends on the etiology and severity of the hyponatremia and hypovolemia. The patient may complain of vomiting, muscle cramps, headache, orthostatic hypotension, confusion, or outright coma with shock.

Uygun et al. [5], were the first to propose diagnostic criteria:

1. Central nervous system injury,
2. Na <130mmol/L,
3. Urine Na >80mmol/day or >20mmol/L
4. Osmotic pressure of plasma <270mmol/L,
5. Urine osmotic pressure / blood osmotic pressure >1,
6. Urine volume > 1800ml/day.

More recently, in 2015, Jan Leonard et al [5], proposed 4 criteria including brain injury, hypotonic hyponatremia, absolute hypovolemia and renal sodium loss.

Table 2 – Clinical and biological elements that make the difference between SIADH and CSW.

Variable	CWS	SIADH
Blood pressure	Decreased	Normal or increased
Heart rate	Increased	Normal
Body weight	Decreased	Normal
Albumin	Increased	Normal
Hematocrit	Increased	Normal
CVP	Decreased	Normal or increased
Serum Na ⁺	Decreased	Decreased
Plasmatic osmolality	Decreased	Decreased
Urine volume	Increased	Normal
Urine Na ⁺	Increased	Increased or normal
Urinary osmolality	Increased	Increased
Urea	Increased	Normal or low
BNP	Increased	Normal
Management	Volume replacement Fludrocortisone	Fluid restriction

CVP: Central venous pressure

The main differential diagnosis remains SIADH. Which makes it possible to distinguish the two entities is blood volume [2]. SIADH presents with hypotonic hyponatremia but without signs of hypovolemia. (Table 2) shows the points of difference between CSW and SIADH [1,6].

According to a cohort done by Tobin et Al., NT-Pro BNP is a very good marker of hypovolemia in patients with hyponatremia in CSW, with a cutoff value of 125 pg/ml, a positive predictive value of 93.33% and a negative predictive value of 87.50%, which makes it possible to differentiate between SIADH and CSW [7].

The main etiology of CSW remains SAH but, any brain injury can cause this syndrome like neuro-meningeal infections especially tuberculosis, stroke, brain tumors, head injury and post-operative neurosurgery [1].

Management of CSW consists of correcting hypovolemia and at the same time correcting hyponatremia depending on the severity of symptoms [8]. According to European recommendations, 0.9% isotonic saline should be administered if symptoms are mild [8], but if hyponatremia is accompanied by moderate to severe symptoms, 3% hypertonic saline should be administered at a rate of 150ml in 20min without exceeding a correction of 10mmol/l during the first 24 hours [8].

Fludrocortisone was shown to be effective in the treatment of hyponatremia secondary to CSW. In 2018, a randomized study led by Misra et al. proved the role of fludrocortisone in the early correction of hyponatremia secondary to neuro-meningeal tuberculosis, but without effect on the results at 6 months (class II evidence). The dose used is 0.1 to 0.4 mg [8]. Good results were reported by Hasan et al. concerning the role of fludrocortisone in the treatment of hyponatremia of CSW secondary to SAH [9]. The role of fludrocortisone on hyponatremia remains evident given the physiology of Na⁺ regulation in the kidney [10].

In our case, our patient first received only physiological saline correction, but due to the worsening of his state of consciousness with no other explanation other than hypona-

tremia, he received hypertonic saline correction as well as treatment with fludrocortisone at a dose of 0.2 mg per day with an impressive improvement in his condition from the 3rd day of treatment.

Conclusion

The diagnosis of CSW in hyponatremia secondary to cerebral injury remains a challenge given the diagnostic difficulty between CSW and SIADH. But it is crucial to distinguish between the two, because if the treatment of CSW is volume replacement, SIADH on the other hand requires total water restriction. If this restriction is applied in patients with CSW, the evolution will be fatal.

Consent for publication

Obtained

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2021.08.049](https://doi.org/10.1016/j.radcr.2021.08.049).

REFERENCES

- [1] Cui H, et al. Inappropriate antidiuretic hormone secretion and cerebral salt-wasting syndromes in neurological patients. *Front. Neurosci* 2019;13. doi:[10.3389/FNINS.2019.01170](https://doi.org/10.3389/FNINS.2019.01170).
- [2] Cerdà-Esteve M, et al. Cerebral salt wasting syndrome: Review. *Eur J Intern Med* 2008;19:249–54. doi:[10.1016/j.ejim.2007.06.019](https://doi.org/10.1016/j.ejim.2007.06.019).
- [3] Misra U K, Kalita J, Singh R K, Bhoi S K. A study of hyponatremia in acute encephalitis syndrome: a prospective study from a tertiary care center in india. *J Intensive Care Med* 2019;34:411–17. doi:[10.1177/0885066617701422](https://doi.org/10.1177/0885066617701422).
- [4] Williams C N, Riva-Cambrin J, Bratton S L. Etiology of postoperative hyponatremia following pediatric intracranial tumor surgery. *J neurosurg Pediatr* 2016;17:303–9. doi:[10.3171/2015.7.PEDS15277](https://doi.org/10.3171/2015.7.PEDS15277).
- [5] Junhai Z, Jing Y, Li L. Cerebral salt-wasting syndrome in a critically ill patient: an easily neglected syndrome in Intensive Care Unit (ICU). *J Natl Med Assoc* 2020;112:258–61. doi:[10.1016/j.jnma.2020.03.013](https://doi.org/10.1016/j.jnma.2020.03.013).
- [6] Oh JY, Il Shin J, Ho J, Zieg J, Moritz M L, Maesaka J. Pediatrics mini review article syndrome of inappropriate antidiuretic hormone secretion and cerebral/renal salt wasting syndrome: similarities and differences. *Front Pediatr* 2015. doi:[10.3389/fped.2014.00146](https://doi.org/10.3389/fped.2014.00146).
- [7] Tobin G, Chacko A G, Simon R. Evaluation of NT-ProBNP as a marker of the volume status of neurosurgical patients developing hyponatremia and natriuresis: pilot study. *Neurol India* 2018;66:1383–8. doi:[10.4103/0028-3886.241401](https://doi.org/10.4103/0028-3886.241401).

- [8] Spasovski G, et al. Clinical practice guideline clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrol Dial Transpl* 2014;1–39. doi:[10.1093/ndt/gfu040](https://doi.org/10.1093/ndt/gfu040).
- [9] Hasan D, et al. Effect of fludrocortisone acetate in patients with subarachnoid hemorrhage. *Stroke* 2021;20:1156–61.
- [10] Misra U K, Kalita J, Kumar M. Trial registration clinical trials registry of India (ctri.nic.in) Identifier: CTRI/2017/10 /010255. *JAMA Neurol* 2018;75:1383–91. doi:[10.1001/jamaneurol.2018.2178](https://doi.org/10.1001/jamaneurol.2018.2178).