Received: 22 April 2021 | Revised: 12 October 2021 | Accepted: 3 November 2021

DOI: 10.1002/ccr3.5171

Clinical Case Reports Open Access WILEY

CASE REPORT

A rare case of neurological dysfunction due to severe hyponatremia after carotid artery endarterectomy: A review of the clinical approach to hyponatremia

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Funding information
None

Abstract

Development of severe hyponatremia after carotid endarterectomy procedure is rare. Several pathophysiological mechanisms related to the carotid endarterectomy procedure may infer an increased risk of developing this complication in specific populations.

KEYWORDS

carotid endarterectomy, hyponatremia, neurological dysfunction, post-operative

1 | INTRODUCTION

Hyponatremia is a common electrolyte disturbance encountered in the postoperative period. However, severe hyponatremia defined as serum sodium <120 mmol/L, following surgery is rare.[1] If untreated it can lead to serious neurologic complications including encephalopathy, seizures, and death. Conversely, a rapid correction of sodium levels may result in a major neurological sequelae due to osmotic demyelination syndrome.[1] Thus, it is important for perioperative clinicians to be familiar with the appropriate management of severe hyponatremia. Here, we present a patient who developed neurological dysfunction due to severe hyponatremia following carotid endarterectomy (CEA) surgery. Using this case example, we describe the pathophysiological mechanisms that place these patients at a higher risk for the development of this complication and review the clinical management of severe hyponatremia.

HIPPA Authorization: A written HIPAA authorization consent was obtained from the patient for the publication of this manuscript.

2 | CASE HISTORY

A 73-year-old woman with medical problems of hypertension, hyperlipidemia, and coronary artery disease underwent left CEA for asymptomatic carotid artery stenosis. Preoperative computed tomography (CT) angiogram showed severe calcification of the aortic arch and the proximal left common carotid artery. Her preoperative

laboratory workup was unremarkable with a baseline sodium of 139 mmol/L (Table 1). The operation was performed under regional anesthesia with sedation, and there were no intraoperative complications. The patient was discharged on postoperative day (POD) one in a stable condition.

On POD four, the patient presented to the emergency room with a three-day history of lethargy, confusion, nausea, and emesis. Given the patient's altered mentation, the initial history was provided by her family. On examination, the patient was somnolent and lacked orientation to person, place, or time. No other focal neurological deficits were appreciated. There was no peripheral edema, and the skin turgor was normal. Initial laboratory evaluation showed severe hyponatremia (109 mmol/L), hypokalemia, and normal renal function (Table 2).

3 | DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS, AND TREATMENTS

Patient's laboratory workup was significant for plasma hypoosmolality (224 mOsm/kg), inappropriate urinary concentration for the given plasma osmolality (405 mOsm/kg), a low serum uric acid level (1.5 g/dL), hypokalemia (2.9 mmol/L), and elevated urinary sodium excretion (83 mmol/L) (Table 2). The patient had normal cortisol and thyroid function tests. A CT scan of the head and chest radiographs showed normal findings. Our patient denied any increased water intake. A review of the patient's home medications revealed that she was prescribed chlorthalidone and carvedilol for hypertension for the past year.

The patient was admitted to the intensive care unit due to acute neurological symptoms. In light of this medical emergency, a 100 ml bolus of 3% saline was administered. She became alert and regained orientation to person, place, and time. Approximately four hours after hypertonic therapy, the sodium levels increased to 115 mmol/L. Additionally, a free water restriction of 1 liter per day was instituted and no further treatments with hypertonic saline were needed. Twenty-four hours after hypertonic therapy, the sodium level rose to 119 mmol/L. At this time, patient was initiated on oral urea-sodium at 45 grams per day. Sodium levels improved gradually over the course of the patient's hospitalization with a discharge value of 129 mmol/L. On admission, potassium chloride was started for hypokalemia and repletion was based on the concurrent increase in the sodium levels. Furthermore, patient's thiazide diuretic therapy was discontinued at the time of her admission. At the time of discharge, the patient was also provided with instructions not to restart her chlorthalidone.

TABLE 1 Patient's Preoperative Laboratory Workup

Sodium (mmol/L)	139
Potassium (mmol/L)	4.0
Chloride (mmol/L)	103
BUN (mg/dl)	15
Creatinine (mg/dl)	0.62
Hemoglobin (gm/dl)	12.4
Platelet Count (10^3/mcL)	276

4 | DISCUSSION

This case highlights the need for heightened vigilance for the possibility of hyponatremia as the cause of neurological dysfunction after CEA. Previously, only three cases of significant hyponatremia following CEA have been reported.[2–4] Of these, only one report described severe hyponatremia with a sodium of 119 mmol/L. Unlike previous cases, our patient developed profound hyponatremia with a sodium level of 109 mmol/L.

Patients undergoing CEA may be at increased risk for developing hyponatremia postoperatively due to higher vasopressin levels.[5] A relationship between carotid baroreceptor activity and increased plasma antidiuretic hormone (ADH) levels has been demonstrated in patients status post-CEA.[6] It is suggested that the endarterectomy-related arterial injury results in the activation of platelets and humoral factors that are transported to the hypothalamus via carotid circulation stimulating ADH secretion.[5] Additionally, it is postulated that the decreased wall distension of the carotid arterial walls or the aortic arch due to atherosclerosis lowers baroreflex-mediated afferent nerve traffic to the nucleus tractus solitarii which causes an increased efferent sympathetic nerve activity and ADH release.[7] Interestingly, an increased incidence of Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) after neck dissections has been described as well.[8] It is hypothesized that elevated cerebral venous pressures as a result of jugular vein ligation during neck dissections results in an increase in the ADH secretion.[8]

In any case of hyponatremia, the initial diagnostic approach includes a serum osmolality evaluation. A serum osmolarity of 280–295 mOsm/kg defines isotonic hyponatremia. Isotonic hyponatremia can be seen with bladder irrigation and pseudohyponatremia where normal plasma sodium concentration is erroneously reported as low due to the presence of hyperlipidemia or hyperproteinemia. Differential diagnosis for hypertonic hyponatremia, defined as serum osmolarity >295 mOsm/kg,

includes hyperglycemia, mannitol, or contrast agents. Hypotonic hyponatremia is defined as a serum osmolarity of <280 mOsm/kg.[9] However, determination of etiology and appropriate management for hypotonic hyponatremia first requires a thorough assessment of volume status.[9] In contrast to isotonic and hypertonic hyponatremia, the development of hypotonic hyponatremia may be secondary to a multitude of pathologies impacting fluid balance. As such, hypotonic hyponatremia may be dilutional due to volume overload or the result of drugs and/or conditions that cause volume contraction.

TABLE 2 Patient's Laboratory Values at the time of Presentation to the Emergency Room on the Post-operative Day Four

Laboratory Investigation	Patient Result	Reference Range
Serum Sodium	109	136–145 mmol/L
Urine Sodium	83	<20 mmol/L
Serum Osmolality	224	275–295 mOsm/kg
Urine Osmolality	405	38–1400 mOsm/kg
Blood Urea Nitrogen	10	7–25 mg/dl
Serum Creatinine	0.60	0.6–1.2 mg/dl
Urine Specific Gravity	1.010	1.016–1.022
Serum Potassium	2.9	3.5–5.1 mmol/L
Serum Uric Acid	1.5	2.3–7.6 g/dl
Serum Glucose	132	70–105 mg/dl

As seen in this case, hypotonic hyponatremia may occur in euvolemic states as well. SIADH remains the leading cause of euvolemic hyponatremia although other etiologies may also be responsible (Figure 1).[9] As in this patient, adrenal insufficiency and hypothyroidism must be excluded prior to reaching the diagnosis of SIADH.[9] Given the severe decline in sodium, laboratory findings, and medication review, the development of hyponatremia in our patient was likely SIADH exacerbated by the use of thiazide diuretics.

Since 1957, thiazide diuretics have been widely prescribed for the management of hypertension.[10] Though adverse effects such as hypokalemia are generally appreciated, thiazide-associated hyponatremia (TAH) is a frequently occurring electrolyte abnormality that has been well described yet not widely known.[10–12] Diagnosis of TAH can be difficult as the laboratory data of individuals with TAH are compatible with those of SIADH. In both etiologies, a state of euvolemia is accompanied by hyponatremia and serum hypoosmolality, inappropriate hyperosmolality of the urine for the associated plasma tonicity, and an inappropriate urinary sodium excretion (usually >40 mmol/L).[13] Measurement of serum uric acid levels can be helpful to determine the presence of TAH with coexistent SIADH. Individuals with serum uric acid levels <4 gm/dl usually exhibit SIADH with concurrent TAH, as the case here.[14]

Although a number of risk factors for TAH have been proposed, female gender, low body weight, and advanced

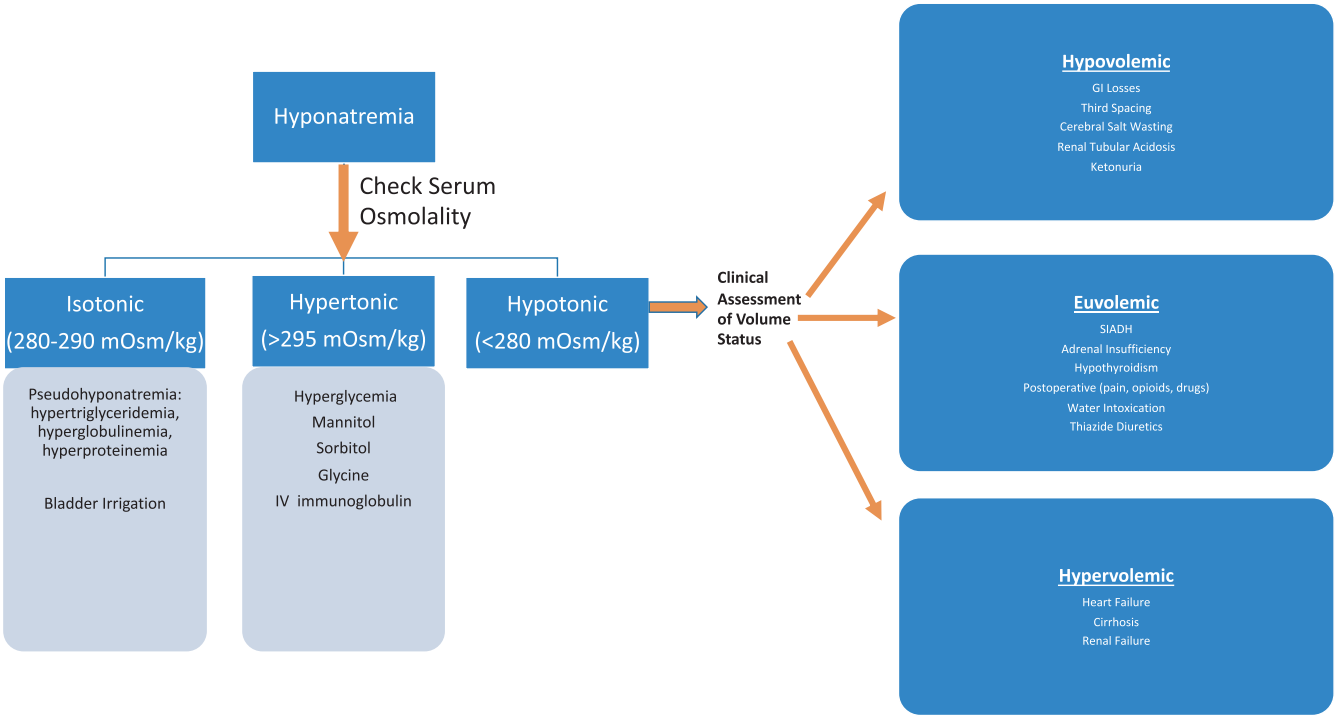

FIGURE 1 Practical Diagnostic Approach to Hyponatremia in the Perioperative Period

age are the most frequently reported.[10–12,14] Our patient was a 73-year-old female who weighed 54.5 kg and was taking chlorthalidone. The relative risk for TAH is 3-4-fold higher in those 70 years or older. This is likely the result of age-related reductions in the glomerular filtration rate and subsequent impairment of free water excretion.[12,14] Though not fully elucidated, low body weight is suggested to impair the renal diluting capacity.[14] Within the class of thiazide diuretics, chlorthalidone is observed to have a higher incidence of TAH.[14] The onset of TAH is typically within 14–19 days of starting therapy; however, it has been reported to occur as early as 1–2 days or be delayed with an onset of months to years.[11,12]

Several proposed mechanisms describe the pathophysiology of TAH. These include reduced sodium reabsorption in the distal tubules, impaired free water excretion, or both. Impaired free water excretion in TAH is potentially secondary to impaired regulation of ADH. Studies have shown that water reabsorption in the collecting duct of the renal tubule is inducible by thiazide administration. Specifically, thiazides upregulate ADH-mediated water permeable transporters or aquaporins, which increase water permeability of apical cells in the renal collecting duct. This increase in water permeability is inhibited by the ADH antagonist prostaglandin-E_2.[11,12,14]

While the causes of hyponatremia may be multifactorial, the primary treatment strategy remains consistent for both thiazide and non–thiazide-associated euvolemic hyponatremia which is the removal or correction of the underlying etiology along with free water restriction. For patients with severe symptomatic hyponatremia, hypertonic saline and vasopressin receptor antagonists (VRAs) have been found to be effective.[10,11,14–17] However, the role of VRAs for TAH has yet to be established.[10,14]

Additionally, urea oral powder has been used to treat both thiazide and non–thiazide-associated hyponatremia.[1,15] Greater than 90% of oral urea is readily absorbed from the upper gastrointestinal tract and is freely filtered by the glomerulus.[1,15] Approximately 50% of urea is passively reabsorbed within the nephron and the remaining filtered urea is excreted in the urine. Urea promotes sodium homeostasis by increasing free water elimination through osmotic diuresis and by reducing sodium loss from natriuresis.[15] Urea is generally safe and well tolerated. The most commonly reported adverse effects are dysgeusia, nausea, and hypokalemia.[15] When compared to hypertonic saline and VRAs, urea has not been associated with the development of osmotic demyelinating syndrome even in the setting of rapid correction of sodium. Urea does not induce hepatotoxicity, and it can be administered in high doses without precipitating acute renal failure.[15]

Furthermore, potassium repletion in patients with hyponatremia must be carried out cautiously as increased potassium results in the shift of sodium from the cell into the extracellular fluid. Thus, treatment strategies must be altered to account for the potassium supplementation as osmotic demyelination following potassium repletion has occurred.[18]

In summary, perioperative clinicians must maintain vigilance for severe hyponatremia as the cause of postoperative neurological decline and be familiar with the clinical management of hyponatremia to prevent devastating neurological injury.

ACKNOWLEDGMENT

None.

CONFLICT OF INTEREST

None.

AUTHOR'S CONTRIBUTION

NF: This author helped with the data analysis, writing the first draft of the manuscript, and critical revisions of the final manuscript. CW, RG, and AP: These authors helped with writing the first draft of the manuscript and critical revisions of the final manuscript. BF: This author helped with conception and development of the manuscript idea, data collection, data analysis, writing the first draft of the manuscript, and critical revisions of the manuscript.

ETHICAL APPROVAL

We hereby confirm that the present study conforms to the ethical standards and guidelines of the journal.

DATA AVAILABILITY STATEMENT

Data sharing not applicable – no new data generated

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How to cite this article: Ferrero NA, Ward CT, Groff RF, Prabhakar A, Fiza B. A rare case of neurological dysfunction due to severe hyponatremia after carotid artery endarterectomy: A review of the clinical approach to hyponatremia. *Clin Case Rep*. 2021;9:e05171. doi:10.1002/ccr3.5171