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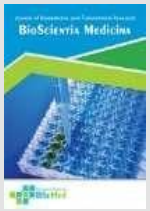

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Hyponatremia After Intracranial Hemorrhage: Cerebral Salt Wasting Syndrome (CSWS) or The Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)?

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A B S T R A C T

Background: Hyponatremia is a common electrolyte disorder encountered in neurosurgical patients, often associated with significant morbidity and mortality. This case report highlights the importance of recognizing and appropriately managing cerebral salt wasting syndrome (CSWS), a rare but important cause of hyponatremia in neurosurgical patients, often following intracranial hemorrhage (ICH). Distinguishing CSWS from the syndrome of inappropriate antidiuretic hormone secretion (SIADH) is crucial for appropriate management. **Case presentation:** A 56-year-old male with a history of hypertension and diabetes mellitus presented with sudden-onset left-sided weakness and decreased consciousness following an ICH. He underwent a ventriculoperitoneal (VP) shunt placement for hydrocephalus. Post-operatively, he developed hyponatremia with elevated urine sodium levels and hypovolemia, suggestive of CSWS. The patient was treated with fluid replacement therapy, including hypertonic saline, and desmopressin, resulting in improvement in his hyponatremia. **Conclusion:** CSWS is an important cause of hyponatremia in neurosurgical patients. Prompt diagnosis and appropriate management, including fluid replacement and potentially desmopressin, can improve patient outcomes. This case underscores the need for a high index of suspicion for CSWS in neurosurgical patients presenting with hyponatremia and highlights the importance of careful monitoring and individualized treatment strategies.

1. Introduction

Hyponatremia, defined as a serum sodium concentration below 135 mEq/L, is a frequently encountered electrolyte disturbance in hospitalized patients, and it is particularly prevalent among those in intensive care units (ICUs). This condition carries the potential for serious complications and can significantly impact patient outcomes. In the context of neurosurgical patients, hyponatremia is especially concerning due to its association with increased morbidity and mortality. The underlying causes of hyponatremia in this patient population are diverse, encompassing a range of conditions such as cerebral salt wasting syndrome (CSWS), syndrome of inappropriate antidiuretic hormone secretion (SIADH), and others.[1,2]

CSWS is a clinical entity characterized by the inappropriate renal excretion of sodium, leading to hyponatremia in conjunction with hypovolemia. This syndrome is often observed following severe brain injury, including subarachnoid hemorrhage, intracranial hemorrhage, traumatic brain injury, and

neurosurgical procedures. The precise mechanisms underlying CSWS remain incompletely understood, but current research suggests that it may involve the release of natriuretic peptides, primarily brain natriuretic peptide (BNP), in response to brain injury. These peptides promote natriuresis, or the excretion of sodium in the urine, and contribute to the development of hyponatremia and hypovolemia. The impairment of the renin-angiotensin-aldosterone system (RAAS), a key regulator of fluid and electrolyte balance, may also play a role in the pathogenesis of CSWS. SIADH, in contrast, is characterized by the excessive release of antidiuretic hormone (ADH), also known as vasopressin. This hormone acts on the kidneys to increase water reabsorption, leading to dilutional hyponatremia. SIADH is associated with euvolemia or hypervolemia, distinguishing it from CSWS. Various factors can contribute to SIADH in neurosurgical patients, including intracranial tumors, infections, and medications.[3-5]

The accurate differentiation between CSWS and SIADH is of paramount importance for guiding appropriate management strategies. CSWS typically necessitates fluid replacement therapy, often with hypertonic saline, to address both hypovolemia and hyponatremia. SIADH, on the other hand, is generally managed with fluid restriction. In certain cases, medications such as vaptans, which are ADH receptor antagonists, or demeclocycline, which inhibits the renal response to ADH, may be employed to block the effects of ADH and promote water excretion. The clinical presentation of CSWS can be variable, ranging from subtle findings to more overt symptoms. Common manifestations include hyponatremia, hypovolemia, polyuria (excessive urination), and signs of dehydration such as dry mucous membranes and decreased skin turgor. In severe cases, hypotension and tachycardia may be observed. The diagnosis of CSWS is established based on a combination of clinical features, laboratory findings, and the exclusion of other potential causes of hyponatremia. Key laboratory findings include hyponatremia, elevated urine sodium concentration, and high urine osmolality.[6-8]

The management of CSWS focuses on correcting both hypovolemia and hyponatremia. Fluid replacement therapy is the cornerstone of treatment, with the choice of fluid depending on the severity of hyponatremia and the patient's clinical status. Isotonic saline (0.9% sodium chloride) may be used for mild hyponatremia, while hypertonic saline (3% sodium chloride) is often reserved for severe or symptomatic cases. In addition to fluid replacement, desmopressin, a synthetic analogue of ADH, may be considered in some cases to reduce urine output and conserve sodium.[9,10] In this case report, we present a case of a 56-year-old man with intracranial hemorrhage who developed hyponatremia during his ICU stay. His clinical presentation and laboratory findings were consistent with CSWS. The patient was treated with fluid replacement therapy and desmopressin, resulting in an improvement in his hyponatremia. This case highlights the importance of recognizing and appropriately managing CSWS in neurosurgical patients.

2. Case Presentation

A 56-year-old male presented to the Emergency Department of Arifin Achmad Regional General Hospital in Riau Province, Indonesia, with complaints of sudden-onset left-sided weakness and decreased consciousness. The patient had a history of controlled hypertension and diabetes mellitus, managed with regular medications including Candesartan 16 mg, Amlodipine 10 mg, and Metformin 500 mg three times daily. He had been referred from another hospital in Pekanbaru due to complaints of headaches. Upon arrival at the ICU, the patient was conscious but disoriented, with a Glasgow Coma Scale (GCS) score of E4M6V4. His vital signs were as follows: blood pressure 155/77 mmHg, heart rate 72 beats per minute, respiratory rate 16 breaths per minute, and temperature 36.7°C. Oxygen saturation was 97%. Physical examination revealed no abnormalities in the head, neck, or chest. A neurological examination revealed left-sided weakness. Initial laboratory

investigations showed hyponatremia (serum sodium 127 mmol/L) and hyperglycemia (serum glucose 372 mg/dL), with no signs of infection. A non-contrast head CT scan performed on December 13, 2021, revealed a hyperdense lesion in the right lateral ventricle, a hyperdense lesion in the right basal ganglia, and signs of intraventricular and intracerebral hemorrhage. There was also evidence of hydrocephalus (Figures 1 and 2).

Based on these findings, the patient underwent a VP shunt placement to alleviate intracranial pressure. Post-operatively, he was admitted to the ICU. His initial post-operative course was stable, with a reduction in headache intensity. However, on the third post-operative day, the patient's family reported increased thirst and a significant rise in urine output, reaching approximately 4600 ml in 24 hours, compared to 2200 ml in the previous 24 hours. Further investigations were initiated, including serum electrolyte monitoring, urinalysis, and urine output measurement. Urine output over the next 24 hours was measured at 4100 ml, with a total fluid intake of 4341.3 ml to compensate for the high urine output. The estimated urine production rate was 2.45 ml/kg body weight per hour. Urinalysis revealed elevated levels of sodium (258 mmol/24 hours), potassium (89 mmol/24 hours), and chloride (258 mmol/24 hours). Serum electrolyte levels were as follows: sodium 133 mmol/L, potassium 3.5 mmol/L, and calcium 1.05 mmol/L (Table 1).

In response to these findings, fluid replacement therapy with 0.9% sodium chloride solution was initiated, along with close monitoring of fluid balance and serial electrolyte checks. On the 11th day of hospitalization, repeat urine electrolyte measurements showed a further increase in sodium (407 mmol/24 hours), potassium (108 mmol/24 hours), and chloride (361 mmol/24 hours). Serum electrolyte levels were sodium 144 mmol/L, potassium 4.1 mmol/L, and calcium 1.20 mmol/L. Urine output remained high at approximately 4550 ml, with a fluid intake of 5972.5 ml and a urine production rate of 2.37 ml/kg body weight per hour. On the following day, the patient's clinical condition remained stable, but urine output increased further to approximately 12300 ml in 24 hours, with a urine production rate of 6.4 ml/kg body weight per hour (Figures 3 and 4). Fluid balance was closely monitored, and desmopressin 0.3 mg every 8 hours was added to the treatment regimen. Serum and urine osmolality were measured, revealing a serum osmolality of 303 mOsmol/kg H_2O and a urine osmolality of 417 mOsmol/kg H_2O. Based on the clinical presentation, laboratory findings, and elevated urine sodium levels despite hyponatremia, a diagnosis of cerebral salt wasting syndrome (CSWS) was made (Table 2). The patient's underlying conditions, including intraventricular hemorrhage, intracerebral hemorrhage, hypertension, diabetes mellitus, and recent VP shunt placement for acute hydrocephalus, were also considered. The patient's management was intensified, including the placement of a urinary catheter and a central venous line for close monitoring of fluid balance and volume status. Correction of hyponatremia was initiated with intravenous 3% sodium chloride solution, and dexamethasone 4 mg every 6 hours was added to the treatment regimen.

3. Discussion

Hyponatremia, defined as a serum sodium concentration below 135 mEq/L, is a prevalent electrolyte disturbance encountered in neurosurgical patients. This condition frequently arises in individuals who have undergone brain surgery or experienced a neurological event, such as a stroke or traumatic brain injury. The incidence of hyponatremia in this patient population can vary depending on the specific underlying condition and the type of neurosurgical intervention. Studies have reported that hyponatremia occurs in approximately 15-30% of patients following brain surgery and in up to 70% of patients with subarachnoid hemorrhage. The presence of hyponatremia in neurosurgical patients is associated with a range of adverse outcomes, including increased morbidity and mortality.

Table 1. Timeline of disease.

Day	Clinical events	Laboratory findings	Imaging findings	Treatment
1	Admission to hospital with decreased consciousness and left-sided weakness. History of hypertension and diabetes mellitus.	Hyponatremia (serum sodium 127 mEq/L) Hyperglycemia No evidence of infection	Head CT scan: Intraventricular hemorrhage, intracerebral hemorrhage, and hydrocephalus	VP shunt placement
2	Postoperative care in ICU. Headache improved. Blood pressure 130/70 mmHg, heart rate 84 bpm, temperature 36.8°C, VAS 2, GCS E4M6V4. Left-sided weakness persists. Pupils isochoric.	-	-	Pain management
3	Condition stable. Blood pressure 140/90 mmHg, heart rate 68 bpm, VAS 2, GCS E4M6V4.	-	-	Continued postoperative care
4	Blood pressure 160/100 mmHg, heart rate 90 bpm, VAS 3, GCS E4M6V4. Increased thirst and urine output (4600 ml/24h). The family is concerned about increased urine output.	Urine output: 4600 ml/24h	-	Serum electrolytes, urinalysis, and urine volume measurement planned.
5	Urine output: 4100 ml/24h Diuresis: 2.45 ml/kg/h	Urinalysis: Sodium 258 mMol/24h (reference range 40-220) Potassium 89 mMol/24h (reference range 25-125) Chloride 258 mMol/24h (reference range 110-250) Serum electrolytes: Sodium 133 mEq/L Potassium 3.5 mEq/L Calcium 1.05 mEq/L	-	Fluid replacement with 0.9% NaCl, fluid balance monitoring, and serial electrolyte checks. Other therapies continued.
11	Urine output: 4550 ml/24h Diuresis: 2.37 ml/kg/h	Urinalysis: Sodium 407 mMol/24h Potassium 108 mMol/24h Chloride 361 mMol/24h Serum electrolytes: Sodium 144 mEq/L Potassium 4.1 mEq/L Calcium 1.20 mEq/L	-	Continued fluid management and monitoring.
12	No clinical deterioration. GCS E4M6V. Increased urine output (12300 ml/24h). Diuresis: 6.4 ml/kg/h.	-	-	Fluid balance monitoring. Desmopressin 0.3 mg every 8 hours. Serum and urine osmolality are planned.
13	-	Serum osmolality: 303 mOsmol/kgH2O (reference range 275-295) Urine osmolality: 417 mOsmol/kgH2O (reference range 300-900)	-	Diagnosis of CSWS confirmed. Urinary catheter placement. Central line placement for volume monitoring. Fluid balance monitoring. Sodium correction with 3% NaCl drip. Dexamethasone 4 mg every 6 hours.
21	-	-	Follow-up head CT scan	-

Table 2. Detailing the diagnostic approach CSWS Vs SIADH.

Clinical Feature	CSWS	SIADH
History	Intracranial hemorrhage, trauma, neurosurgery	Similar to CSWS, also medications, lung disease, malignancy
Volume status	Hypovolemia	Euvolemia or hypervolemia
Urine output	Increased	Normal or decreased
Urine sodium	Elevated (>40 mEq/L)	Elevated (>40 mEq/L)
Serum osmolality	Decreased (<275 mOsm/kg)	Decreased (<275 mOsm/kg)
Urine osmolality	Increased (>100 mOsm/kg)	Increased (>100 mOsm/kg)
Response to fluid replacement	Improves hyponatremia	No improvement or worsening of hyponatremia

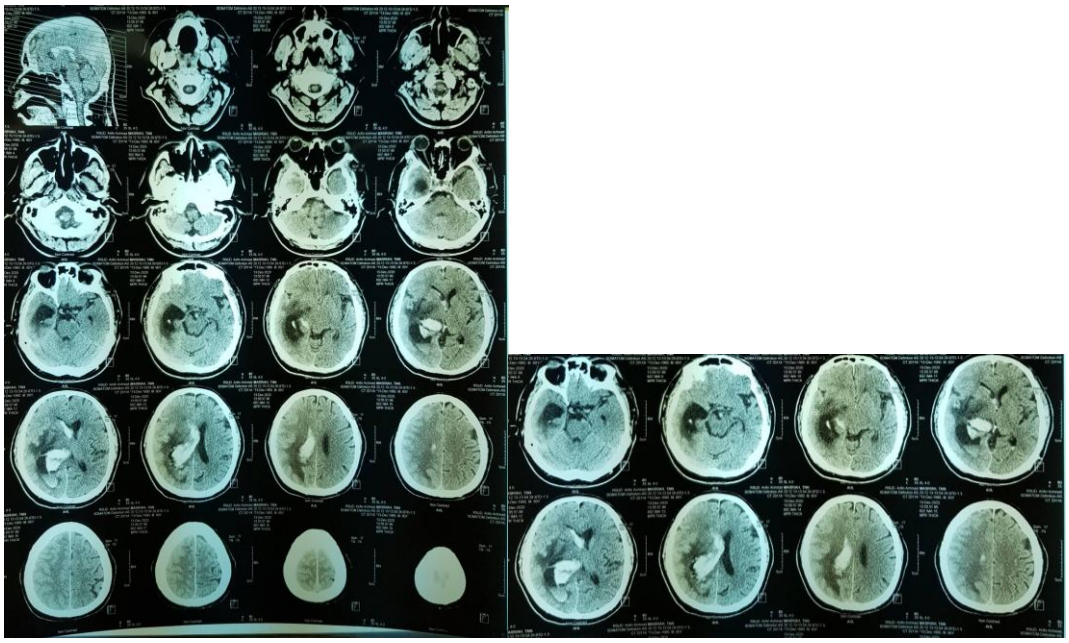

Figure 1. Head CT scan of the patient obtained on admission to the intensive care unit.

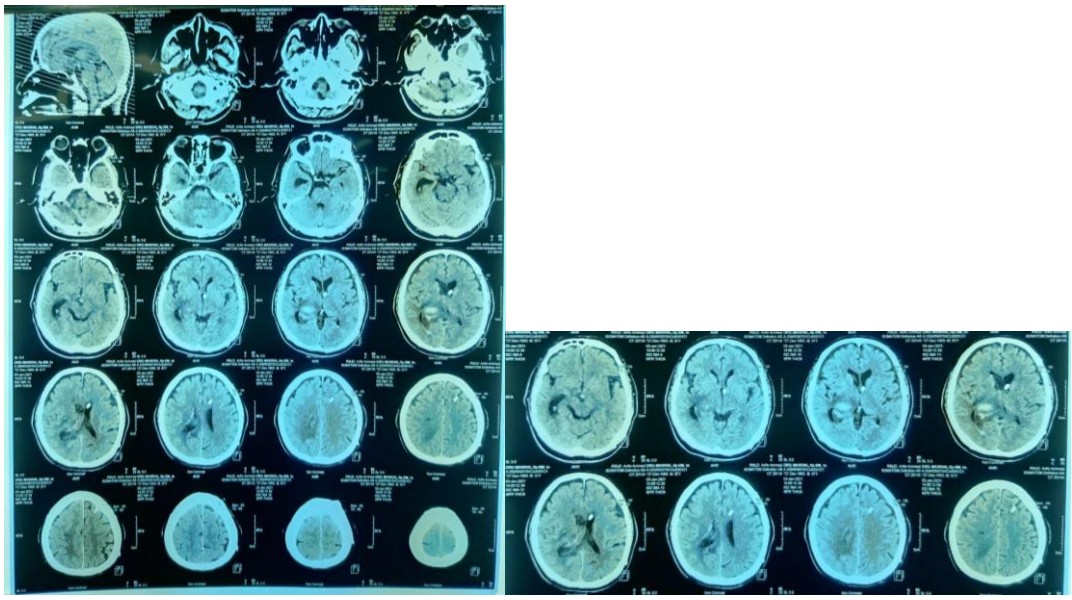

Figure 2. Follow-up head CT scan obtained on day 21 of the patient's hospital stay.

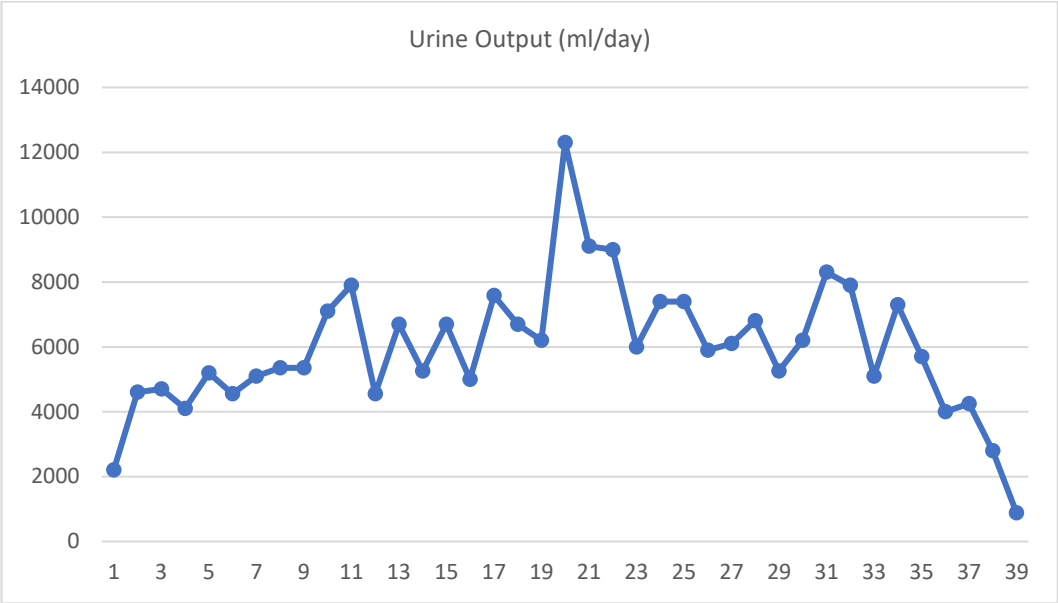

Figure 3. Daily urine output.

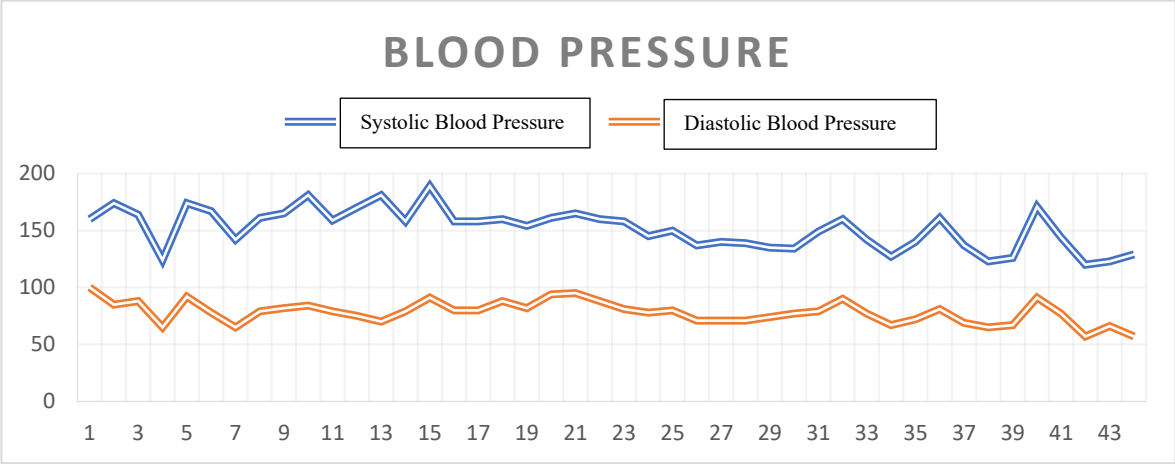

Figure 4. Monitoring of blood pressure.

Hyponatremia can exacerbate cerebral edema, a condition characterized by swelling of the brain tissue, which can lead to elevated intracranial pressure and potentially life-threatening complications. Moreover, hyponatremia can disrupt neuronal function, resulting in neurological deficits such as seizures, confusion, and coma. Studies have demonstrated that hyponatremia is an independent predictor of poor outcomes in neurosurgical patients, including prolonged hospital stays, increased risk of complications, and higher mortality rates. SIADH is characterized by the excessive release of antidiuretic hormone (ADH), leading to increased water reabsorption by the kidneys and dilutional hyponatremia. SIADH is often associated with euvolemia or hypervolemia, meaning that the total body sodium content is normal or even elevated, but the excess water retention leads to a decrease in serum sodium concentration. In neurosurgical patients, SIADH can be triggered by various factors, including intracranial tumors, infections, and medications. CSWS is characterized by the

inappropriate renal excretion of sodium, leading to hyponatremia in conjunction with hypovolemia. The exact pathophysiology of CSWS is not fully understood but is thought to involve the release of natriuretic peptides, primarily brain natriuretic peptide (BNP), in response to brain injury. These peptides promote natriuresis, or the excretion of sodium in the urine, and contribute to the development of hyponatremia and hypovolemia. Other conditions that can contribute to hyponatremia in neurosurgical patients include hypothyroidism, adrenal insufficiency, and medications such as diuretics and antiepileptic drugs. Accurate diagnosis of the underlying cause of hyponatremia is crucial for appropriate management and improved patient outcomes. This often involves a combination of clinical assessment, laboratory investigations, and imaging studies. Clinical assessment may reveal signs of hypovolemia, such as dry mucous membranes, decreased skin turgor, and hypotension, which may suggest CSWS. Laboratory investigations typically include serum electrolyte levels, urine sodium concentration, and serum and urine osmolality. Imaging studies, such as head CT scans or MRI, may be performed to identify any underlying neurological conditions. The management of hyponatremia in neurosurgical patients depends on the underlying cause and the severity of the hyponatremia. In general, the goals of treatment are to correct the underlying cause, restore serum sodium levels to the normal range, and prevent complications such as cerebral edema and seizures. Fluid management is a cornerstone of hyponatremia treatment. In patients with hypovolemia, such as those with CSWS, fluid replacement therapy is essential. The choice of fluid depends on the severity of hyponatremia and the patient's clinical status. Isotonic saline (0.9% sodium chloride) may be used for mild hyponatremia, while hypertonic saline (3% sodium chloride) is often reserved for severe or symptomatic cases. In patients with euvolemia or hypervolemia, such as those with SIADH, fluid restriction may be necessary. In some cases, medications may be used to treat hyponatremia. Vaptans, which are ADH receptor antagonists, can be used to promote water excretion in patients with SIADH. Demeclocycline, which inhibits the renal response to ADH, may also be used in SIADH. In patients with CSWS, desmopressin, a synthetic analogue of ADH, may be considered in some cases to decrease urine output and conserve sodium. If an underlying condition is contributing to hyponatremia, such as hypothyroidism or adrenal insufficiency, treatment of that condition is essential. Close monitoring of fluid balance, electrolyte levels, and clinical status is essential in managing hyponatremia in neurosurgical patients. This monitoring helps to ensure appropriate fluid replacement, prevent complications such as overcorrection of hyponatremia, and guide adjustments to the treatment plan as needed.[11,12]

Cerebral salt wasting syndrome (CSWS) is a rare but serious condition characterized by the inappropriate renal excretion of sodium, leading to hyponatremia (low blood sodium levels) and hypovolemia (decreased blood volume). This syndrome typically occurs in individuals who have experienced a brain injury, such as a stroke, traumatic brain injury, or brain surgery. Hyponatremia can lead to fatigue, nausea, vomiting, headache, confusion, seizures, and coma. Hypovolemia can cause thirst, dry mouth, decreased urine output, low blood pressure, and rapid heart rate. Despite being hypovolemic, patients with CSWS may have increased urine output due to the impaired ability of the kidneys to conserve sodium. Diagnosing CSWS can be challenging, as it often mimics other conditions that cause hyponatremia, such as the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Patients with CSWS are typically hypovolemic, while those with SIADH are euvolemic or hypervolemic. Patients with CSWS typically respond to fluid replacement with an increase in serum sodium levels, while those with SIADH may not. Urine sodium concentration is typically high in CSWS due to the inappropriate renal excretion of sodium. Brain natriuretic peptide (BNP) is a hormone that is released in response to brain injury. BNP

promotes natriuresis (excretion of sodium in the urine), which can lead to hyponatremia and hypovolemia. The RAAS is a hormonal system that plays a crucial role in regulating fluid and electrolyte balance. Brain injury can disrupt the RAAS, leading to decreased aldosterone secretion. Aldosterone is a hormone that promotes sodium reabsorption in the kidneys. Reduced aldosterone levels can contribute to sodium loss and hyponatremia. Brain injury can activate the sympathetic nervous system, which can lead to increased renal blood flow and glomerular filtration rate. This can result in increased sodium excretion and hyponatremia. The primary goal of CSWS treatment is to correct hyponatremia and hypovolemia. This is typically achieved through fluid replacement therapy, often with hypertonic saline (3% sodium chloride solution). Hypertonic saline helps to increase serum sodium levels and expand blood volume. In some cases, desmopressin (a synthetic form of antidiuretic hormone) may be used to reduce urine output and conserve sodium. The prognosis for patients with CSWS varies depending on the severity of the condition and the underlying brain injury. With prompt diagnosis and appropriate treatment, many patients can recover fully. However, in some cases, CSWS can lead to serious complications, such as seizures, coma, and even death.[13,14]

Cerebral salt wasting syndrome (CSWS) and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) are two conditions that can lead to hyponatremia (low sodium levels in the blood) in neurosurgical patients. Distinguishing between these two conditions can be challenging due to overlapping clinical and laboratory features. However, accurate differentiation is crucial as the treatment approaches for CSWS and SIADH differ significantly. Misdiagnosis can lead to inappropriate management and potentially worsen patient outcomes. Volume status refers to the amount of fluid in the circulatory system, specifically the blood volume within the blood vessels. It is a critical physiological parameter that reflects the body's fluid balance and plays a crucial role in maintaining blood pressure, tissue perfusion, and overall cardiovascular function. In the context of hyponatremia, assessing volume status is essential for differentiating between cerebral salt wasting syndrome (CSWS) and the syndrome of inappropriate antidiuretic hormone secretion (SIADH), two conditions with distinct pathophysiological mechanisms and treatment approaches. CSWS is characterized by hypovolemia, a state of decreased blood volume. This occurs due to the inappropriate excretion of sodium and water by the kidneys, leading to a net loss of fluid from the body. The hypovolemia in CSWS can range from mild to severe, depending on the extent of sodium and water loss. In contrast to CSWS, SIADH is associated with euvolemia (normal blood volume) or hypervolemia (increased blood volume). This is because SIADH involves the excessive retention of water by the kidneys, without a corresponding increase in sodium excretion. The retained water dilutes the blood, leading to hyponatremia, but the overall blood volume remains normal or even increases. Assessing volume status is an important step in evaluating patients with hyponatremia. It involves a combination of clinical findings and laboratory tests. An elevated heart rate (tachycardia) can be a sign of hypovolemia, as the body tries to compensate for the decreased blood volume by increasing cardiac output. Low blood pressure (hypotension) can also indicate hypovolemia, although it may not be present in all cases, especially if the patient is lying down. Orthostatic hypotension, a drop in blood pressure upon standing, can be a more sensitive indicator of hypovolemia. Jugular venous pressure (JVP) is the pressure in the jugular veins, which reflects the right atrial pressure and overall fluid status. A low JVP suggests hypovolemia, while a high JVP suggests hypervolemia. Decreased skin turgor, where the skin remains tented after being pinched, can be a sign of dehydration and hypovolemia. Dry mucous membranes, such as a dry mouth or tongue, can also indicate dehydration and hypovolemia. Decreased urine output (oliguria) can be a sign of hypovolemia, as the body tries to conserve fluid. However, in some cases of CSWS, urine output

may be normal or even increased (polyuria) due to the impaired ability of the kidneys to conserve sodium. In addition to clinical assessment, laboratory tests can provide objective measures of volume status. Elevated blood urea nitrogen (BUN) and creatinine levels can indicate dehydration and hypovolemia. Hematocrit is the percentage of red blood cells in the blood. An elevated hematocrit can suggest hypovolemia due to hemoconcentration, where the blood becomes more concentrated as the fluid volume decreases. Urine sodium concentration is typically high in CSWS due to the inappropriate renal excretion of sodium. In SIADH, urine sodium concentration may be variable but is often lower than in CSWS. Accurate assessment of volume status is crucial for differentiating between CSWS and SIADH and guiding appropriate treatment. In CSWS, the primary treatment is fluid replacement to correct the hypovolemia and hyponatremia. In SIADH, the primary treatment is fluid restriction to reduce the excess water retention. Misdiagnosis and inappropriate treatment can lead to serious complications, such as worsening hyponatremia, cerebral edema, and seizures. Fluid management is a cornerstone in treating hyponatremia, especially in the context of neurosurgical conditions like Cerebral Salt Wasting Syndrome (CSWS) and Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH). The response to fluid management strategies, particularly the administration of intravenous fluids, can be a pivotal factor in differentiating between these two conditions and guiding appropriate treatment decisions. In CSWS, the underlying pathophysiology involves the inappropriate excretion of sodium by the kidneys, leading to hyponatremia and hypovolemia (decreased blood volume). Therefore, fluid replacement therapy is central to managing CSWS. The type and rate of fluid administration depend on the severity of hyponatremia and the patient's overall clinical status. For patients with mild hyponatremia, isotonic saline (0.9% sodium chloride solution) is often the initial fluid of choice. Isotonic saline expands the intravascular volume and helps to restore sodium balance without causing rapid changes in serum sodium levels. In cases of severe or symptomatic hyponatremia, hypertonic saline (3% sodium chloride solution) may be necessary. Hypertonic saline is more effective in rapidly raising serum sodium levels but requires careful monitoring to avoid overcorrection and potential complications like osmotic demyelination syndrome. Patients with CSWS typically respond favorably to fluid replacement therapy. The administration of isotonic or hypertonic saline helps to restore the depleted intravascular volume, improve renal perfusion, and promote sodium retention. This leads to an increase in serum sodium levels and improvement in clinical symptoms. In contrast to CSWS, SIADH involves the excessive retention of free water by the kidneys due to the inappropriate release of antidiuretic hormone (ADH). This leads to dilutional hyponatremia, where the serum sodium concentration is decreased due to an excess of water relative to sodium. In SIADH, fluid restriction is often the primary treatment strategy. Limiting fluid intake helps to reduce the excess water in the body and allows the kidneys to excrete the excess water while conserving sodium. The degree of fluid restriction depends on the severity of hyponatremia and the patient's clinical condition. Patients with SIADH may not respond well to fluid replacement therapy and may even experience a further decrease in serum sodium levels. This is because additional fluid administration can exacerbate the dilutional effect, leading to a further decrease in serum sodium concentration. The response to fluid management can be a valuable tool in differentiating between CSWS and SIADH. If a patient with hyponatremia shows improvement in serum sodium levels and clinical symptoms after receiving fluid replacement therapy, it suggests that the underlying cause is likely CSWS. This indicates that the hyponatremia was due to hypovolemia and sodium depletion, which responded to fluid and sodium replacement. If a patient with hyponatremia experiences a further decrease in serum sodium levels or shows no improvement after receiving fluid

replacement, it suggests that the underlying cause is likely SIADH. This indicates that the hyponatremia was due to dilutional effects of excess water retention, and additional fluid administration worsened the dilution. Urine sodium concentration is a crucial laboratory test used to evaluate the body's sodium balance and diagnose the underlying cause of hyponatremia (low blood sodium levels). It measures the amount of sodium excreted in the urine, providing valuable insights into the kidneys' handling of sodium. In differentiating between cerebral salt wasting syndrome (CSWS) and the syndrome of inappropriate antidiuretic hormone secretion (SIADH), two common causes of hyponatremia in neurosurgical patients, urine sodium concentration plays a pivotal role. Both CSWS and SIADH can present with elevated urine sodium levels, but the underlying mechanisms differ significantly. In CSWS, the elevated urine sodium concentration is a direct consequence of the inappropriate renal excretion of sodium. Despite the body's need to conserve sodium due to the existing hyponatremia, the kidneys fail to reabsorb sodium effectively, leading to its excessive loss in the urine. This inappropriate sodium excretion contributes to the development and maintenance of hyponatremia and hypovolemia (decreased blood volume) characteristic of CSWS. In SIADH, the elevated urine sodium concentration is often multifactorial and related to the expanded intravascular volume caused by excessive water retention. The increased blood volume leads to an increased glomerular filtration rate (GFR), the rate at which the kidneys filter blood. This increased GFR can result in an increased filtered load of sodium, overwhelming the kidneys' ability to reabsorb sodium fully, even though the kidneys are functioning normally in terms of sodium handling. Furthermore, the expanded intravascular volume in SIADH can suppress the renin-angiotensin-aldosterone system (RAAS), a hormonal system that regulates fluid and electrolyte balance. Aldosterone, a hormone produced by the adrenal glands, promotes sodium reabsorption in the kidneys. Suppression of the RAAS leads to decreased aldosterone levels, further contributing to increased sodium excretion in the urine. Interpreting urine sodium concentration in isolation can be misleading. It is essential to consider the patient's volume status and other clinical and laboratory findings to accurately differentiate between CSWS and SIADH. In a hypovolemic patient with hyponatremia and elevated urine sodium concentration, the diagnosis of CSWS is strongly suggested. This indicates that the kidneys are inappropriately excreting sodium despite the body's need to conserve it. In a euvolemic or hypervolemic patient with hyponatremia and elevated urine sodium concentration, the diagnosis of SIADH is more likely. The elevated urine sodium in this context is likely due to the increased GFR and suppressed aldosterone levels associated with the expanded intravascular volume. In addition to the key differentiating features discussed earlier, such as volume status and response to fluid management, several other laboratory tests can aid in distinguishing between cerebral salt wasting syndrome (CSWS) and the syndrome of inappropriate antidiuretic hormone secretion (SIADH). These tests provide further insights into the underlying pathophysiological mechanisms and help to guide appropriate treatment decisions. Serum osmolality measures the concentration of solutes in the blood. In both CSWS and SIADH, serum osmolality is typically low due to the presence of hyponatremia. Hyponatremia, or low blood sodium levels, is the primary driver of decreased serum osmolality in both conditions. While serum osmolality alone cannot differentiate between CSWS and SIADH, it helps to confirm the presence of hyponatremia and assess the severity of the condition. Urine osmolality measures the concentration of solutes in the urine. It reflects the kidneys' ability to concentrate urine and conserve water. In SIADH, urine osmolality is usually high due to the excessive reabsorption of water by the kidneys. This leads to the production of concentrated urine, even in the presence of hyponatremia. In CSWS, urine osmolality may be variable depending on the severity of hypovolemia and the degree of renal sodium and water loss. In some cases, urine osmolality may be

high due to the body's attempt to conserve water in response to hypovolemia. However, in other cases, urine osmolality may be normal or even low due to the impaired ability of the kidneys to concentrate urine effectively. Serum uric acid is a byproduct of purine metabolism. Measuring serum uric acid levels can be helpful in differentiating between CSWS and SIADH. In SIADH, serum uric acid levels are often low due to increased urinary excretion of uric acid. This is thought to be related to the increased glomerular filtration rate and the suppressed renin-angiotensin-aldosterone system associated with SIADH. In CSWS, serum uric acid levels may be normal or even elevated. This is because the hypovolemia in CSWS can lead to decreased renal blood flow and reduced uric acid clearance. Fractional Excretion of Uric Acid (FEUA) is a more specific test that assesses the renal handling of uric acid. It is calculated using the serum and urine uric acid levels and creatinine clearance. FEUA is often elevated in SIADH due to the increased urinary excretion of uric acid. In CSWS, FEUA is typically normal or low. Despite the distinct clinical and laboratory features that differentiate cerebral salt wasting syndrome (CSWS) from the syndrome of inappropriate antidiuretic hormone secretion (SIADH), distinguishing between these two conditions can still be challenging in some cases. This diagnostic difficulty arises due to several factors, including overlapping clinical presentations, similarities in some laboratory findings, and the dynamic nature of these conditions, particularly in the early stages. Both CSWS and SIADH can present with similar neurological symptoms, such as confusion, lethargy, and seizures. These symptoms are primarily attributed to the hyponatremia (low blood sodium levels) that occurs in both conditions. Hyponatremia can disrupt neuronal function and lead to cerebral edema (swelling of the brain tissue), which can manifest as neurological deficits. This overlap in clinical presentation can make it difficult to distinguish between CSWS and SIADH based on neurological symptoms alone. While some laboratory findings can help differentiate between CSWS and SIADH, others may overlap, particularly in the early stages of the conditions. Both conditions can present with elevated urine sodium levels, although the underlying mechanisms differ. This overlap in urine sodium concentration can create diagnostic confusion, especially if the patient's volume status is not carefully assessed. CSWS and SIADH are dynamic conditions, meaning that their clinical and laboratory features can evolve. In the early stages, the differentiating features may be subtle or less pronounced, making it challenging to arrive at a definitive diagnosis. For instance, a patient with CSWS may initially present with euvolemia or even mild hypervolemia due to the compensatory mechanisms activated in response to hypovolemia. This can mimic the volume status typically seen in SIADH. Given these diagnostic challenges, a thorough clinical assessment, careful monitoring of fluid balance and electrolyte levels, and dynamic testing may be necessary to accurately differentiate between CSWS and SIADH. A detailed clinical assessment, including a review of the patient's medical history, neurological examination, and assessment of volume status, is crucial. Careful attention should be paid to signs of hypovolemia, such as dry mucous membranes, decreased skin turgor, and orthostatic hypotension. Close monitoring of fluid intake and output, body weight, and serum electrolyte levels, particularly sodium, is essential. This helps to track the patient's fluid balance and assess the response to fluid management strategies. In challenging cases, dynamic testing, such as assessing the response to fluid challenges, may be necessary. This involves administering a controlled amount of intravenous fluid, such as isotonic saline, and monitoring the patient's serum sodium levels and clinical response. A significant increase in serum sodium levels after fluid administration suggests CSWS, while a lack of improvement or worsening of hyponatremia suggests SIADH.[15-17]

Desmopressin is a synthetic analog of vasopressin, also known as antidiuretic hormone (ADH). It is a medication that acts on the kidneys to regulate water balance and reduce urine output. In the context of

cerebral salt wasting syndrome (CSWS), where there is inappropriate renal sodium and water loss, desmopressin can play a role in mitigating excessive water loss and potentially improving hyponatremia (low blood sodium levels). Desmopressin exerts its effects by binding to vasopressin V2 receptors in the renal collecting ducts. These receptors are located on the surface of cells that line the collecting ducts, which are the final tubules responsible for concentrating urine and conserving water. Upon binding to V2 receptors, desmopressin triggers a signaling cascade that leads to the insertion of aquaporin-2 water channels into the cell membranes. Aquaporin-2 water channels are protein channels that facilitate the movement of water across cell membranes. Their insertion into the cell membranes of the renal collecting ducts increases the permeability of these cells to water. As a result, water is reabsorbed from the urine back into the bloodstream, leading to a reduction in urine output and conservation of water. Desmopressin can be administered intravenously, subcutaneously, intranasally, or orally. The route of administration affects its onset of action and duration of effect. Intravenous administration provides the most rapid onset, while intranasal and oral administration have a slower onset but a longer duration of effect. Desmopressin is metabolized in the liver and kidneys and excreted primarily in the urine. Its half-life is approximately 1.5 to 2.5 hours, depending on the route of administration and individual factors. In CSWS, the inappropriate renal sodium and water loss can lead to hypovolemia (decreased blood volume) and hyponatremia. Desmopressin can help to mitigate the excessive water loss by increasing water reabsorption in the kidneys. This can help to restore fluid balance and potentially improve hyponatremia. While desmopressin can be beneficial in some cases of CSWS, its use should be carefully considered and monitored. Desmopressin can potentially worsen hyponatremia if fluid intake is not adequately monitored. Close monitoring of fluid balance, electrolyte levels, and clinical status is essential when using desmopressin in CSWS. One of the primary reasons for considering desmopressin in CSWS is the observation that some patients with CSWS exhibit elevated levels of ADH despite having hyponatremia. This seemingly paradoxical finding suggests a state of renal resistance to ADH, where the kidneys do not respond adequately to the circulating ADH. Consequently, the kidneys continue to excrete excessive amounts of water, leading to hyponatremia and hypovolemia. Desmopressin, being a more potent and longer-acting form of ADH, may help to overcome this renal resistance. By binding to vasopressin V2 receptors in the renal collecting ducts with higher affinity and for a longer duration, desmopressin can potentially stimulate water reabsorption more effectively than endogenous ADH. This can lead to a reduction in urine output and conservation of water, thereby mitigating the excessive water loss associated with CSWS. Another rationale for using desmopressin in CSWS is to manage significant polyuria (excessive urination). Polyuria is a common symptom in CSWS due to the impaired ability of the kidneys to conserve sodium and water. The excessive urine output can contribute to hypovolemia and electrolyte imbalances, further complicating the clinical picture. Desmopressin's ability to reduce urine output can be particularly beneficial in patients with CSWS who experience significant polyuria. By decreasing urine volume, desmopressin can help to restore fluid balance, prevent dehydration, and potentially improve hyponatremia. The decision to use desmopressin in CSWS should be made on a case-by-case basis, considering the patient's clinical condition, severity of hyponatremia, and response to other treatment measures. Desmopressin is not a first-line therapy for CSWS and should be reserved for patients who have significant polyuria or those who do not respond adequately to fluid replacement therapy alone. When desmopressin is used in CSWS, close monitoring of fluid balance, electrolyte levels, and clinical status is crucial. Serum sodium levels should be checked frequently, and fluid intake and output should be carefully monitored. If hyponatremia worsens or does not improve with desmopressin, the medication

should be discontinued. The evidence supporting the use of desmopressin in cerebral salt wasting syndrome (CSWS) is currently limited and primarily based on case reports, small case series, and retrospective studies. While some studies have shown promising results, with desmopressin effectively reducing urine output and improving hyponatremia in some patients with CSWS, the overall evidence base remains weak and inconclusive. Several case reports have documented the successful use of desmopressin in managing CSWS, particularly in patients with significant polyuria (excessive urination) and hyponatremia. In these reports, desmopressin was often added to the treatment regimen after fluid replacement therapy alone failed to adequately control urine output and improve sodium levels. The reported benefits of desmopressin included a reduction in urine volume, an increase in urine osmolality (indicating improved water conservation by the kidneys), and an improvement in serum sodium levels. A few small case series have also reported positive outcomes with desmopressin in CSWS. These studies typically involved a small number of patients with CSWS who were treated with desmopressin in addition to standard fluid management. The results generally showed that desmopressin was well-tolerated and associated with a decrease in urine output and an increase in serum sodium levels. Some retrospective studies have evaluated the use of desmopressin in CSWS by reviewing medical records of patients who received desmopressin as part of their treatment. These studies have generally reported that desmopressin was associated with a reduction in urine output and an improvement in hyponatremia. However, the retrospective nature of these studies limits their ability to establish a cause-and-effect relationship between desmopressin use and clinical outcomes. There is a lack of randomized controlled trials, which are considered the gold standard for evaluating the efficacy of interventions. Most studies on desmopressin in CSWS have been observational and have not included a control group, making it difficult to determine the true effectiveness of desmopressin. Patients with CSWS can have varying underlying conditions and severities of illness, which can affect their response to desmopressin. This heterogeneity makes it challenging to draw definitive conclusions about the effectiveness of desmopressin across different patient populations. Desmopressin can potentially worsen hyponatremia if fluid intake is not adequately monitored. Some studies have reported cases of worsening hyponatremia with desmopressin use, highlighting the importance of careful monitoring and fluid management. Desmopressin, a synthetic analog of antidiuretic hormone (ADH), is a medication that can be used in the management of cerebral salt wasting syndrome (CSWS) under certain circumstances. However, its use requires careful consideration and monitoring due to potential risks and complications. Desmopressin's primary mechanism of action is to increase water reabsorption in the kidneys, which can lead to dilutional hyponatremia if fluid intake is not adequately monitored. Dilutional hyponatremia occurs when the concentration of sodium in the blood is lowered due to an excess of water relative to sodium. In CSWS, where there is already an underlying risk of hyponatremia due to inappropriate renal sodium loss, the use of desmopressin can further exacerbate hyponatremia if fluid intake exceeds urine output. This risk is particularly significant in patients with impaired thirst mechanisms or those who are unable to regulate their fluid intake effectively. Desmopressin can also lead to fluid overload, especially in patients with compromised cardiac or renal function. Fluid overload occurs when the body retains excess fluid, leading to increased blood volume and potential complications such as heart failure and pulmonary edema. In patients with CSWS who may already have underlying cardiac or renal dysfunction, the use of desmopressin requires careful monitoring of fluid balance and clinical status to prevent fluid overload. Desmopressin can affect the balance of other electrolytes in the body, such as potassium and magnesium. Hypokalemia (low potassium levels) and hypomagnesemia (low magnesium levels) can occur with desmopressin use,

especially in patients with underlying electrolyte disturbances or those receiving medications that can affect electrolyte balance. Monitoring electrolyte levels and correcting any imbalances is essential when using desmopressin in CSWS. Desmopressin can cause other adverse effects, such as headache, nausea, flushing, and nasal congestion. These side effects are usually mild and transient but can be more pronounced in some patients. In rare cases, desmopressin can cause more serious adverse effects, such as seizures and hyponatremic encephalopathy (brain dysfunction due to severe hyponatremia). The use of desmopressin in CSWS should be carefully considered and individualized based on the patient's clinical condition, severity of hyponatremia, and response to other treatment measures. Desmopressin is not a first-line therapy for CSWS and should be reserved for patients who have significant polyuria or those who do not respond adequately to fluid replacement therapy alone. Close monitoring of fluid balance, electrolyte levels, and clinical status is essential when using desmopressin in CSWS. If hyponatremia worsens or does not improve with desmopressin, the medication should be discontinued.[18-20]

4. Conclusion

This case report highlights the importance of recognizing and appropriately managing cerebral salt wasting syndrome (CSWS) in neurosurgical patients. CSWS is an uncommon but important cause of hyponatremia in neurosurgical patients. It is often challenging to differentiate CSWS from the syndrome of inappropriate antidiuretic hormone secretion (SIADH), but careful assessment of the patient's volume status, response to fluid management, and other laboratory findings can help to guide the diagnosis. Prompt diagnosis and appropriate management, including fluid replacement and potentially desmopressin, can improve patient outcomes. The use of desmopressin in CSWS should be carefully considered and monitored due to potential risks such as hyponatremia and fluid overload.

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