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SIADH in Hemorrhagic Stroke Patients: A Case Series

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Abstract: *Hyponatremia is common in acute stroke, possibly syndrome of inappropriate antidiuretic hormone (SIADH) or cerebral salt-wasting syndrome (CSWS). Hyponatremia is defined as a condition in which the sodium concentration is below 135 mEq/L. Hyponatremia can cause hypoosmolality in cerebral blood vessels and cause an increase in intracranial pressure resulting in cerebral edema which can be life threatening. Patient 1, 47 years old male with a hemorrhagic stroke came to the emergency room at Zainoel Abidin Hospital with acute weakness in the right side (2 hours' onset) and headache when the patient was working in the office followed by a decrease in consciousness (GCS 14), he is an uncontrolled hypertensive patient, active smoker and rarely physical exercise. His blood pressure was 230/140 mmHg, heart rate, respiration and body temperature were normal, right side neurologic deficit with positive Babinsky reflex. The head CT scan shows intracerebral hemorrhage (ICH) in the left hemisphere. Laboratory examination revealed serum sodium levels of 130 mmol/L, potassium 3.9 mmol/L. During the treatment period, the patient often complained of headaches and frequent vomiting. There were no symptoms of hypovolemia, so it was suspected that the cause of hyponatremia was SIADH and the symptoms improved after fluid restriction and sodium chloride supplementation. After 2 weeks of treatment, the patient was allowed to go home. Patient 2, aged 60 years male with hemorrhagic stroke, came to the emergency room at Zainoel Abidin Hospital with a sudden loss of consciousness on activity (onset 4.5 hours, GCS 11), with vomiting twice, left side weakness, dysarthria, and headache. The patient is an uncontrolled hypertension and diabetes mellitus, blood pressure is 158/102 mmHg with normal heart rate, breathing and body temperature. The Head CT scan showed massive intracerebral and intraventricular hemorrhage in the right hemisphere, serum sodium level of 129 mmol/L, potassium 3.8 mmol/L, and chloride 106 mmol/L, and random blood sugar 226 mg/dL, no hypovolemia was found. The patient had SIADH. After fluid restriction, furosemide and sodium chloride supplementation, the patient's condition improved. Hyponatremia in stroke can be either SIADH or CSWS. These two conditions are similar but require different treatment, therefore they must be determined precisely. Monitoring serum sodium levels and determining the etiology of hyponatremia in stroke patients is very important.*

Keywords: *SIADH; CSWS; hemorrhagic stroke; hyponatremia*

I. Introduction

Stroke is a clinical condition in which there is an acute decrease in brain blood perfusion due to a blockage or rupture in blood vessels which causes a decrease in neurological function focally or globally.[1] Stroke disease is the most dominant health complication resulting in death and disability[29]. Stroke is a medical condition ranked second in the cause of mortality around the world. This disorder is heterogenic making it difficult to detect the etiology which causes it, increasing the burden of medical services and the economy of a country. [2]

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The most common complications which often occur in acute stroke patients are neurological complications, such as intermittent stroke, seizure, and electrolyte imbalances.[3,4] Those complications participate in affecting the degree of stroke and outcome of hemorrhagic stroke patients. Disturbance in electrolyte balance, especially hyponatremia is a complication that commonly occurs in acute stroke patients.[5] Several studies reports that hyponatremia in stroke patients is a predictor of poor prognosis.[6] The pathophysiologic mechanism is still unclear, but several theories show that hyponatremia promotes cerebral edema and affects cerebral perfusion.[7]

Hyponatremia is defined as a condition in which sodium concentration is below 135 mEq/L and manifests in patients as severe sweating, vomiting, diarrhea, burn, and diuresis.[8] Hyponatremia often occurs in a patient with intracranial disease and after a hypophyseal operation, occurring in 9-35% of patients.[9] This is also observed in 30-40% of patients with subarachnoid hemorrhage (SAH).[10] The common cause of hyponatremia is Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) and cerebral salt-wasting syndrome (CSWS).[11] The main risk for hyponatremia and hypoosmolality in the brain is cerebral edema, which causes an increase in intracranial pressure (ICP) which can threaten life and occurs when there is an increase in intracranial volume to extracranial volume exceeding 10%.[12]

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) was found to be the most common cause of hypernatremia in inpatients as well as outpatients.[13] The diagnostic criteria which are accepted for SIADH need evaluation on blood volume status, serum sodium concentration, and serum osmolality, urine sodium concentration, urine osmolality, thyroid function test, and serum cortisol, as well as medical history to check the salt and water intake, kidney function, and diuretics usage. All this examination is needed to eliminate alternative causes of hyponatremia.[14]

II. Case

2.1 Case 1

A patient of age 47 years old male came to the Emergency Room of Zainoel Abidin Hospital with acute weakness in right limbs 2 hours before admission. The complaints start when the patient was working in the office and was accompanied by a headache hence the patient was diagnosed with hemorrhagic stroke. The patient was also known to be an active smoker and rarely does physical exercise. It was also found history of hypertension that is not controlled. Glasgow Coma Scale score is 14 with E4M5V5, blood pressure 230/140 mmHg, heart rate 80 times/minute, respiratory rate 22 times/minute, and temperature of 36.5˚C. ECG results and thoracic X-ray is within normal limit. Babinsky reflex was positive on neurological exam. CT scan examination shows intracerebral hemorrhage (ICH) in the left hemisphere which leads to the diagnosis of hemorrhagic stroke type intracerebral hemorrhage (Figure 1). Laboratory examination found a serum sodium level to be 130 mmol/L, potassium 3, 9 mmol/L, and chloride 107 mmol/L which indicates that the patient is in hyponatremia. (Table 1).

During the period of care, the patient often complains of headache and persistent nausea and vomiting. Administration of analgesics does not show a significant change. Another laboratory examination shows that the serum sodium level is still in the range of 130 mmol/L. There are no symptoms of hypovolemia that can be found hence it is suspected that the cause of hyponatremia is SIADH. The patient only reported improvement in symptoms after fluid restrictions and administration of sodium chloride supplement. After 2 weeks of care, the patient was allowed to go home.

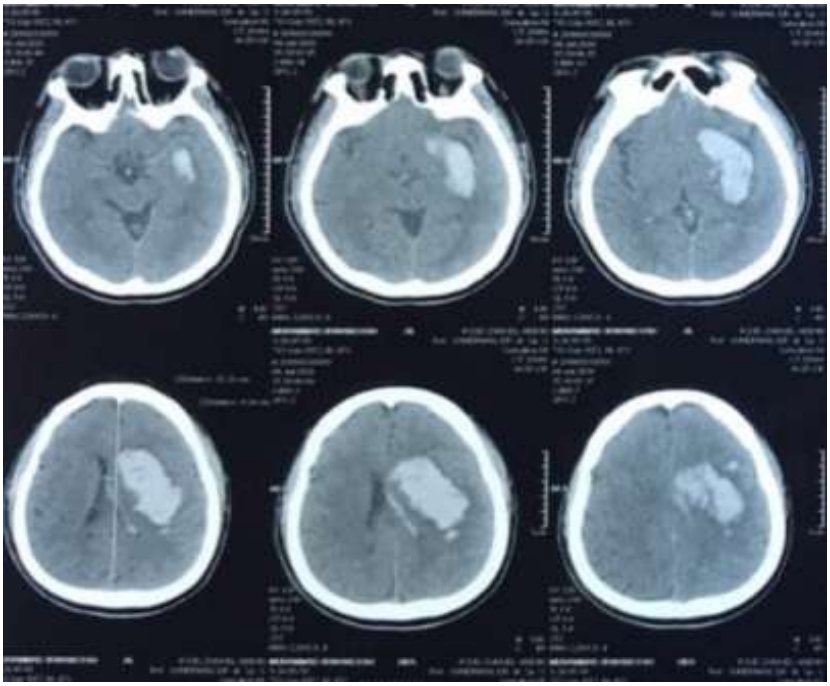

Figure 1. *CT Scan of Patient 1 Shows Intracerebral Hemorrhage in the Left Hemisphere of the Brain*

2.2 Case 2

A patient age 60 male came to the emergency room of Zainoel Abidin Hospital with decreased awareness approximately 4.5 hours before admission to the hospital. Decreased awareness occurred suddenly while doing an activity and occurred with vomiting twice. Other complaints include weakness of the left limbs, dysarthria, weakness in talking muscles, and headache hence patient is diagnosed with hemorrhagic stroke. The patient also has a history of hypertension and uncontrolled diabetes mellitus. GCS examination resulted in a score of 11 with E2M5V4, blood pressure 158/102 mmHg, heart rate 105 times/minute, respiratory rate 24 times/minute, and temperature of 36,7˚C.

ECG result and thoracic X-ray of patient shows normal outcomes. CT scan examination shows that there is an intracerebral and intraventricular hemorrhage that is massive in the right hemisphere which signifies a diagnosis of hemorrhagic stroke type intracerebral hemorrhage (Figure 2). Upon laboratory examination, it is found serum sodium concentration of 129 mmol/L, potassium 3,8 mmol/L, and chloride 106 mmol/L, and random blood sugar 226 mg/dL which shows that patient also is in a hyponatremia condition (Table 1).

The first management given is the administration of intravenous infusion of ringer lactate, perdipin, piracetam, and insulin injection. The patient is then consulted to neurosurgery to undergo craniotomy. After several days of care, the patient's condition has not shown improvement, after further examination, it is found that the serum sodium level of patient is still low, which is 129 mmol/L. There are no symptoms of hypovolemia found hence it is suspected that the cause of hyponatremia in the patient is SIADH. Administration of intravenous infusion was discontinued and the patient was given furosemide and sodium chloride supplement. Combination of fluid restriction and administration of furosemide resulted in improvement of patient's symptoms.

Table 1. Sodium, Potassium and Chloride Level of Case 1 and 2 Patients

	Case 1	Case 2	Normal limit
Sodium	130	129	132 - 146 mmol/L
Potassium	3,9	3,8	3,7 - 5,4 mmol/L
Chloride	107	106	98 - 106 mmol/L

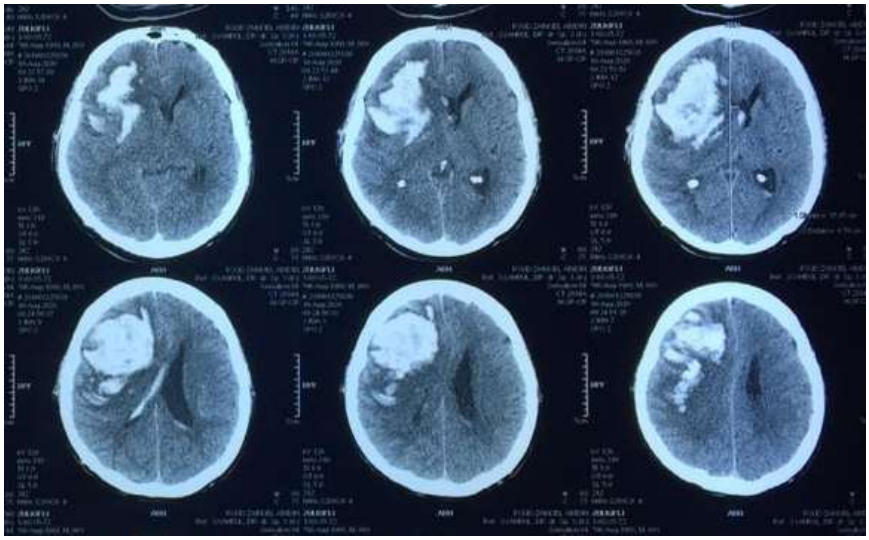

Figure 2. *CT Scan or Patient 2 Shows Intracerebral and Intraventricular Hemorrhage in the Right Hemisphere of the Brain*

III. Discussion

Stroke is a condition that is caused by a disturbance in cerebrovascular which is defined as an acute onset of neurological deficit originating from focal vascular. Stroke causes neurological deficit that lasts long and is one of the most common causes of life-long disability and death.[15] Hemorrhagic stroke is most commonly caused by a rupture in blood vessels which degenerates due to chronic hypertension.[16]

In neurological deficits like stroke, hyponatremia is an electrolyte imbalance that is commonly faced by and commonly related to SIADH and CSWS.[15] Both patients in this report came with hemorrhagic stroke and were given management which is according to the diagnosis of hemorrhagic stroke. After three days of care, both patients in this report do not show improvement although adequate therapy has been administered. Laboratory testing shows that both patients suffers a reduced serum sodium concentration (patient 1: 130 mmol/L and patient 2: 129 mmol/L).

Hyponatremia is reported to be one of the complications of stroke. Studies have shown that hyponatremia is a predictor of poor diagnosis.[17] A stroke patient with hyponatremia is related to an elongated period of hospital care compared to stroke patients with normal serum sodium level. [15] Mortality in a patient with brain damage and severe hyponatremia (<130 mmol/L) is 50 times higher compared to those patients with normal sodium concentration.[18] Stroke incidents related to hyponatremia often found in acute geriatric patients.[6] Gray et al. reported that most of the patients will suffer from hyponatremia within one week after spontaneous intracerebral hemorrhage.[18] The etiology of hyponatremia which occurs in stroke patients has not been identified completely. Several studies claimed that SIADH could become one of the main reasons for hyponatremia in stroke patients, especially stroke from spontaneous intracerebral

hemorrhage. [11,18] SIADH is caused by the over secretion of antidiuretic hormone (ADH) or similar substance to ADH that is related to water retention, hypervolemia, and secondary diuresis and natriuresis.[19]

The first patient complains of headache and nausea-vomiting while the second patient does not show improvement in his state of awareness. Headache which occurs in stroke patients is caused by increased intracranial pressure due to cerebral edema.[20] Cerebral edema is the most dangerous hyponatremia complication, especially in acute hyponatremia (onset <48 hours).[15]

Hyponatremia in patients with neurological damage could worsen cerebral edema through osmotic fluid movement from hypotonic extracellular space to relatively hypertonic intracellular space hence causing brain edema, reduced blood flow, and increased intracranial pressure and could potentially cause a worsening neurological deficit. [18,21] Side effects of cerebral edema could worsen the quality of awareness due to increased intracranial pressure which puts pressure on the center of awareness. Hyponatremia which causes cerebral edema often occurs in 1 to 3 days after reduced-sodium plasma concentration.[22] Increased intracranial pressure could also cause a disturbance in blood flow, mechanical deformation, neurotransmitter secretions, dysfunction of mitochondria, and cell membrane depolarization. Due to the damage of neurons in perihematomal area and inflammatory means will fill the site of the lesion.[23] Patients with acute hyponatremia could die of herniation. [24]

Aside from reduced serum concentration of sodium, the absence of hypovolemia symptoms on both patients caused them to be diagnosed with hyponatremia due to SIADH. The diagnostic criteria for SIADH include hyponatremia (concentration of sodium <135 mEq/L), serum hypo-osmolarity (<280 mOsm/L) which is caused by the expansion of extracellular volume, increased plasma volume, and urine osmolarity that is relatively higher to plasma, sodium excretion >20-25 mEq/L, no dehydration is proven clinically, and the urine sodium concentration of less than 25 mEq/L.[12] Proper diagnosis of SIADH needs laboratory examination of urine and serum osmolality, urine sodium, cortisol, and thyroid hormone.[25] However, several studies in the United States and European Union show that there is only 21% of patients which were diagnosed with SIADH have done appropriate and comprehensive laboratory exams.[11] Other studies show that less than half of surveyed clinicians could use the biochemical parameter to conclude SIADH diagnosis.[11,26] This shows that electrolyte imbalances like hyponatremia are often missed when diagnosing patients. Monitoring of sodium concentration is very important to be done, especially within the first week in geriatric patients who suffers from spontaneous intracerebral hemorrhage.[11,27]

Fluid restriction is recommended to be the first-line treatment in chronic moderate or severe hyponatremia which is caused by SIADH; although fluid restriction is either not enough or impractical.[28] Tolvaptan, which is an oral vasopressin receptor V2 antagonist, may be considered as one of the choices to correct hyponatremia caused by SIADH.[11,15] Fluid restriction and administration of sodium chloride supplement cause both patients to show visible improvement hence they could return home after 7 days of care (patient 1) and 10 days of care (patient 2).

IV. Conclusion

Hyponatremia is a complication that is often observed in hemorrhagic stroke patients and could cause significant exacerbations if not detected and managed early. Hyponatremia can be caused by SIADH and CSWS, hence the etiology of hyponatremia

should also be determined because these two conditions require different management. Hence, monitoring of serum sodium level and determining the etiology of hyponatremia in stroke patients become very important.

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