

Severe hyponatremia in ischemic stroke with COVID-19: Case report

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ABSTRACT

Hyponatremia could be found in an ischemic stroke patient. We, herein, report series of cases on ischemic stroke patients with COVID-19 who developed hyponatremia. A diagnosis of hyponatremia was made due to COVID-19 pneumonia. The patients were managed conservatively with a significant improvement during the course of hospitalization and on follow-up.

Keywords: hyponatremia, COVID-19, cerebral infarction

BACKGROUND

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered SARS-CoV-2 virus. As of July 20, 2021, the number of confirmed COVID-19 positive cases has risen by 38.325 from the previous day to 2,950,058 cases. In that same period, the number of deaths rose by 1.280 to 76200, while the number of recovered patients rose by 29.791 to 2,323,666 [1]. The clinical spectrum of COVID-19 varies from asymptomatic or paucisymptomatic forms to clinical illness characterized by acute respiratory failure requiring mechanical ventilation, septic shock, and multiple organ failure. In some cases, hyponatremia can be found as a clinical manifestation of COVID-19.

The previous study shows COVID-19 is able to induced comorbidities, such as pneumonia, respiratory failure, stroke etc., which can also contribute to the development of SIADH [2]. Another study reported two cases of SIADH found in COVID-19 patients who suffered pneumonia [3]. Another study also found a case of a patient with COVID-19 who developed sudden exertional dyspnea and hypoxia and was found to be hyponatremic [4]. A similar study of A 65-year-old female patient presented to the emergency department with shortness of breath and fever, an oropharyngeal swab for the COVID-19

PCR test was positive and after the initiation of treatment, the patient developed hyponatremia [5].

A better understanding of hyponatremia in a patient with COVID-19 is needed to prevent complications and unwanted results. The purpose of this report is to inform the clinician about an uncommon condition found in a patient with COVID-19 such as hyponatremia.

METHODS

We consecutively collected cases of an ischemic stroke patient with COVID-19 who has hyponatremia. The data of clinical diagnosis was made by a neurologist. The imaging studies were performed for all patients. The data of blood analysis and electrolytes were obtained in 24 hours in hospital administration.

CASES PRESENTATIONS

A 69 years old female, admitted to the emergency room (ER) of Bethesda Hospital Yogyakarta, complain of drowsiness, nausea, and vomiting. Previously, the patient had a history of non-hemorrhagic stroke that cause weakness on the right side of the patient's body (Hemi-paresis dextra). Physical ex-

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amination showed drowsiness and disorientation. Laboratory findings confirmed positive for COVID-19 through a rapid antigen SARS-CoV-2 test. A complete blood count shows a low level of erythrocyte and platelets. White blood cell count shows an increase segmented neutrophil and neutrophil-lymphocyte ratio. D-dimer was presented high on a D-dimer test, C-reactive protein test also show a low value. Electrolyte test showed a low level of sodium (106.9 mmol/l) and a low level of potassium (2,67 mmol/l) Plain computer tomography (CT) brain imaging showed hypodensity lateral paraventricle dextra et sinistra and calcification on the pineal body, plexus choroid, and lentiform nuclei.

A 74 years old male, admitted to the emergency room (ER) of Bethesda Hospital Yogyakarta, complain of dizziness and lethargy. Physical examination exhibited drowsiness, nausea, and vomiting Rapid Antigen SARS-CoV-2 test confirmed the patient have COVID-19. A complete blood count reveals low hemoglobin (9.9 g/dl), low hematocrit (26,9%). White blood cell count shows a high value of segmented neutrophils (79,4%) and a high level of neutrophil-lymphocyte ratio (6.18). Electrolyte tests show a low level of sodium (113.5 mmol/l) and potassium (3.44 mmol/l). Plain computer tomography (CT) brain imaging displays hypodensity periventricular and calcification of pineal gland and choroid plexus.

A 75 years old woman, admitted to the emergency room (ER) of Bethesda Hospital Yogyakarta, with symptoms such as drowsiness, decreased alertness, and disoriented. Physical examination showed dizziness and lethargy. The patient is diagnosed with COVID-19 through a Rapid Antigen SARS-CoV-2 test. Laboratory findings such as complete blood count show low hemoglobin (9,9 g/dl), low level of hematocrit (26,9%), and erythrocyte (3,63 million cells per microlitre (cells/mcL)). White blood cell count shows a high level of segmented neutrophils (79.4%) and Neutrophil-lymphocyte ratio (6.18). Electrolyte tests exhibit a low level of sodium (113,5 mmol/l) and potassium (3,44 mmol/l). Plain computer tomography (CT) brain imaging display hypodensity on periventricle and posterior crus internal capsule bilateral, calcification of lenticular nuclei, pineal gland, and choroid plexus.

A 67 years old man, admitted to the emergency room (ER) of Bethesda Hospital Yogyakarta, with symptoms such as lethargy and headache over the last 2 days. The patient is diagnosed with COVID-19 by rapid antigen SARS-CoV-2 test. Laboratory tests such as complete blood count exhibit low hemoglobin (9,9 g/dl) and erythrocyte (3,63 million cells per microlitre (cells/mcL)). White blood cell count shows an increase in segmented neutrophil (79%), Neutrophil-lymphocyte ratio (6,18). Electrolyte test exhibit

low level of sodium (124,2 mmol/l) and potassium (2,47 mmol/l).

A 68 years old man, admitted to Bethesda Hospital Yogyakarta, with a headache and drowsiness. The patient is diagnosed with COVID-19 by Rapid Antigen SARS-CoV-2 test. Complete blood count test evince a low haemoglobin (12.6 g/dl) and hematocrit (32.7%). White blood count shows an increased ($20.13 \times 10^9/l$), similar neutrophil-lymphocyte ratio (22.13) which is also increased. Electrolyte test exhibit low level of sodium (101.5 mmol/l) and potassium (2.21 mmol/l). Plain computer tomography (CT) brain imaging display hypodensity on parenchymal occipital Sinistra and calcification of pineal gland and choroid plexus.

A 46 years old man, admitted to Bethesda Hospital Yogyakarta, with seizures. The patient is diagnosed with COVID-19 by rapid antigen SARS-CoV-2 test. Complete blood count test shows a high level of neutrophil to lymphocyte ratio (22.13), high level of ureum (60,3 mg/dl), and a high level of creatinine (1,97 mg/dl). Electrolyte tests exhibit a low level of sodium (101,5 mmol/l) and a low level of potassium (2,21 mmol/l).

A 55 years old man, admitted to Bethesda Hospital Yogyakarta, with symptoms such as right-side weakness and dysarthria. The patient is diagnosed with COVID-19 through the rapid antigen SARS-CoV-2 test. Complete blood count test shows low percentage of hematocrit (31%), high neutrophil and lymphocyte ratio (5,38), high level of C-reactive protein (5.29 mg/l), high level of D-Dimer (1.70 ng/ml), low level of creatinine (0.47 mg/dl). Electrolyte tests exhibit a very low level of sodium (106.9 mmol/l) and potassium (2.67 mmol/l).

DISCUSSION

We reported 7 cases of patients who were diagnosed with ischemic stroke and developed hyponatremia due to COVID-19. All of the patients showed a low serum level of sodium below 130 mEq/l which indicates hyponatremia that is often found in COVID-19 patients. SIADH has been identified as a predominant cause of hyponatremia in up to 50% of cases of common lung pathologies such as pulmonary malignancy, severe obstructive lung disease, acute respiratory failure, and pneumonia (3). COVID-19 pneumonia has just been identified as a possible cause of SIADH. According to preliminary findings, the production of certain pro inflammatory cytokines, notably IL-6, is responsible for the development of SIADH in COVID-19 pneumonia. These cytokines enhance ADH synthesis by two mechanisms: first, direct stimulation of non-osmotic ADH release, second, a direct insult to the alveolar basement membrane can activate the hypoxic pulmo-

TABLE 1

Patient	Initial	Symptoms	Hb (g/dL)	Hct (%)	Leucocyte Count (10 ³ /mm ³)	Platelets (10 ³ /mm ³)	NLR	CRP (mg/L)	D-dimer	Ur (mg/dL)	Cr (mg/dL)	Na (Mmol/L)	K (Mmol/L)
1	W	Drowsiness, disoriented,	9,9	26,9	9,56	318	6.18	0.85	0,86	25,9	0,9	113,5	3,44
2	TJH	Drowsiness, nausea and vomiting	12.5	31	5,69	165	5.38	5,29	1,7	26,1	0,47	106,9	2,67
3	AN	Dizziness, Lethargy	10,4	30	7,91	190	5.64	71,53	1,36	38,9	1.64	128,6	6,8
4	P	Lethargy, Headache	12,6	33.1	3,25	151	-	9.44	1,14	16,3	0.61	124,2	2,47
5	S	Headache, Drowsiness	12,6	32.7	20,52	284	22,13	60.15	-	25,7	0.67	101,5	2,21
6	TAP	Seizure	13.7	35.9	8.48	227	8.86	-	-	60.3	1.97	110.5	2.09
7	NTF	Right side weakness, Dysarthria	12.5	31	5.69	165	5.38	5.29	1.70	26.1	0.47	106.9	2.67



FIGURE 1. Patient 5 – Chest X-ray showed basal pneumonia in both lungs

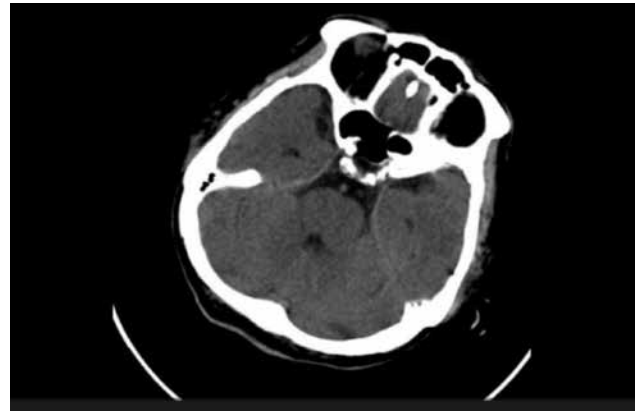


FIGURE 2. Patient 5 – Brain CT scan showing infarct in the left temporal lobe

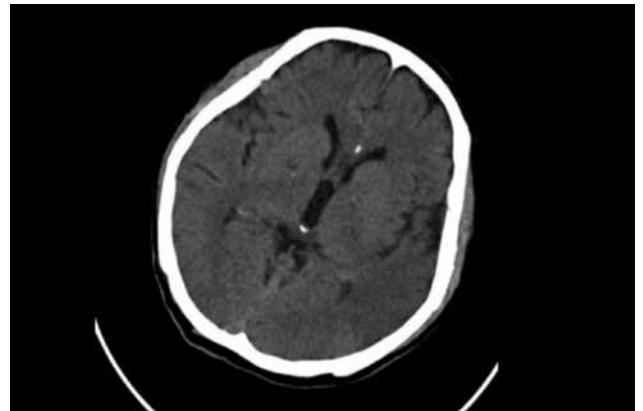


FIGURE 3. Patient 5 – Brain CT scan showing multiple lacunar infarctions in basal ganglia

nary vasoconstriction pathway, resulting in an increase of ADH production (6). This theory is supported by the findings of a study that found hyponatremia was common among patients with COVID-19 and occurred in 30% of patients (7). Other studies that support these findings also discover an ischemic stroke patient and COVID-19 exhibit extreme hyponatremia with a sodium of 106 mmol/l (8). Hyponatremia is commonly found in a stroke patient, conditions related to stroke per se such as

secondary adrenal insufficiency due to pituitary ischemia or hemorrhage, SIADH, and cerebral salt wasting (CSW) could lead to hyponatremia (9). COVID-19's patient may experience inflammatory cytokine-induced impairment of the kidney that could potentially contribute to developing hyponatremia (10).

One patient showed increased creatinine serum level which can indicate impaired kidney function. This was also found in a study where a 64-year-old man with no preexisting conditions, diagnosed with COVID and exhibit an increased creatinine and SUN (saliva urea nitrogen) levels from 1.2 and 21 mg/dl, respectively, to 9.9 and 160 mg/dl by day 4 (11). This may happen due to the destruction of the kidney cell from the virus SARS-CoV-2. A study showed polymerase chain reaction fragments of the viruses in the blood and urine of SARS and COVID-19 patients which may indicate the presence of the virus in the urinary system (12).

High NLR was noted in all of our case report. These findings are consistent with a previous study which also presented COVID-19 patients exhibit a high Neutrophil-to-Lymphocyte Ratio especially on patients with moderate-severe symptoms (13). One study shows that older age and NLR can present as a

biomarker for poor outcomes in patients with COVID-19 (14).

The C-reactive protein was increased in 4 out of 5 patients on the complete blood count. These findings are consistent with the previous report that hyponatremia in SARS-CoV-2 positive patients was associated with a greater predisposition to fever and nausea, and in terms of biological changes, with increased leukocytes, neutrophils, and high sensitivity C-reactive protein (HS-CRP) (10).

CONCLUSION

COVID-19 patients with ischemic stroke who presented with hyponatremia exhibit a variety of neurological symptoms such as drowsiness, unalert, disoriented, lethargy, nausea, dizziness and headache. Other findings such as elevated D-dimer, C-reactive protein and creatinine serum are also exhibited in patients.

These findings could hopefully help the clinician to be aware of a condition such as hyponatremia in a COVID-19 patient. Further research and study is needed to determine the exact pathomechanism, risk factor, and specified treatment for this particular condition

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REFERENCES

1. Indonesian Covid Task Force. Distributional Map [Internet]. Committee on COVID-19 response and national economic recovery. 2021. Available at: <https://www.covid19.go.id/>
2. Using Osmolality to Diagnose and Treat Hyponatremia in COVID-19 Patients. Available at: https://www.aicompanies.com/wpcontent/uploads/2020/05/Using_Osmolality_Diagnosis_and_Treat_Hyponatremia_in_COVID_19_patients_PCNO1369.pdf
3. Ravioli S, Niebuhr N, Ruchti C et al. The syndrome of inappropriate antidiuresis in COVID-19 pneumonia: report of two cases. *Clin Kidney J*. 2020 May 17;13(3):461-462.
4. Sheikh MM, Ahmad E, Jeelani HM et al. COVID-19 Pneumonia: Emerging Cause of Syndrome of Inappropriate Antidiuretic Hormone. *Cureus*. 2020 Jun 26;12(6):e8841.
5. Gemcioglu E. A Case of Inappropriate Antidiuretic Hormone Secretion Syndrome Associated with Covid-19 Pneumonia. *Acta Endocrinologica* (Bucharest). 2020;16(1):110-111.
6. Qin C, Zhou L, Hu Z et al. Dysregulation of Immune Response in Patients With Coronavirus 2019 (COVID-19) in Wuhan, China. *Clinical Infectious Diseases*. 2020;71(15):762-768.
7. Frontera J, Valdes E, Huang J et al. Prevalence and Impact of Hyponatremia in Patients With Coronavirus Disease 2019 in New York City. *Critical Care Medicine*. 2020;48(12):e1211-e1217.
8. Alam S, Dharia R, Miller E et al. Coronavirus Positive Patients Presenting with Stroke-Like Symptoms. *Journal of Stroke and Cerebrovascular Diseases*. 2021;30(4):105588.
9. Liamis G, Barkas F, Megapanou E et al. Hyponatremia in Acute Stroke Patients: Pathophysiology, Clinical Significance, and Management Options. *European Neurology*. 2019;82(1-3):32-40.
10. Gheorghe G, Ilie M, Bungau S et al. Is There a Relationship between COVID-19 and Hyponatremia? *Medicina*. 2021;57(1):55.
11. Patel N, Rein J, Sanchez-Russo L et al. COVID-19–Associated Acute Kidney Injury: A Case Series. *Kidney Medicine*. 2020;2(5):668-669.
12. Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020;395(10223):497-506.
13. Fuad M, Oehadian A, Prihatni D, Marthoenis M. Neutrophil-to-Lymphocyte Ratio and COVID-19 Symptom-based Severity at Admission. *Althea Medical Journal*. 2021;8(1).
14. Yang A, Liu J, Tao W, Li H. The diagnostic and predictive role of NLR, d-NLR, and PLR in COVID-19 patients. *International Immunopharmacology*. 2020;84:106504.