Case Report

Stroke vs. SIADH: A case of symptomatic hyponatremia secondary to SIADH in association with COVID-19 infection

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Abstract

A 66-year-old male with no known past medical history presented with history of two days of throbbing frontal headache associated with nausea, vomiting and left-sided facial droop. The patient also reported dizziness, subjective chills without cough, shortness of breath, or sputum production. Laboratory findings revealed elevated inflammatory markers but normal thyroid, kidney, and liver function tests. Initial sodium level was 126 mEq/L. Urine studies showed elevated urine osmolality of 647 mOsm/Kg and urine sodium level of 175 mEq/L, both suggestive of syndrome of inappropriate secretion of antidiuretic hormone (SIADH). The TSH and ACTH stimulation tests both came back as normal. CT scan of the chest showed no evidence of lung infiltrates. Diffusion weighted MRI of the brain showed no evidence of acute or subacute CVA. SARS-CoV-2 nasal swab test was resulted positive. With these findings we diagnosed our patient with SIADH. Patient was initially started on 3% saline infusion for symptomatic hyponatremia. A fluid restricted diet was enforced. Patient was also started on salt tablets in order to increase solute intake. Sodium slowly corrected throughout the hospitalization. Of note, our patient never became hypoxic, neither did he show evidence of clinical pneumonia. A CT imaging of the chest showed no lung infiltrates, and an MRI of the brain was negative for any acute intracranial abnormalities. This case highlights the role of early recognition of SIADH in the setting of SARS-CoV-2 infection even in the absence of hypoxemia or lung pathology.

Introduction

Hyponatremia is defined as serum sodium concentration level below the reference limit of 135 mEq/L and has been described as the most commonly known water-electrolyte abnormality among hospitalized patients [1]. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is suspected when serum osmolality is less than 275 mOsm/Kh (hypoosmolality), while urine osmolality is inappropriately high. This is in the absence of renal salt wasting or hypovolemia, in an individual with normal organ function [2]. A new body of evidence is rapidly emerging regarding the new clinical and laboratory presentations of severe acute respiratory syndrome related to coronavirus 2 (SARS-CoV-2) among hospitalized patients. Recently, acute hyponatremia has been reported among patients infected with SARS-CoV-2, mainly in patients with either gross lung involvement or those who require positive pressure ventilation [3,4].

Hyponatremia from SIADH in the setting of pneumonia is a common finding. Here, we present an isolated case of SIADH in a patient with SARS-CoV-2 infection without signs of blatant lung involvement or hypoxemia.

Case report

A 66-year-old Spanish-speaking man with no known prior medical history presented to the emergency department with two-day history of a new left sided facial droop and unstable gait. These symptoms were associated with moderate throbbing frontal headache. Other associated symptoms included nausea, multiple bouts of vomiting, subjective chills along with a left sided facial droop. Patient did not report any ear pain, tinnitus, acute loss of consciousness or laterized sensory deficit or weakness. He also denied recent history of significant weight loss, chronic cough, hemoptysis, urinary symptoms, back pain, black stools or family history of cancer. Social history was negative for chronic alcohol use, tobacco use, chronic SSRI or narcotic medication use. Medical History was negative for decompensated liver disease or chronic kidney disease.
On presentation, vital signs were as followed: A blood pressure of 175/91 mmHg, Oxygen saturation was 98% on room air and oral temperature was 38.1 °C (99.7 °F). Physical examination revealed a left sided facial droop and mild weakness on bilateral upper extremities. No peripheral edema, JVD was noted on physical examination.

Laboratory findings were significant for serum sodium of 126 mEq/L (normal range 136-145 mEq/L), Creatinine and BUN levels were within normal limits. Inflammatory markers including Ferritin, LDH, and CRP were elevated at presentation. A nasopharyngeal swab for SARS-CoV-2 PCR was resulted positive. Urine sodium and osmolality were obtained. An overview of laboratory results at presentation is provided in table 1.

Chest imaging did not show any infiltrates. An MRI of the brain revealed normal age-related changes without any evidence of brain mass or infarction on diffusion weighted imaging.

Patient was given a bolus of 1,000 ml of normal saline in ED. The repeat serum sodium dropped to 120 mmol/L. Urine osmolality and sodium was re-checked which showed a urine osmolality of 647 mOsm/kg and urine sodium of 175 mmol/L, respectively. A thyroid stimulating hormone (TSH) and ACTH stimulation test were obtained both of which were within normal limits.

Considering symptomatic hyponatremia, patient was started on 3% saline infusion. A fluid restricted was enforced and sodium chloride tablets were started. Following these measures, serum sodium slowly corrected. The patient remained stable with no signs of hypoxia during his hospital stay. Patient never received any treatment related to COVID-19 infection during the hospitalization either.

One month after his presentation, our patient is asymptomatic with normal sodium levels.

**Discussion**

Hyponatremia is among the most common electrolyte abnormalities observed among hospitalized patients, ranging between 15% to 30% on the floors and up to 40% among patients admitted to ICU [5,6]. Euvolemic hyponatremia is probably the most common form of hyponatremia in the inpatient setting with SIADH being the most common underlying mechanism [2]. SIADH should be suspected in a euvolemic patient with normal thyroid function tests and no evidence of hormonal derangement.

Common lung pathologies such as lung primary cancers, severe COPD, acute respiratory failure and pneumonia are among the most common conditions leading to SIADH [7]. In one study, identifiable causes of SIADH were reported as medications (26.5%), malignancy (27.7%), lung infections (12.3%), pain and nausea (10.4%), idiopathic (15.9%), and CNS disorders (7.2%) [2].

Recently SARS-CoV-2 pneumonia has emerged as a potential cause of SIADH, and multiple recent case studies have reported the association between SARS-CoV-2 pneumonia and SIADH [7]. However, the underlying pathophysiology is yet to be clearly understood. Intravascular volume depletion or low extracellular osmolality are potent stimulators of ADH release. In pneumonia-induced lung injury causes hypoxia induced pulmonary vasoconstriction which leads to a decrease in filling of left atrium and ADH secretion [8]. A. Berni, et al. showed that among patients hospitalized with SARS-CoV-2 infection, the IL-6 levels inversely correlated with sodium levels. It seems that IL-6 leads to non-osmotic ADH stimulation which in turn results in hyponatremia [8]. Another postulated mechanism is hypoxic pulmonary vasoconstriction caused by direct alveolar basement membrane insult from SARS-CoV-2 pneumonia leading to increased ADH production [7]. Also, positive airway pressure (PAP) therapy in patients with SARS-CoV-2 pneumonia, is a well-known cause of ADH release through baro-receptor activation resulting from pulmonary congestion as well as decreased venous return because of positive pressure [9].

While SIADH could be a common cause of hyponatremia among hospitalized patients with SARS-CoV-2 infection, in many circumstances the cause of hyponatremia is multifactorial. One study in France reported 75% of patients hospitalized with SARS-CoV-2 infection had at least two proximal collecting tubule function abnormalities [10]. This could be secondary to 100-fold higher ACE-2 expression in kidneys than that of the respiratory system, which can potentially lead to kidney injury and electrolyte abnormalities [10].
While most common symptoms related to SARS-CoV-2 infection are fever, sore throat, dry cough, malaise, myalgia, SOB, and GI symptoms, many patients present with less classic features [11]. In a study from Wuhan, China, among 214 patients admitted to the hospital for SARS-CoV-2 infection, 36.4% were found to have some sort of neurological manifestation at presentation. These included headache, nausea, vomiting, confusion, seizure, ataxia, cranial nerve damage, with acute ischemic cerebrovascular accident ranging between 1% - 3% based on different studies [12-16]. Hanafi, et al. reported diffuse subcortical ischemic lesions in the brain resembling cerebral vasculitis with a characteristic lower extremity skin rash [17]. Our patient presented with recent onset dizziness, a left sided facial droop and a frontal headache associated with nausea and vomiting that started two days prior to presentation. MRI of the brain and CTA of the head and neck were negative for acute CVA and showed patent intracranial vasculature.

Our patient had no prior known history of chronic kidney or liver disease, cancer, and was not taking any diuretic medication, SSRI, narcotics etc. He never required any supplemental oxygen during his entire hospitalization. Thyroid function studies and cosyntropin stimulation test were normal. HIV was negative. These findings along with unremarkable diffusion weighted brain MRI for acute stroke and chest CT scan for pneumonia (Figure 1), pointed towards the diagnosis of isolated SIADH in the setting of SARS-CoV-2 infection. We believe nausea and vomiting in our patient was the result of acute hyponatremia as it completely resolved with treatment of this condition at time of discharge. Habib, et al. lately reported a patient with hyponatremia associated with SARS-CoV-2 infection in the absence of respiratory symptoms or fever [13]. Here we report the first case of symptomatic hyponatremia caused by SARS-CoV-2-induced SIADH in United States.

**Conclusion**

To date, a myriad of different manifestations of SARS-CoV-2 infection have been reported, many of which have amazed clinicians. SIADH is the most common cause of hyponatremia in hospitalized patients. Regardless of etiology, it appears that hyponatremia is associated with worse outcomes. This case report further emphasizes the role of early recognition of SIADH in the setting of SARS-CoV-2 infection even in the absence of hypoxia or lung pathology. Further studies are needed to investigate the pathophysiology of SIADH in this new phenomenon.

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