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Case Series

Internal Medicine Section

Hyponatremic Unconsciousness as a Presenting Symptom of COVID-19: A Case Series

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ABSTRACT

The novel Coronavirus Disease-2019 (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection can present with a multitude of clinical symptoms. The virus, disease symptomatology, pathogenesis and complications are being studied and new concepts are evolving rapidly. The current worldwide situation caused by the disease makes it exceedingly important to recognise varied presentations of the disease. Three cases are being discussed hereby, wherein the patients presented with altered sensorium secondary to hyponatremia as the initial and only presentation of SARS-CoV-2 infection, in the absence of fever or any respiratory involvement. Acute symptomatic hyponatremia is an under-recognised presentation with only a few cases reported till date and needs further awareness and understanding.

Keywords: Altered sensorium, Coronavirus disease-2019, Electrolyte imbalance, Severe acute respiratory syndrome coronavirus 2

INTRODUCTION

The Coronavirus Disease-2019 (COVID-19), has taken the form of a global pandemic. It is transmitted via droplet/airborne route and commonly involves respiratory system and presents with fever, cough and breathlessness [1]. Various unfamiliar clinical manifestations of COVID-19 are being brought to light every day and the fact still remains that the virus itself and its pathogenesis, systemic involvement and complications are a grey area that need to be further explored.

Pneumonia is one of the many infective causes of hyponatremia secondary to inappropriate antidiuretic hormone secretion. Syndrome of Antidiuretic Hormone Secretion (SIADH) associated with COVID-19 is one of the complications of this disease. It has also been reported to be related to severity of the disease [2-4].

Authors hereby discuss three patients who presented with altered sensorium. The aetiology turned out to be severe hyponatremia secondary to SIADH attributable to COVID-19, in absence of fever or other classical symptoms of the disease.

CASE SERIES

Case 1

A 70-year-old male patient presented to Emergency Department with complaints of altered sensorium for 15 days in the form of decreased responsiveness, drowsiness and inability to recognise relatives. There was no history of seizures, headache, vomiting, facial deviation, limb weakness or loss of consciousness. He did not have any history of trauma, drug intake or similar episode in the past. There was no history of fever, cough, expectoration or breathlessness.

The patient was a chronic smoker. He was a known case of Chronic Obstructive Pulmonary Disease (COPD) with history of Metered Dose Inhaler (MDI) use for last 10 years. He had a history of cerebrovascular accident (infarct) 15 years back, due to which he suffered from left sided hemiparesis, from which he recovered over time with physiotherapy. The patient had been prescribed low dose aspirin and statin which was taken by him for five years. There was no history of intake of diuretics or any other drugs in the past.

At presentation, he was drowsy with Glasgow Coma Scale (GCS)-E3V3M5. His Blood Pressure (BP) was 124/70 mmHg, pulse rate 78 beats/minute and SpO_2 was 98% on room air. Pupils were bilaterally normally sized and reactive. He was moving all four limbs equally and plantar response was flexor bilaterally. There was no neck rigidity/Kernig's/Brudzinski's sign. Chest auscultation revealed bilateral diffuse rhonchi. Rest of the examination was normal.

Non-Contrast Computerised Tomography (NCCT) head was done which was suggestive of old gliotic changes. Random blood glucose was 126 mg/dL. Arterial Blood Gases (ABG) was within normal limits with pH 7.436, pCO_2 44, HCO3- 26. Chest roentgenogram was normal. Blood investigations revealed Haemoglobin (Hb) 12.7 g/dL, Total Leukocyte Count (TLC) 11700/mm^3 (Neutrophils 83%, Lymphocytes 14%, Monocytes 3%), Platelet count 2 lacs/mm^3. Kidney and liver function tests were normal. Hyponatremia was noted with serum sodium 114.5 mmol/L. Serum potassium was normal (3.8 mmol/L).

Further investigations showed low serum osmolality 265 mOsm/kg and urinary osmolality 136 mOsm/kg. Urine routine examination was normal and urinary sodium was elevated 46 mmol/L. Thyroid function tests and serum cortisol were within normal limits. The patient was managed with 3% NaCl infusion with oral free water restriction. Following that a COVID-19 Reverse Transcription-Polymerase Polymerase Chain Reaction (RT-PCR) was sent which came out positive.

Patient showed considerable improvement in the following days. On the third day of admission, the patient was conscious and oriented. The patient was asymptomatic at discharge with serum sodium 129 mmol/L and advised home isolation.

Case 2

A 60-year-old male patient, chronic smoker and known case of COPD (using MDIs for three years) presented with complaints of altered sensorium for two days in the form of disorientation and decreased responsiveness. He had no history of preceding fever, headache, vomiting, seizures, loss of consciousness, cough, breathlessness, chest pain or focal neurological complaints. He did not have any trauma or similar complaint in the past. There was no history of intake of diuretics or any other drugs.

At presentation, the patient had pulse rate 84 beats/minute, BP-110/76 mmHg, SpO_2-97% on room air and GCS was E3V2M5. There were no signs of fluid overload or dehydration. Pupils were bilaterally normal sized and reactive. There was no focal neurological deficit or neck rigidity/Kernig's/Brudzinski's sign and bilateral plantar were flexor. Other systemic examination was normal.

Electrocardiogram (ECG) and chest x-ray were done which were normal. Blood investigations revealed Heamoglobin 9.9 g/dL, Total Leukocyte Count (TLC) 8000/mm^3, Differential Leukocyte Count (DLC) was 72% polymorphs, 22% lymphocytes, 2% eosinophils, 4% monocytes and platelet count 5.3 lacs/mm^3. Kidney Function Test (KFT) was normal with urea 20 mg/dL and serum creatinine 1.0 mg/dL. Liver function tests were normal. Serum sodium was 125 mmol/L and potassium 4.83 mmol/L. Serum and urinary osmolality was 268 mOsm/kg and 124 mOsm/kg, respectively and urinary sodium 50 mmol/L. Urine routine and microscopic examination was normal. The NCCT head was suggestive of age-related atrophic changes. The RT-PCR for COVID-19 of patient was positive.

He was started on 3% NaCl infusion in view of symptomatic hyponatremia. His sensorium improved during the course of stay following electrolyte correction. The patient was discharged for home isolation. He was conscious and oriented with serum sodium 134 mmol/L at the time of discharge.

Case 3

A 77-year-old gentleman presented to the Emergency Department with the chief complaints of altered sensorium for one day. He was apparently well one day before the presentation when he started showing signs of easy irritability and aggressive behaviour. There was no history of any weakness or loss of consciousness or projectile vomiting or seizures. There was no history of fever, cough, breathlessness or chest pain. On examination his blood pressure was 110/70 mmHg, pulse rate was 89 beats/minute and saturation was 98% on room air. His Central Nervous System (CNS) examination and other systemic examinations were within normal limits.

The patient was a known hypertensive and diabetic and had been taking Metformin and ACE inhibitor (Enalapril) for last 15 years. No history of diuretic, SGLT2 inhibitor or other drug use was there.

The ECG and chest x-ray were normal. The NCCT head was normal study. Routine investigations showed significantly decreased serum sodium of 115 mEq/L. A diagnosis of acute severe symptomatic hyponatremia was made and cause of hyponatremia was further evaluated. Hb- 11.5 g/dL, TLC- 9600/mm^3, DLC- 74% neutrophils, 26% lymphocytes, Platelets- 1.6lac/mm^3. His kidney function tests (Uric acid was 3.1) and liver function tests were within normal limits. He was clinically euvolemic. His serum osmolality calculated at that time was 267mOsm/Kg and urine osmolality was 212 mOsm/Kg with a urinary sodium of 62mmol/L. This has confirmed a diagnosis of SIADH. Patient improved with 3% NaCl infusion followed by fluid restriction. His serum cortisol and thyroid function tests were sent which were normal. No underlying medical conditions causing SIADH could be identified in the patient. In light of the ongoing pandemic, nasopharyngeal swab for COVID-19 RT-PCR was sent which came out to be positive. The patient was discharged for home isolation when he was asymptomatic, conscious and oriented with serum sodium level 134 mEq/L.

DISCUSSION

Hyponatremia is a commonly encountered electrolyte disbalance in the clinical practice. The SIADH is the most common cause of euvolemic hyponatremia. The established criteria for diagnosis of SIADH requires the presence of euvolemic state, low serum osmolality with concurrent elevated urinary osmolality and sodium levels. In addition, thyroid and adrenal diseases, renal insufficiency and diuretic use need to be ruled out [2].

Community acquired pneumonia is a recognised cause of SIADH, however, the underlying mechanisms are disputed. Hypoxic pulmonary vasoconstriction with subsequent reduced left atrial filling is important mechanism contributing to inappropriate ADH secretion [3]. Emotional, physical, or psychological stresses and pain associated with infections may stimulate the hypothalamo-hypophyseal axis, leading to ADH release.

Berni A et al., conducted a study where he correlated hyponatremia with Interleukin-6 (IL-6) levels and pO_2/FiO_2 ratio (an important indicator of respiratory performance) and found that serum sodium levels inversely correlated with IL-6 levels, while directly correlated with pO_2/FiO_2 ratio [4].

Hyponatremia has been found in COVID-19 patients in a number of studies and case reports, as discussed further. One of them is a large retrospective study by Frontera JA et al., which reported 30% prevalence of hyponatremia in SARS-CoV-2 RT-PCR positive patients along with an association of hyponatremia with increased risk of encephalopathy and mechanical ventilation. However, in the index cases, all three patients made a full recovery. Frontera JA et al., also found a significant correlation between IL6 levels and hyponatremia, and implicated IL6 related non osmotic release of ADH as the cause of hyponatremia [5].

Yousaf Z et al., described a case series of patients with SIADH and hyponatremia in patients presenting with pneumonia related to COVID-19 [6]. Another retrospective study by Ruiz-Sanchez JG et al., reported a prevalence of 20% in patients admitted with COVID-19 pneumonia. They also found that hyponatremia was independently associated with increased risk of sepsis and mortality [7].

In our cases, the patients presented with altered sensorium as a manifestation of hyponatremia, in the absence of fever or any respiratory manifestations of COVID-19 disease. None of the patients ever had any history of episode of unconsciousness or hyponatremia earlier in their lifetime. Hence, after excluding other causes, hyponatremia was attributed to SIADH secondary to SARS-CoV-2 infection.

Only a handful of similar cases of altered sensorium secondary to hyponatremia as the sole presentation of COVID-19 have been reported. One of the reports by Habib MB et al., discussed the case of a middle-aged male patient presenting with altered sensorium which was investigated and ascribed to acute severe hyponatremia (Serum sodium levels 112 mEq/L) due to SIADH secondary to COVID-19 infection [8].

A case of severe hyponatremia with serum sodium levels 116 mEq/L manifesting as mental confusion in the absence of lung and CNS involvement has been reported by Sherazi A et al., in a 55-year-old female patient with COVID-19 [9].

CONCLUSION(S)

Syndrome of Antidiuretic Hormone Secretion (SIADH) is an important complication of the COVID-19 disease. It can be the sole manifestation and thus serve as a clue for diagnosing COVID-19. In light of the current situation of COVID-19 pandemic and magnitude of burden of the disease, with rapidly evolving concepts and information, such uncommon presentations warrant recognition and sensitisation of physicians.

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