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# Kidney Transplant Recipient with Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) Secondary to COVID-19 Pneumonia: A Case Report

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## ABSTRACT

**Background.** Currently, COVID-19 is becoming one of the most common causes of viral pneumonia worldwide. In the medical literature, very few case reports describe the association between COVID-19 and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) in kidney transplant patients.

**Methods.** A 74-year-old immunocompromised man post–kidney transplant presented with nonspecific symptoms consisting of fatigue, malaise, and anorexia. He was also found to have hyponatremia in the context of pulmonary insults. SIADH in the setting of COVID-19 pneumonia was diagnosed after exclusion of other causes of hyponatremia. He was treated for COVID-19 pneumonia with antiviral therapy, secondary bacterial infection prophylaxis, dexamethasone and ventilatory support in addition to modification of antirejection medications.

**Results.** The patient has improved and his serum sodium normalized with management of primary insult.

**Conclusions.** SIADH should be suspected in transplant patients with COVID-19 pneumonia once they develop hyponatremia. The decision of intravenous fluid administration should be taken carefully in these settings.

**T**HE current COVID-19 pandemic, caused by SARS-CoV-2, is a serious public health concern worldwide [1].

The clinical presentation of COVID-19 ranges from mild disease with upper respiratory tract symptoms to a severe form of the disease with pneumonia and organ failure. Pulmonary manifestations of COVID-19 include fever, fatigue, shortness of breath, and cough [2].

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is characterized by impaired water excretion secondary to the inability to inhibit antidiuretic hormone (ADH) secretion [3]. SIADH, characterized by uncontrolled release of ADH, occurs when the total body water content exceeds urinary excretion, commonly referred to as euvoletic dilutional hyponatremia [3,4].

The mechanism underlying hyponatremia in patients with COVID-19 is excessive release of inflammatory cytokines, including interleukin (IL)-1 $\beta$ , IL-6, and the tumor necrosis factor. IL-6 triggers hypothalamic arginine vasopressin production with consequent hyponatremia [5,6].

In addition to infections, SIADH may occur in neurologic disorders including head injury and stroke, as well as paraneoplastic syndromes and may be associated with the administration of medications such as tricyclic antidepressants and selective serotonin reuptake inhibitors [7–9].

SIADH should be considered in the differential diagnosis in patients with hyponatremia (serum sodium levels <135 mmol/L) associated with plasma hypo-osmolality, urine hyperosmolality (>100 mosmol/kg), and high urinary sodium (>40 mEq/L). Notably, the serum potassium level is normal, no acid-base disturbance is observed, and the serum uric acid level is frequently low in patients with SIADH [4,8].

A systematic review and meta-analysis reported that SIADH-induced hyponatremia was associated with longer length of

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intensive care unit (ICU) stay and was shown to be associated with a high mortality rate in patients with COVID-19. The prognostic value of this finding remains unclear and requires further investigation [10].

Few case reports have described COVID-19–associated SIADH and hyponatremia. We present a case of hyponatremia secondary to SIADH in a patient with COVID-19 pneumonia and a history of kidney transplantation.

## CASE PRESENTATION

A 76-year-old man with a medical history of living-related kidney transplant in 2011, type 2 diabetes mellitus, and hypertension presented to the emergency department with nonspecific symptoms, including malaise, headache, poor oral intake, and fatigue. He denied a history of fever, confusion, seizures, chest, or gastrointestinal symptoms and denied the administration of any new medications or changes to his usual prescription. He had recently received the first dose of the COVID-19 vaccine. Current medications included prednisone, tacrolimus, mycophenolate mofetil, nifedipine, losartan, metoprolol, atorvastatin, glipizide, Januvia/Metformin, magnesium oxide, and omeprazole.

Physical examination showed normal vital signs, and volume status evaluation showed euvoemia. Systemic evaluation including chest and neurologic examination was unremarkable.

Initial chemistry, urinalysis and brain computed tomography were unremarkable (Table 1). The patient was admitted to the hospital for appropriate hydration, with a tentative diagnosis of mildly symptomatic hyponatremia secondary to poor oral intake. We initiated intravenous fluid (IVF) administration, and a Foley catheter was inserted to monitor fluid status. Blood work obtained 6 hours later showed worsening hyponatremia with a serum sodium level of 120 mEq/L but normal renal function; therefore, the patient underwent workup for hyponatremia (Table 2).

The patient's condition worsened 24 hours later, with progressive shortness of breath and low-grade fever but normal blood pressure. Arterial blood gas evaluation results were consistent with severe hypoxemia (type 1 respiratory failure) with anion gap metabolic acidosis. Chest radiography revealed bilateral diffuse interstitial infiltrates (Fig 1). We performed reverse transcriptase-polymerase chain reaction testing for COVID-19,

**Table 2. Follow-up Laboratory Test Results**

Laboratory Studies	
Serum sodium	120 mEq/L
Serum potassium	4.4 mEq/L
Urinary sodium	67 mmol/L
Serum osmolality	230 mosm/kg
Urine osmolality	590 mosm/kg
Serum thyroid stimulating hormone	Normal
Serum cortisol	Normal

and the patient was transferred to the ICU for monitoring and respiratory support after discontinuation of IVF. The patient was tentatively diagnosed with respiratory failure secondary to COVID-19 pneumonia. Hyponatremia was likely secondary to SIADH in the setting of chest infection, which was supported by the laboratory test results. Despite trials of continuous positive airway pressure, the patient's respiratory status continued to deteriorate, which eventually necessitated intubation. The patient also received full empirical therapy for suspected COVID-19 pneumonia, including dexamethasone, favipiravir, tocilizumab, and nebulizers, secondary bacterial infection prophylaxis, and modifications to his anti-rejection medications. He remained hemodynamically stable and did not require inotropic or vasopressor support. The patient's COVID-19 test showed positive results, 12 hours later. The patient's respiratory status improved slightly the following day, and ventilator settings were adjusted to wean the patient from mechanical ventilatory support. He remained intubated in the ICU for 5 days.

**Table 1. Initial Laboratory Test Results**

Laboratory Studies	
WBC count ( $\times 10^6 \mu\text{L}$ )	8,500
Lymphocytes	35%
Neutrophils	45%
Serum hemoglobin	13 g/dL
Platelets ( $\times 10^6 \mu\text{L}$ )	230,000
Serum urea	10 mg/dL
Serum creatinine	0.9 mg/dL
Serum potassium	4.4 mEq/L
Serum sodium	123 mEq/L
Serum uric acid	3 mg/dL

WBC, white blood cells.



**Fig 1.** Chest radiograph (anteroposterior view) showing bilateral diffuse interstitial infiltrates in a patient with COVID-19 pneumonia and a history of kidney transplantation.

**Table 3. Trend of Serum Sodium Level**

Serum [Na+] level					
First Day	Second Day	Third Day	Fourth Day	Fifth Day	Sixth Day
120 mEq/L	123 mEq/L	125 mEq/L	128 mEq/L	131 mEq/L	136 mEq/L

His condition gradually improved, and he was successfully extubated and transferred to the general ward following stabilization of his general condition. The patient's kidney function remained normal throughout admission, and serum sodium level improved gradually with a parallel improvement in his respiratory status (Table 3).

## DISCUSSION

Several studies have reported pneumonia associated with SIADH [11–13]; however, few case reports have discussed SIADH secondary to COVID-19 pneumonia [14,15]. To our knowledge, this is the first case report that describes SIADH-induced hyponatremia in a patient with SARS-CoV-2 infection and a history of kidney transplantation.

Our patient was an elderly man with a history of long-standing diabetes and hypertension and kidney transplantation, who received potent immunosuppressant agents including mycophenolate mofetil. Therefore, the patient was not administered the complete COVID-19 vaccine course.

Immunocompromised patients are known to show greater susceptibility to COVID-19 breakthrough infections [16,17]. Interestingly, the highest risk was observed among recipients of solid organ transplant [16–18].

Furthermore, immunocompromised patients tend to present with atypical clinical manifestations, as observed in the present case [17,19]. Diagnosis of COVID-19 infection was confirmed using reverse transcriptase-polymerase chain reaction testing, and pneumonia was confirmed based on chest radiography findings, which revealed diffuse bilateral pulmonary infiltrates in our patient.

SIADH should be suspected in patients with hyponatremia (serum sodium levels <135 mmol/L), and low plasma osmolality (<280 mosmol/kg), high urine osmolality (>100 mosmol/kg), and high urinary sodium levels (>20 mmol/L) are useful for diagnostic confirmation [3,20].

In the present case, laboratory test results revealed severe hyponatremia (serum sodium 120 mmol/L), serum osmolality 230 mosmol/kg, urine osmolality 590 mosmol/kg, high urinary sodium levels (67 mmol/L), and low serum uric acid levels, all of which were consistent with diagnosis of SIADH [3,4].

Habib et al observed that SIADH may often be an initial presentation of COVID-19 infection [21]. COVID-19-induced hyponatremia is attributed to sepsis and cytokine storm (excessive IL-6 release), which consequently activates the hypothalamic-pituitary-adrenal axis and upregulates arginine vasopressin expression [5,6].

A variety of medications can cause SIADH-induced hyponatremia [7–9]. However, no medication administered by our patient is reported to cause hyponatremia or SIADH.

Severe hyponatremia can precipitate a variety of neurologic symptoms, including lethargy, drowsiness, seizures, and loss of consciousness [19,22] and may even result in brain stem herniation secondary to cerebral edema. Moreover, rapid correction of hyponatremia can lead to serious neurologic insult such as the osmotic demyelination syndrome [23]. Fortunately, supportive management in the ICU and optimal treatment of the primary injury (pneumonia) led to gradual improvement in our patient's condition, and his serum sodium levels returned to the normal range.

Hyponatremia observed in recipients of kidney transplants may be multifactorial in origin [24,25]. Patients who undergo solid organ transplantation show greater susceptibility to infections and may be predisposed to SIADH-induced hyponatremia. Poor oral intake may contribute to hyponatremia in these patients and may lead to hypovolemic hypo-osmolar hyponatremia [16–18]. This condition is often therapeutically challenging. IVF administration can worsen hyponatremia in patients with SIADH owing to the desalination phenomenon [26,27], although IVF is known to improve serum sodium levels in patients with hypovolemia. IVF administration initially led to worsening of serum sodium levels in our patient; however, these improved gradually parallel with improvement in the patient's respiratory status, all of which support the diagnosis of SIADH-induced hyponatremia in this case.

## CONCLUSIONS

COVID-19 is associated with the development of SIADH; therefore, this condition should be considered in the differential diagnosis in patients with hyponatremia. Administration of IVF warrants cautious decision-making in these settings to avoid worsening of hyponatremia. Moreover, vaccination of immunocompromised patients (such as those with a history of kidney transplant) plays a key role in reducing the transmission of the virus and controlling the COVID-19 pandemic.

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