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Case Report

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Unusual Presentation of Hyponatremia: Persistent Hiccups

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ABSTRACT

Hyponatremia is a common electrolyte disturbance with well-recognized neurological and gastrointestinal symptoms. However, it rarely presents with atypical manifestations, such as persistent hiccups. We report a case of a 36-year-old woman with necrotizing tonsillitis who developed persistent hiccups 3 days prior to hospitalization. Laboratory evaluation revealed severe hyponatremia (serum sodium [Na] 122.4 mEq/L), consistent with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). Despite symptomatic treatment, hiccups persisted until serum Na levels were gradually corrected with hypertonic saline and fluid restriction. Hiccups resolved with improved Na levels. This case underscores the importance of considering hyponatremia in the differential diagnosis of persistent hiccups and highlights SIADH as a potential underlying cause.

Keywords: Hiccup; Hyponatremia; Inappropriate ADH syndrome; Tonsillitis

INTRODUCTION

Hyponatremia, defined as a serum sodium (Na) concentration < 135 mEq/L, is the most common electrolyte disorder in clinical practice [1]. It typically presents with a range of neurological and gastrointestinal symptoms, particularly in acute cases, including headache, confusion, nausea, seizures, and even coma. However, in rare instances, hyponatremia may present with atypical or nonspecific symptoms.

Persistent hiccups, often regarded as benign and self-limiting, can occasionally serve as subtle clinical indicators of a more serious underlying pathology. Although uncommon, intractable hiccups have been associated with various conditions including intracranial lesions, gastrointestinal disorders, and metabolic and electrolyte abnormalities [2].

The underlying pathophysiological mechanism remains unclear; however, it has been postulated that hyponatremia contributes to the development of hiccups through its effects on central nervous system (CNS) excitability and brainstem function.

Conflicts of interest
All authors have no conflicts of interest to declare.

Data sharing statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions
Supervision: SWH; Writing - original draft: SL; Writing - review & editing: HWS, JL, MYY.

Here, we report a case of persistent hiccups as the initial manifestation of severe hyponatremia that resolved after correction of underlying electrolyte abnormalities.

CASE REPORT

A 36-year-old woman presented to the emergency department with a 14-day history of sore throat, cough, sputum production, and dyspnea. She had been on treatment for a severe sore throat, and a biopsy confirmed necrotizing tonsillitis (**Figs. 1** and **2**). Three days before admission, she developed persistent hiccups that did not respond to the initial symptomatic management.

On physical examination, the patient was hemodynamically stable with no signs of dehydration or edema. Her vital signs were as follows: blood pressure, 149/77 mmHg; heart

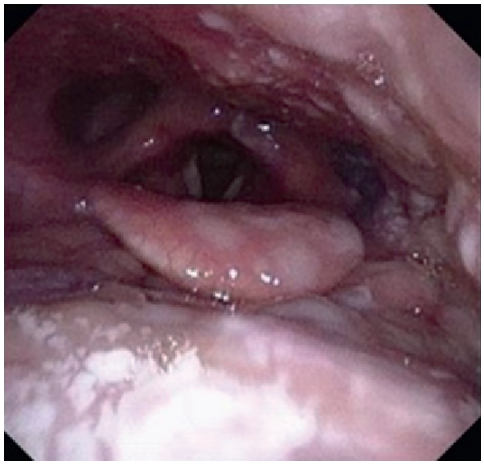

Fig. 1. On physical examination of the larynx, the endoscopic photo showed multiple ulcerative lesions on the left epiglottic surface and oropharynx.

Fig. 2. Neck CT axial image reveals mild asymmetric swelling with heterogeneous enhancement of the left palatine tonsil and aryepiglottic folds, probable pharyngotonsillitis.
CT, computed tomography.

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rate, 74 beats per minute; respiratory rate, 18 breaths per minute; and body temperature, 37.0°C. The initial laboratory evaluation revealed significant electrolyte abnormalities, including severe hyponatremia (serum Na 122.4 mEq/L) and hypokalemia (serum K 2.9 mEq/L). Additional findings included low serum osmolality (246 mOsm/kg) and reduced serum uric acid (1.7 mg/dL). Renal function was within normal limits (serum creatinine 0.4 mg/dL, blood urea nitrogen 6.4 mg/dL), and inflammatory markers were unremarkable (C-reactive protein 0.1 mg/dL). Urinalysis showed elevated urine Na (Na 103 mEq/L) and osmolality (241 mOsm/kg), consistent with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). The fractional excretion of uric acid was 12.7%. The endocrine evaluation revealed a normal thyroid-stimulating hormone (0.30 μIU/mL), adrenocorticotropic hormone (25.4 pg/mL), and basal cortisol level (26.0 μg/dL), with a mildly elevated free T4 (2.13 ng/dL). These results rule out adrenal insufficiency and hypothyroidism. The plasma antidiuretic hormone (ADH) concentration was 4.51 pg/mL, which was inappropriately normal in the context of hyponatremia. Arterial blood gas analysis revealed respiratory alkalosis. The complete blood count, brain CT and chest radiography findings were unremarkable, and no lesions that could have caused hyponatremia were identified.

The patient was managed with fluid restriction, an intravenous bolus, and a continuous infusion of 3% hypertonic saline. Despite corrective efforts, hiccups persisted, Na level decreased to 118.3 mEq/L on day 2 and 116.4 mEq/L on day 3 (**Fig. 3**). Pharmacological interventions included baclofen, and metoclopramide for hiccup control.

The hiccups lasted until the fifth day, and resolved on the sixth day of hospitalization. Serum Na level began to improve slowly 2 days before the resolution of hiccups, without overcorrection. Serum Na concentrations were 120 mEq/L on day 4, 123.1 mEq/L on day 5, 127.7 mEq/L on day 6, and 131.4 mEq/L on day 7, when hypertonic saline administration was discontinued (**Fig. 3**). The patient was discharged in a stable condition on the eighth day of hospitalization.

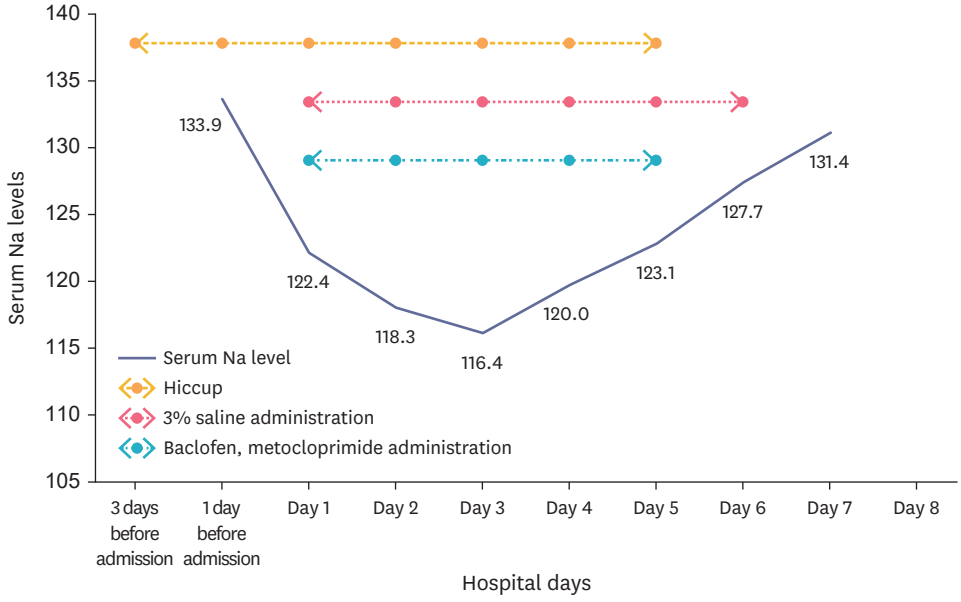

Fig. 3. Symptoms, therapeutic drugs, fluid administration, and changes in serum Na levels.
Na, sodium.

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DISCUSSION

Hiccups are repeated involuntary, spasmodic, and temporary contractions of the diaphragm accompanied by sudden closure of the glottis [3]. They are mediated by a reflex arc that involves afferent pathways (phrenic, vagal, and sympathetic nerves), a central processing center in the medulla oblongata, and efferent pathways to the respiratory muscles. Physical and chemical irritants, inflammatory, and neoplastic conditions involving the hiccup reflex may cause hiccups [4].

Persistent hiccups have been associated with a variety of central and peripheral causes. The central causes of hiccups include stroke, space-occupying lesions, and injury, whereas peripheral causes include lesions along the arc such as tumors, myocardial ischemia, herpes infection, gastroesophageal reflux disease, and instrumentation applied to the human body [4]. Notably, metabolic and electrolyte disturbances have been implicated in disrupting the reflex arc [2].

Although rare, hyponatremia has been reported to cause persistent hiccups, likely through interference with CNS inhibitory mechanisms. Hyponatremia may precipitate hiccups by disrupting normal neuronal function in the brainstem hiccup reflex arc [2]. Several case reports have described persistent hiccups as early signs of hyponatremia, especially in the elderly or neurologically compromised individuals [2]. A case-control study involving hospitalized patients reported that the likelihood of developing hiccups increased 17-fold with every 10 mEq/L reduction in serum Na levels [5].

In the present case, the diagnosis of the SIADH was made based on the patient's euvolemic status, decreased serum osmolality, inappropriately concentrated urine with elevated Na levels, and normal adrenal and thyroid function. Plasma ADH levels were inappropriately normal, given the degree of hyponatremia, further supporting the diagnosis.

The underlying etiology of hyponatremia in this patient was likely multifactorial. First, non-osmotic stimuli, such as pain, nausea, and emotional stress are known to provoke vasopressin (ADH) secretion, leading to dilutional hyponatremia. Although excessive water intake due to hiccup-related discomfort could be a contributing factor, the patient had no history of polydipsia. Second, pharyngotonsillitis may have played a role. Hyponatremia is a frequently observed abnormality in pediatric and adult patients with respiratory tract infections. Although the exact mechanism remains unclear, SIADH is thought to result from inflammatory cytokine-mediated ADH secretion or transient resetting of the osmostat in response to fever and dehydration. Recent studies have suggested that interleukin (IL)-mediated pathways contribute to inappropriate hormone release [6]. Furthermore, previous studies have shown that inflammatory cytokines such as IL-1β and IL-6 can cause hyponatremia in inflammatory conditions. In a study evaluating the hypothalamic–pituitary–adrenal axis response following intravenous administration of IL-6 in cancer patients, an increase in plasma arginine vasopressin levels was observed [7]. Additionally, an animal study demonstrated that IL-1β stimulates both central and peripheral vasopressin release [8]. Although CRP elevation was not observed in our patient, leukocytosis was present—white blood cell count was initially 11,300 × 10^3/μL on day 1, increased to 15,900 × 10^3/μL on day 3, then decreased to 11,700 × 10^3/μL on day 6 and 8,400 × 10^3/μL on day 7—and the timing of its normalization closely corresponded to the improvement of hyponatremia. Third, opioid use may have exacerbated SIADH. The patient was prescribed tramadol 5 days before admission,

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which is 2 days before hiccup appeared, for neck pain. Tramadol was discontinued at the time of hospitalization, Dihydrocodeine was initiated on hospital day 3 to control her cough, continued for 7 days during the hospital stay, and further prescribed for 15 days at discharge. In this patient, tramadol may be considered one of the causes because it was administered before the onset of symptoms. Opioids are well-documented SIADH inducers. Tramadol may increase ADH secretion directly via opioid receptors and indirectly via enhanced serotonin activity, which in turn promotes vasopressin release. However, most reported cases of tramadol-induced hyponatremia occurred in elderly patients and often involved higher doses [9,10]. Fourth, although evidence is limited regarding hypokalemia as an isolated cause of hiccups, other accompanying electrolyte imbalances such as hypokalemia may also contribute to their development. Hypokalemia can cause neuromuscular irritability and has been implicated in various arrhythmias and muscle disorders [11]. In this patient, the potassium levels were 2.9 mEq/L on day 1, 3.4 mEq/L on day 2, and 3.0 mEq/L on day 3, respectively and potassium was supplemented through both intravenous administration on day 1 to 2, and oral medication on day 3 to 7. The temporal correlation between the onset of persistent hiccups and the development of hyponatremia and their resolution following correction of serum Na levels supports the hypothesis that hiccups may be an early and underrecognized symptom of severe hyponatremia in some patients.

In this patient, hyponatremia was not severe on the day before admission. Initially, tonsillitis may have been the cause of the hiccups. It can be presumed that severe hyponatremia during hospitalization, caused by multiple factors, acted as a sustaining factor for the intractable hiccups. This case highlights a rare and atypical presentation of SIADH-induced hyponatremia, with persistent hiccups as the initial symptom. Clinicians should be vigilant for metabolic and electrolyte abnormalities in patients presenting with unexplained or intractable hiccups. In addition to symptomatic and pharmacological management, a thorough evaluation of the underlying causes, including hyponatremia, should be a part of the diagnostic approach in such cases.

In conclusion, the present report emphasizes the importance of evaluating serum electrolytes—particularly Na—in patients with persistent hiccups, since prompt recognition and management of hyponatremia (as seen here in the context of SIADH) may alleviate an otherwise unexplained symptom.

REFERENCES

1. Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. *Am J Med* 2013;126:S1-S42. PUBMED | CROSSREF
2. Jones JS, Lloyd T, Cannon L. Persistent hiccups as an unusual manifestation of hyponatremia. *J Emerg Med* 1987;5:283-287. PUBMED | CROSSREF
3. Sampath V, Gowda MR, Vinay HR, Preethi S. Persistent hiccups (singultus) as the presenting symptom of lateral medullary syndrome. *Indian J Psychol Med* 2014;36:341-343. PUBMED | CROSSREF
4. Chang FY, Lu CL. Hiccup: mystery, nature and treatment. *J Neurogastroenterol Motil* 2012;18:123-130. PUBMED | CROSSREF
5. George J, Thomas K, Jeyaseelan L, Peter JV, Cherian AM. Hyponatraemia and hiccups. *Natl Med J India* 1996;9:107-109. PUBMED
6. Park SW, Shin SM, Jeong M, et al. Hyponatremia in children with respiratory infections: a cross-sectional analysis of a cohort of 3938 patients. *Sci Rep* 2018;8:16494. PUBMED | CROSSREF

https://doi.org/10.5049/EBP.2025.23.e6

7. Mastorakos G, Weber JS, Magiakou MA, Gunn H, Chrousos GP. Hypothalamic-pituitary-adrenal axis activation and stimulation of systemic vasopressin secretion by recombinant interleukin-6 in humans: potential implications for the syndrome of inappropriate vasopressin secretion. *J Clin Endocrinol Metab* 1994;79:934-939. PUBMED | CROSSREF

8. Landgraf R, Neumann I, Holsboer F, Pittman QJ. Interleukin-1 beta stimulates both central and peripheral release of vasopressin and oxytocin in the rat. *Eur J Neurosci* 1995;7:592-598. PUBMED | CROSSREF

9. Akl A, Alwagdani M, Aziz AA, Saad R, Baslaim G, Aldhaheri F. Tramadol-induced hyponatremia: case report highlighting the mechanism and review of literature. *Urol Nephrol Open Access J* 2021;9:75-77. CROSSREF

10. Falhammar H, Calissendorff J, Skov J, Nathanson D, Lindh JD, Mannheimer B. Tramadol- and codeine-induced severe hyponatremia: a Swedish population-based case-control study. *Eur J Intern Med* 2019;69:20-24. PUBMED | CROSSREF

11. Kardalas E, Paschou SA, Anagnostis P, Muscogiuri G, Siasos G, Vryonidou A. Hypokalemia: a clinical update. *Endocr Connect* 2018;7:R135-R146. PUBMED | CROSSREF