## CONCLUSION

A fever of unknown origin may be a manifestation of the hepatosplenic form of CSD and such cases can be a diagnostic and also a treatment challenge despite the antibiotic treatment. The use of corticosteroids could improve the clinical evolution of these patients, reduce their morbidity, and shorten the duration of antibiotic therapy, side effects and hospitalization time. This therapeutic option can be considered in cases of CSD with hepatosplenic abscesses and persistent clinical manifestations.

## REFERENCES


1. Sarno M, Rosanio FM, De Brasi D, et al. Systemic cat-scratch disease: a "Troublesome" diagnosis. *Pediatr Infect Dis J*. 2021;40:e117–e119.
2. Phan A, Castagnini LA. Corticosteroid treatment for prolonged fever in hepatosplenic cat-scratch disease: a case study. *Clin Pediatr (Phila)*. 2017;56:1291–1292.
3. Margileth AM. Recent advances in diagnosis and treatment of cat scratch disease. *Curr Infect Dis Rep*. 2000;2:141–146.
4. Sharma R, Arshad AM, Sardar S, et al. Hepatosplenic bartonellosis in an immunocompetent teenager: an atypical presentation of cat-scratch disease. *Cureus*. 2021;13:e13219.
5. Nawrocki CC, Max RJ, Marzec NS, et al. Atypical manifestations of cat-scratch disease, United States, 2005-2014. *Emerg Infect Dis*. 2020;26:1438–1446.
6. Barros S, de Andrade GC, Cavalcanti C, et al. Cat scratch disease: not a benign condition. *Ocul Immunol Inflamm*. 2018;26:1115–1122.
7. Spach HD, Kaplan LS. Treatment of cat scratch disease. Available at: https://www.uptodate.com/contents/treatment-of-cat-scratch-disease. Accessed February 10, 2022.
8. Florin AT, Zaoutis ET, Zaoutis BL. Beyond cat scratch disease: widening spectrum of *Bartonella Henselae* infection. *Pediatrics* 2008;121;e1413.
9. Sandoval AC, Reyes FT, Prado MA, et al. Cat-scratch disease in the pediatric population: 6 years of evaluation and follow-up in a public hospital in chile. *Pediatr Infect Dis J*. 2020;39:889–893.
10. Bryant K, Marshall GS. Hepatosplenic cat scratch disease treated with corticosteroids. *Arch Dis Child*. 2003;88:345–346.


OPEN

# SYNDROME OF INAPPROPRIATE SECRETION OF ANTIDIURETIC HORMONE ASSOCIATED WITH VARICELLA INFECTION IN CHILDREN

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**Abstract:** A 9-year-old girl with remarkable hyponatremia was diagnosed with SIADH that was likely secondary to varicella. Under appropriate treatment, her serum sodium returned to the normal level. There was no evidence of hyponatremia at a 3-month follow-up. We propose that medical professionals need to consider the existence of that SIADH when treating patients with varicella who present with severe hyponatremia.

**Key Words:** varicella, syndrome of inappropriate antidiuretic hormone secretion, hyponatremia

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## CASE REPORT

A previously healthy 9-year-old girl was taken to the emergency department of our hospital with skin eruption for 9 days and fever for 7 days. She had symptoms of dizziness and nausea-vomiting for the last 2 days and did not have cough or abdominal pain. Oral valacyclovir and cefixime had been started 3 days previously by the clinician of the local hospital to treat her varicella. She was treated with intravenous 3% hypertonic saline for 1 day to treat a serum sodium level of 114.3 mmol/L. However, the patient's hyponatremia showed little improvement. She had never been vaccinated against varicella.

On arrival, she was fully conscious and alert. Physical examination revealed a temperature of 37.5 °C, blood pressure of 110/70 mm Hg, heart rate of 90 beats/min, respiratory rate of 20 times per minute and oxygen saturation of 98% on ambient air. The skin examination was remarkable for a vesicular skin rash over the trunk, head and face. The chest, heart, abdominal and neurological examinations were normal without nuchal rigidity or meningeal signs.

Cerebrospinal fluid (CSF) examination showed no pleocytosis with normal protein and glucose. CSF culture was sterile. CSF polymerase chain reaction investigations were not performed for varicella-zoster virus (VZV) DNA. Blood tests revealed severe hyponatremia (114 mmol/L) (normal, 135–145 mmol/L), with calculated osmolarity of 257 mOsm/kg H2O. Serum blood urea nitrogen level was 2.6 mmol/L (normal, 1.7–8.3 mmol/L), creatinine level of 29 μmol/L (normal, 44–110 μmol/L), uric acid level of 137 μmol/L (normal, 155–360 μmol/L) and uric sodium level of 67.9 mmol/L. Serum procalcitonin was normal. Serologic studies confirmed primary VZV infection (IgG and IgM anti-VZV positive), whereas antibody titers to herpes simplex virus showed no significant changes. Thyroid function tests and tests for adrenal function were normal. Blood cultures were negative. Findings on chest radiograph, magnetic resonance imaging of the head, electrocardiogram and electroencephalogram were normal. Metagenomic next-generation sequencing performed on blood showed *Acinetobacter junii* as the suspicious pathogen.

With an infusion of 3% saline and treatment with furosemide, her serum sodium returned to the normal level within 3 days and all lesions resolved eventually (Fig. 1). She was also treated with intravenous amoxicillin and clavulanate potassium for 3 days followed by oral for 6 days in consideration of *A. junii* infection. On the 12th day, the patient was discharged with a serum sodium of 137 mmol/L. Her hyponatremia did not relapse at the subsequent follow-up to 3 months after discharge.

## DISCUSSION

Hyponatremia is a common electrolyte abnormality in hospital inpatients.[1] Secretion of antidiuretic hormone (SIADH) is a condition characterized by hypotonic and euvolemic hyponatremia caused by impaired free water excretion resulting from antidiuretic hormone release in the absence of adequate stimuli.[2] The underlying causes of SIADH can be categorized as malignancies, pulmonary or central nervous system (CNS) disorders, medications, or other causes, such as infection inflammation, and the postoperative state.[1,2] This patient's elevated urine sodium concentration, euvolemic status, low serum osmolality, declined uric acid and normal cardiac, hepatic, endocrine and adrenal function were consistent with the diagnosis of SIADH. Since the absence of other identifiable causes of SIADH and there was a strong temporal association between the onset of chickenpox and the occurrence of severe hyponatremia, it was hypothesized that a causal relationship did exist between the 2 above.

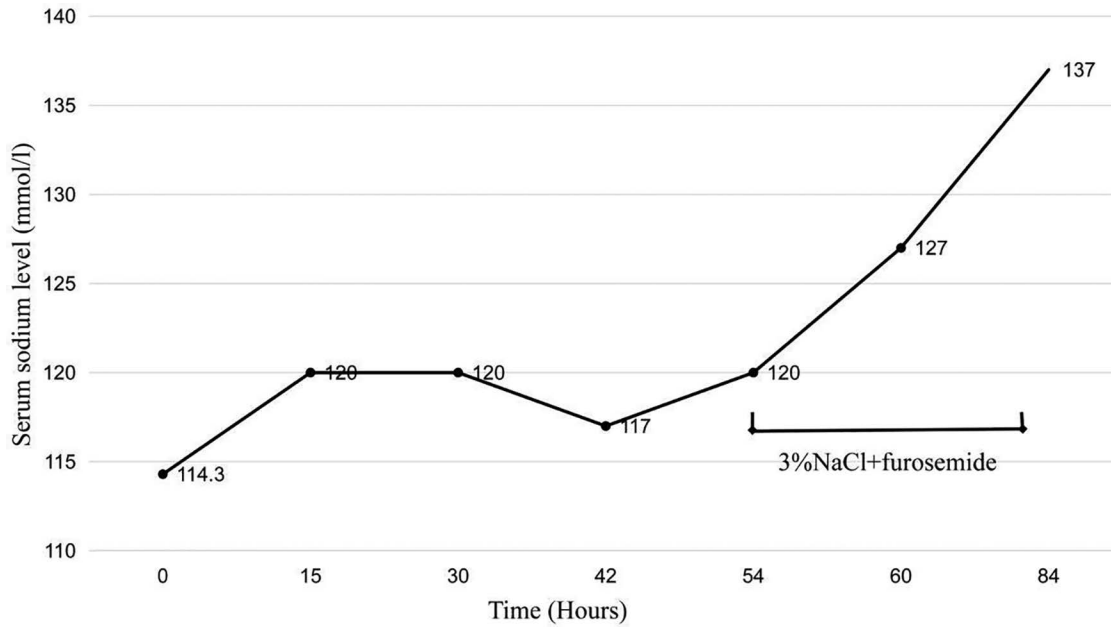


**FIGURE 1.** The serum sodium level and treatment in the patient.

SIADH associated with herpes zoster (shingles) was first described in 1983 by Maze et al.[3] To date, the association of SIADH with localized and disseminated herpes zoster has been well described.[3–8] The time span from the onset of herpes zoster to the identification of hyponatremia is usually 3–7 days with a duration of hyponatremia of 4 days to 4 months. With appropriate management, most cases had favorable prognoses, and a few cases have developed postherpetic neuralgia or even death. As far as we know, there was no report of primary VZV infection with SIADH.

The underlying mechanism of SIADH associated with VZV infection remains unclear. We did not examine the antibody and polymerase chain reaction of VZV in the patient's CSF. Although we could not find any clinical evidence of VZV infection in the CNS such as meningeal irritation signs, pleocytosis, it cannot be ruled out that SIADH in our patient was associated with VZV infection in the CNS. Kageyama et al[5] described a 59-year-old man with SIADH associated with Ramsay Hunt syndrome; the patient's high antibody titers to the VZV in his serum; CSF indicate the CNS involvement.

*A. junii* is rarely responsible for disease in humans, with documented cases of septicemia in neonates and pediatric oncology patients.[9] There is emerging evidence that hyponatremia may alter the immune response and could explain why this patient is infected with *A. junii*.[10] It was considered that *A. junii.* was unlikely to have played a role in our patient's hyponatremia because the *A. junii* infection persisted when the hyponatremia had been corrected.

In conclusion, this case highlights the possible association between SIADH and primary VZV infection. To the best of our knowledge, this is the first report of SIADH associated with varicella in children. Clinicians should be aware of this possible association as prompt diagnosis and effective treatment of SIADH is critical.

## REFERENCES

1. Seay NW, Lehrich RW, Greenberg A. Diagnosis and management of disorders of body tonicity-hyponatremia and hypernatremia: core curriculum 2020. *Am J Kidney Dis*. 2020;75:272–286.
2. Moritz ML. Syndrome of inappropriate antidiuresis. *Pediatr Clin North Am*. 2019;66:209–226.
3. Maze SS, Klaff LJ, Yach D. Syndrome of inappropriate antidiuretic hormone secretion in association with herpes zoster of the chest wall. A case report. *S Afr Med J*. 1983;63:735–736.
4. Ingraham IE Jr, Estes NA, Bern MM, et al. Disseminated varicella-zoster virus infection with the syndrome of inappropriate antidiuretic hormone. *Arch Intern Med*. 1983;143:1270–1271.
5. Kageyama Y, Nakamura M, Sato A, et al. Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) associated with Ramsay Hunt syndrome: report of a case and review of the literature. *Jpn J Med*. 1989;28:219–222.
6. Wang CC, Shiang JC, Chen JT, et al. Syndrome of inappropriate secretion of antidiuretic hormone associated with localized herpes zoster ophthalmicus. *J Gen Intern Med*. 2011;26:216–220.
7. Bassi V, Fattoruso O, Santinelli C. Localized herpes zoster infection: a rare cause of syndrome of inappropriate secretion of antidiuretic hormone. *Oxf Med Case Reports*. 2017;2017:omx065.
8. Foppiani L. SIADH with severe hyponatremia in an elderly man with herpes zoster infection: a causal or casual association? *Intern Med*. 2018;57:3393–3398.
9. Kappstein I, Grundmann H, Hauer T, et al. Aerators as a reservoir of Acinetobacter junii: an outbreak of bacteraemia in paediatric oncology patients. *J Hosp Infect*. 2000;44:27–30.
10. van der Meer JW, Netea MG. A salty taste to autoimmunity. *N Engl J Med*. 2013;368:2520–2521.