JOURNAL OF COMMUNITY HOSPITAL INTERNAL MEDICINE PERSPECTIVES, 2017
VOL. 7, NO. 6, 358–362
https://doi.org/10.1080/20009666.2017.1407209

Taylor & Francis
Taylor & Francis Group

CASE REPORT

Ticks and salt: an atypical case of neuroborreliosis

Nazia Siddiqui, Deidre M. St. Peter and Surendra Marur

Department of Medicine, Greater Baltimore Medical Center, Baltimore, MD, USA

ABSTRACT

It is well documented that central nervous system (CNS) infections may lead to syndrome of inappropriate anti-diuretic hormone secretion (SIADH), but diagnosing these can prove difficult in patients with atypical presentations. We present a case of SIADH and muscle weakness in a patient without typical signs of CNS infection who was tested and diagnosed with neuroborreliosis based largely on her likelihood of exposure. This case indicates the need for Lyme testing in patients with unexplained SIADH who live in endemic areas. The patient was an 83-year-old female with a history of type 2 diabetes and hypertension, who presented from her primary care physician's office when her sodium was found to be 123 mEq/L. Her sole symptom was proximal muscle weakness. The diagnosis of SIADH was reached based on laboratory data. A trial of fluid restriction was initiated, but neither her sodium nor her muscle weakness improved. Lyme testing was performed as the patient lived in an endemic area and was positive. Lumbar puncture showed evidence of neurologic involvement. After realizing the appropriate treatment for hyponatremia in this case, intravenous ceftriaxone was started, and patient's sodium levels improved and muscle weakness resolved. Studies show that SIADH is associated with CNS infections, likely related to the inflammatory cascade. However, the atypical presentation of neuroborreliosis for our patient delayed the appropriate diagnosis and treatment. Our case demonstrates the need to screen for Lyme disease in endemic areas in patients presenting with neurologic symptoms and SIADH.

ARTICLE HISTORY
Received 20 June 2017
Accepted 2 November 2017

KEYWORDS
Neuroborreliosis; Lyme disease; syndrome of inappropriate anti-diuretic hormone; SIADH; hyponatremia; proximal muscle weakness; endemic lyme

1. Introduction

Hyponatremia, defined as a serum sodium level below 135 mEq/L, is an incredibly common finding among hospitalized patients. Up to 30% of those patients have sodium levels below 135 mEq/L and the number of geriatric patients with hyponatremia may be even higher [1,2]. One study showed that up to 50% of nursing home residents have sodium levels below 130 mEq/L [3].

Clinical manifestations of hyponatremia often occur below sodium levels of 125 mEq/L and include confusion, headaches, lethargy, muscle cramps and depressed reflexes. More severe symptoms include seizures, coma, herniation of brain tissue or death, related to cerebral edema [4].

The approach to diagnosing and managing hyponatremia is based on the etiology, which can be determined by serum osmolarity, volume status and urine sodium levels (Table 1). If the serum osmolality is normal or high, glucose, proteins, lipids or exogenous solutes are likely causing dilutional hyponatremia. If the serum osmolarity is low, one must next assess the clinical volume status. Hypovolemic hyponatremia may be caused by renal or non-renal loss of solutes. Hypervolemic hyponatremia is attributable to congestive heart failure, hepatic failure or nephrotic syndrome. Euvolemic hyponatremia can be from the rarer psychogenic polydipsia or beer potomania when the urine is dilute, or from SIADH when the urine is inappropriately concentrated.

Syndrome of inappropriate anti-diuretic hormone secretion (SIADH) is defined as hyponatremia and hypo-osmolarity resulting from inappropriate, continued secretion or action of the hormone despite normal or increased plasma volume, which results in impaired water excretion [8]. The diagnosis of SIADH is made based on Bartter and Schwartz criteria, as follows:

(1) Decreased plasma osmolality (<275 mOsm/L)
(2) Inappropriately concentrated urine (>100 mOsm/L)
(3) Euvolemic
(4) Elevated urine Na (>20 mEq/L)
(5) Euthyroid, eucortisolemic and no diuretic use.

Management of SIADH begins with identification of underlying cause and appropriate treatment. Treatment of SIADH of unknown etiology entails fluid restriction and sodium chloride tablets. For refractory cases, demeclocycline, urea and vaptans are used [9].

In the following, we discuss a case of SIADH with associated muscle weakness diagnosed using the Bartter and Schwartz criteria [9]. Our patient did not respond

CONTACT Nazia Siddiqui n.siddiqui1@saba.edu Department of Medicine, Greater Baltimore Medical Center, Baltimore, MD, USA

Table 1. Causes of hyponatremia [4–7].

Serum osmolarity	Volume status	Urine findings	Cause of hyponatremia
Normal			• Hyperproteinemia • Hyperlipidemia
High (<295 mOsm/L)			• Hyperglycemia • Exogenous solutes (radiocontrast, mannitol)
Low (<280 mOsm/L)	Hypovolemic	Urine Na <10 mEq/L	Non renal salt loss • Dehydration • Vomiting • Diarrhea
		Urine Na >20 mEq/L	Renal salt loss • Diuretics • ACE inhibitor • Mineralocorticoid deficiency
	Euvolemic	Urine Na >20 mEq/L, urine osmolarity <300 mOsm/L	• Psychogenic polydipsia • Beer potomania
		Urine Na >20 mEq/L, urine osmolarity >300 mOsm/L	• SIADH (drugs, neoplasm, CNS disease, pulmonary disease, post-operative state, pain, HIV)
	Hypervolemic		• CHF • Hepatic failure • Nephrotic syndrome

as expected to SIADH treatment; hence, other causes of muscle weakness were considered. The cause of SIADH and muscle weakness was found to be a central nervous system (CNS) infection, though the diagnosis was difficult to reach as the patient was not displaying typical infectious signs and symptoms. Instead, we tested the individual based on exposure risk, leading to the appropriate diagnosis and management of the underlying cause of SIADH.

2. Case

Our patient was an 83-year-old woman with a past medical history of type 2 diabetes mellitus, hypertension and microcytic anemia who lived in rural Maryland and worked at her family's produce stand.

Three weeks prior to her admission for weakness and hyponatremia, she presented with abdominal pain, and was found to have a urinary tract infection and hypontremia. Her sodium on the first admission was 121 mEq/L and she was discharged with sodium of 129 mEq/L. She did well for several weeks until she had sudden onset diffuse body pain followed by arm weakness one week prior to presentation. She presented to her primary care physician after the onset of proximal bilateral arm weakness, and during diagnostic work-up she was found to be hyponatremic.

On presentation on this admission, her vital signs were within normal limits, except for a mildly elevated blood pressure. The exam was grossly normal except for 3/5 muscle strength in the biceps, triceps, deltoids and quadriceps. There were no rashes present and the patient denied any recent history of rashes. She was hyperglycemic, with sodium of 121 mEq/L after correction. She was afebrile with no elevated white blood cell count. Imaging of chest was negative for masses or other abnormalities.

Lab values obtained during her hospitalization are displayed in Tables 2 and 3.

There were two problems we faced: hyponatremia and muscle weakness. To evaluate her hyponatremia, thyroid stimulating hormone, cortisol and computed tomography (CT) head were evaluated and found to be within normal limits. Medications which could have contributed to hyponatremia were discontinued (lisinopril). The physical exam suggested euvolemic hyponatremia, with urine and electrolyte studies confirming SIADH of unknown etiology. In following the management guidelines, she was fluid restricted to 1000 mL/day. After three days, sodium chloride (NaCl) pills three times daily (TID) were added as her sodium levels and symptoms were minimally improved with fluid restriction, alone.

To evaluate her muscle weakness, she was seen by nephrology and neurology. Magnetic resonance images of head, spine and brachial plexus were unrevealing. Lyme screening was performed given her residence in and endemic area and resulted positive with many immunoglobulin IgG and IgM bands appearing. Lumbar puncture was performed, demonstrating lymphocytic pleocytosis. Together with the Lyme serology, the lumbar puncture made neuroborreliosis the leading diagnosis in our patient and infectious disease specialists recommended prompt treatment.

Her sodium was 137 mEq/L when we started treatment with ceftriaxone, having normalized two days prior. The day after antibiotics were started, her sodium trended down to 132 mEq/L. By the time of antibiotic initiation, the patient had been taking NaCl pills 1 g TID for eight days and her muscle weakness was largely unchanged. After 4 days of appropriate treatment with ceftriaxone, her sodium was 143 mEq/L and she was discharged on one NaCl tablet daily. Her muscle weakness had also markedly improved by discharge. Her strength was 5/5 in quadriceps bilaterally, 4/5 in the

Table 2. Sodium levels during hospitalization.

Day of hospitalization	Proximal muscle strength	Sodium (mEq/L)	Urine osmolarity	Urine sodium	Urine creatinine	Intervention
1 (8/8)	Deltoids: 3/5 Biceps: 3/5 Triceps: 3/5 Quadriceps: 3/5	118–120	527	140	96	
2 (8/9)	Deltoids: 2/5 Biceps: 2/5 Triceps: 2/5 Quadriceps: 3/5	118–119				
3 (8/10)	Deltoids: 2/5 Biceps: 2/5 Triceps: 2/5 Quadriceps: 3/5	116–121	550	77	29	Started water restriction to 800 mL and NaCl 1 g TID
4 (8/11)	Deltoids: 1/5 Biceps: 1/5 Triceps: 4/5 Quadriceps: 3/5	124				
5 (8/12)	Deltoids: 1/5 Biceps: 1/5 Triceps: 4/5 Quadriceps: 3/5	128				
6 (8/13)	Deltoids: 1/5 Biceps: 3/5 Triceps: 4/5 Quadriceps: 4/5	130				
7 (8/14)	Deltoids: 1/5 Biceps: 3/5 Triceps: 4/5 Quadriceps: 4/5	129				
8 (8/15)	Deltoids: 1/5 Biceps: 4/5 Triceps: 4/5 Quadriceps: 4/5	129				Water restriction to 1000 mL/day
9 (8/16)	Deltoids: 1/5 Biceps: 4/5 Triceps: 4/5 Quadriceps: 5/5	134				
10 (8/17)	Deltoids: 2/5 Biceps: 4/5 Triceps: 4/5 Quadriceps: 5/5	135				Lumbar puncture
11 (8/18)	Deltoids: 3/5 Biceps: 4/5 Triceps: 4/5 Quadriceps: 5/5	137				Started ceftriaxone 2 g/day
12 (8/19)	Deltoids: 3/5 Biceps: 4/5 Triceps: 4/5 Quadriceps: 5/5	137	271	68	37	
13 (8/20)	Deltoids: 2/5 Biceps: 5/5 Triceps: 5/5 Quadriceps: 5/5	139				
14 (8/21)	Deltoids: 2/5 Biceps: 4/5 Triceps: 4/5 Quadriceps: 5/5	143				

Salt tablets were added on hospital day 3 (8/10) and discontinued on hospital day 11 (8/18). Ceftriaxone was started on hospital day 11 (8/18) for a duration of 21 days (completed 9/8).

Table 3. Cerebrospinal fluid analysis (lumbar puncture on 8/17).

CSF WBC	73
CSF RBC	355
CSF neutrophils	3
CSF lymph	86
CSF glue	61
CSF protein	92

biceps/triceps, 3/5 in deltoids, and she was without any pain. One month after she was discharged, muscle weakness had completely resolved.

Importantly, she decided to forego salt replacement or fluid restriction upon discharge and presented to her primary care physician after two weeks with completely normal sodium levels and no residual weakness.

3. Discussion

It is well known that SIADH is a diagnosis of exclusion. In the case of our patient, suspicion of any infection was low based on her clinical presentation. The question then arises: do all hyponatremic patients need to be tested for Lyme disease?

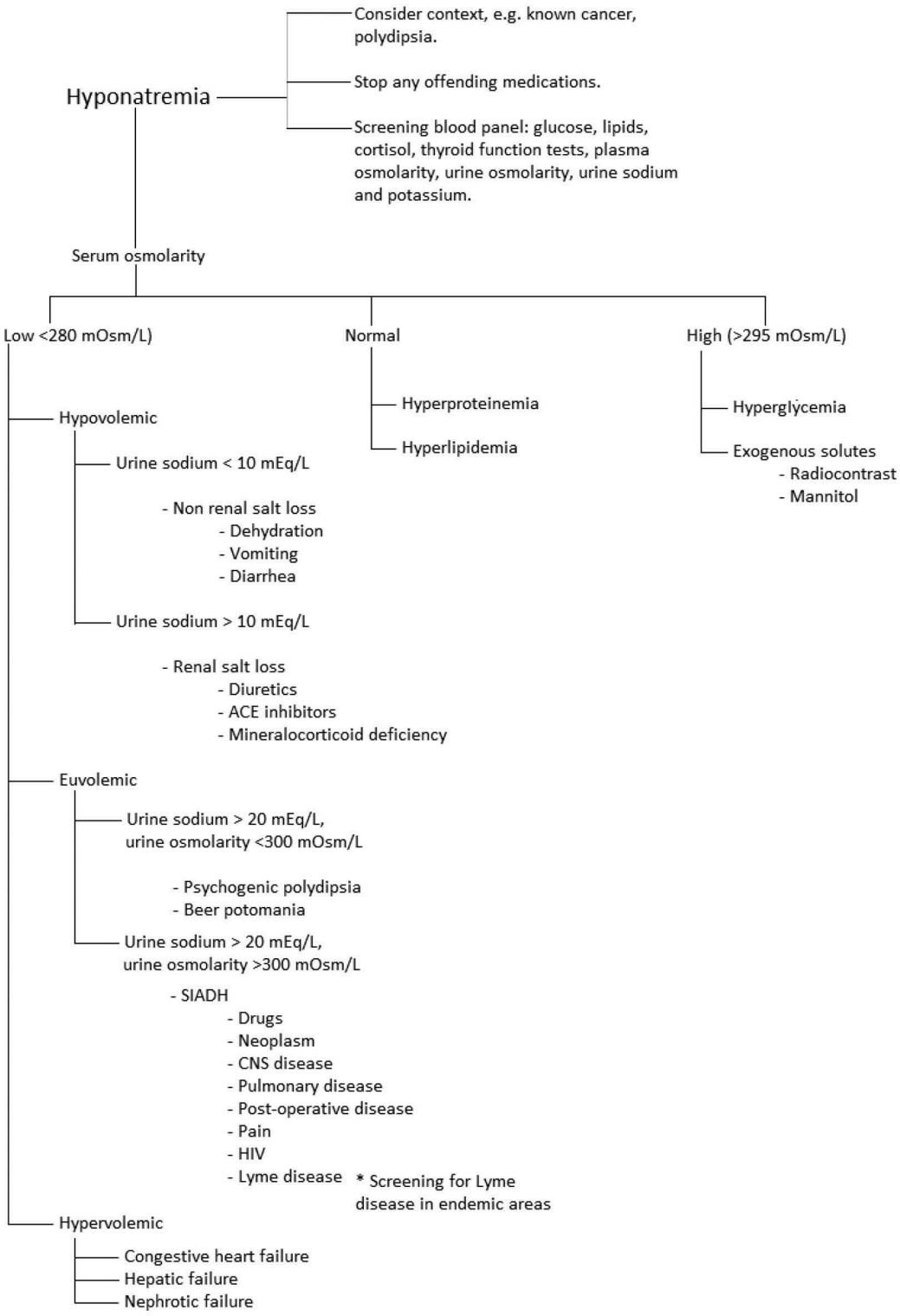

Figure 1. Revised approach to hyponatremia.

*Note the addition of Lyme disease screening for hypo-osmolar euvolemic hyponatremia.

This case is unique in that it demonstrates the challenges of managing SIADH when the underlying cause is not apparent. There was an extensive search for the etiology of her weakness, as she had a CT and MRIs to exclude lesions, malignancy and other causes of SIADH. She was fluid restricted and given exogenous salt to correct the hyponatremia, but her muscle weakness and SIADH did not fully resolve until antibiotic therapy was started appropriately for her neuroborreliosis. Our patient had no signs and symptoms suggestive of infection: no increased white count, no fever, no history of rash nor any memory of tick bite (although tick bites are seldom recalled in patients with Lyme disease). Furthermore, when SIADH is caused by infection, it is more commonly associated with pulmonary disease [9]. In her case, the decision to test for Lyme disease was

based solely on exposure. We argue that in Lyme disease endemic areas, such as rural Maryland, there should be Lyme screening for all hyponatremic patients found to have unexplained SIADH, especially patients with neurologic symptoms. It has been well documented that CNS infections may lead to hyponatremia and it is time this finding makes its way into the minds of young practitioners in the setting of refractory hyponatremia. We propose that in endemic areas, all patients presenting with hypo-osmolar euvolemic hyponatremia, particularly those with coexisting neurologic symptoms, should be screened for Lyme disease (Figure 1).

The relationship between hyponatremia and CNS infections is well documented with many theories about the mechanism. In some cases, it may be from direct loss of electrolytes from fever or vomiting, or from the use of hypo-osmolar fluids for rehydration, rather than from SIADH. Complicating matters further is the fact that other non-osmotic stimulants of ADH release such as diarrhea, vomiting, excessive sweating, systemic vasodilation, and leakage of fluid from the intravascular compartment are all commonly seen with infections and can further decrease serum sodium. A study of tick-borne encephalitis showed that only 5% of hyponatremia during meningoencephalitis was caused by SIADH, the rest was from electrolyte loss [10]. CNS infections that cause SIADH may do so via a 'reset osmostat'. This is when the brain resets its osmostat to maintain serum sodium at a lower concentration than normal, and is facilitated by increased release of ADH [11]. Reset osmostat has been reported in diseases like tuberculosis and malaria [12,13]. In 1995, Patwari et al. studied 60 children diagnosed with bacterial meningitis and demonstrated that approximately 35% were diagnosed with SIADH and that the diagnosis was associated with severe meningeal inflammation [14]. The relationship between intracranial inflammation and ADH may be from increased levels of pro-inflammatory cytokines (i.e., IL-6, IL-1B), as well as of neutrophils, C-reactive protein and brain natriuretic peptide, all leading to increased release of ADH. A very small study done in 1994 including six patients with cancer showed that two hours after injection with IL-6, plasma ADH rose in all patients suggesting that this inflammatory cytokine may directly cause SIADH [15]. When inflammatory processes are responsible for SIADH, the syndrome usually will resolve after treatment of the infection [16,17].

In summary, we propose screening for Lyme disease in endemic areas for all patients with unexplained SIADH, particularly those with neurologic symptoms. The search for infection in an asymptomatic patient is difficult and not always practical (i.e., cannot order tests for every pathogen). We propose that in endemic areas, Lyme testing is a cost-effective test that can be done early on for patients with hyponatremia, in particular that which is being attributed to SIADH. We suggest testing for Lyme disease and managing with antibiotics before concluding SIADH of unknown etiology and managing with fluid restriction, salt pills, and vasopressin receptor antagonists (i.e., vaptans) or demeclocycline.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clin Chim Acta. 2003;337(1–2):169–172.
[2] DeVita MV, Gardenswartz MH, Konecky A, et al. Incidence and etiology of hyponatremia in an intensive care unit. Clin Nephrol. 1990;34(4):163–166.
[3] Miller M, Morley JE, Rubenstein LZ. Hyponatremia in a nursing home population. J Am Geriatr Soc. 1995;43(12):1410–1413.
[4] Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342(21):1581–1589.
[5] Anderson RJ, Chung HM, Kluge R, et al. Hyponatremia: A prospective analysis of its epidemiology and the pathogenetic role of vasopressin. Ann Intern Med. 1985;102(2):164–168.
[6] Chung HM, Kluge R, Schrier RW, et al. Clinical assessment of extracellular fluid volume in hyponatremia. Am J Med. 1987;83(5):905–908.
[7] Goh KP. Management of hyponatremia. Am Fam Physician. 2004;69(10):2387–2394.
[8] Cuesta M, Thompson CJ. The syndrome of inappropriate antidiuresis (SIAD). Best Pract Res Clin Endocrinol Metab. 2016;30(2):175–187.
[9] Verbalis JG, Goldsmith SR, Greenberg A, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. 2013;126(10Suppl 1):S1–S42.
[10] Czupryna P, Moniuszko A, Garkowski A, et al. Evaluation of hyponatraemia in patients with tick-borne encephalitis–a preliminary study. Ticks Tick Borne Dis. 2014;5(3):284–286.
[11] Liamis G, Milionis HJ, Elisaf M. Hyponatremia in patients with infectious diseases. J Infect. 2011;63(5):327–335.
[12] Hill AR, Uribarri J, Mann J, et al. Altered water metabolism in tuberculosis: role of vasopressin. Am J Med. 1990;88(4):357–364.
[13] Miller LH, Makaranond P, Sitprija V, et al. Hyponatraemia in malaria. Ann Trop Med Parasitol. 1967;61(3):265–279.
[14] Patwari AK, Singh BS, Manorama DE. Inappropriate secretion of antidiuretic hormone in acute bacterial meningitis. Ann Trop Paediatr. 1995;15(2):179–183.
[15] Mastorakos G, Weber JS, Magiakou MA, et al. 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(4):934–939.
[16] Perkins MP, Shumway N, Jackson WL Jr. Lyme neuroborreliosis presenting as the syndrome of inappropriate antidiuretic hormone secretion. MedGenMed. 2006;8(3):71.
[17] Wong LL, Verbalis JG. Systemic diseases associated with disorders of water homeostasis. Endocrinol Metab Clin North Am. 2002;31(1):121–140.