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Case Report

CASE REPORT

Localized herpes zoster infection: a rare cause of syndrome of inappropriate secretion of antidiuretic hormone

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Abstract

Hyponatremia is the most common electrolyte abnormality observed in clinical practice and syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is diagnosed in nearly 40% of the hospitalized hyponatremic patients. We present a case report of herpes zoster infection causing a severe hyponatremia/hypokalemia. This rare association between SIADH and varicella-zoster virus infection is described in only few case in the literature. In our case report, the associated hypokalemia was not related to the use of diuretics but, probably, dependent on the frank serum hyposmolality able to induce an aldosterone release.

INTRODUCTION

Hyponatremia is a common electrolyte imbalance in hospitalized patients [1]. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is considered as the most frequent cause. Usually, herpes zoster disease is caused by reactivation of endogenous varicella-zoster virus (VZV) that has persisted in latent form within sensory ganglia following an earlier episode of chickenpox [2]. We present a case report of a patient affected by a SIADH dependent on a herpes zoster infection complicated with hypokalemia.

CASE REPORT

An 82-year-old Caucasian female was taken to the Emergency Department of our Hospital with a 4 days history of mental confusion and a skin eruption in the area of the left tenth thoracic dermatome. The patient had a history of type 2 diabetes mellitus (treated with repaglinide 0.5 mg bid), paroxysmal atrial fibrillation (digoxin 0.125 mg/die and apixaban 2.5 mg bid), arterial hypertension (lecarnidipine 10 mg/die), Hashimoto's thyroiditis (L-tyroxine 75 μg/die) and anxious syndrome (psychotropic drugs: alprazolam 0.5 mg/die, citalopram 20 mg/die, trazodone 60 mg/die); She had been following this therapy since 1 year. Two months before of the admission a routine blood test showed normal serum Na and K levels. Six days before the admission, the patient had gone to the Emergency Department of another hospital for a mild chest pain. The routine blood tests, including serum sodium (Na) and potassium (K) levels, gave results almost in the normal range. A couple of days later, following the onset of skin eruptions, the general practitioner diagnosed an herpes zoster disease with typical shingles, prescribing brivudine 125 mg/die for 1 week. The day after the patient suffered of mental confusion and gait instability in the absence of pain, fever, polydipsia, seizures, diarrhea, nausea, vomiting and an increased water intake with no his-

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tory of a recent use of diuretics. At the admission blood pressure was 170/95 mmHg with a sinus heart rate of 74 beats/min and her body temperature was 36.2°C. Skin examination evidenced a remarkable eruption of dense vesicles ('shingles') on the left side of the chest distributed along the tenth thoracic nerve dermatome. The absence of orthostatic hypotension, jugular vein turgor or edema suggested an euvolemic status. A water load test (2 L of 0.9% NaCl solution in 24 h) did not modify the serum Na level.

The values of the laboratory (Table 1) associated to normal cardiac, hepatic, endocrine and adrenal function, suggested a diagnosis of syndrome of SIADH. Moreover, we found an increased transtubular K gradient (19.7) associated to a metabolic alkalosis. The serum renin and aldosterone levels were not tested.

The anamnestic history and radiological investigations, such as a total-body computed tomography failed to identify other possible causes of SIADH.

Psychotropic drugs were stopped and a mild hypertonic 1.5% NaCl and a KCl solutions were started. The NaCl and KCl solutions were continued until the seventh and fifth day, respectively, obtaining a serum value of 128 and 3.5 mEq/L, with the complete resolution of the mental confusion. On the ninth day, the patient was discharged presenting 134 mEql/L of serum Na and 4.5 mEql/L of K (Fig. 1), suggesting a fluid restriction (800 ml/day). Eleven days after discharge, the patient presented Na and K normal levels, the fluid restriction was stopped and the psychotropic drugs were resumed, scheduling a weekly follow-up. Hyponatremia and hypokaliemia did not relapse at subsequent monthly follow-up up to 6 months.

Table 1: Laboratory values at admission

	Values	Reference range
Serum		
Urea nitrogen	20	10–50 mg/dl
Creatinine	0.4	0.5–0.9 mg/dl
Na	105	135–145 mEq/L
K	2.5	3.5–5.3 mEq/L
Uric acid	3.0	2.4–5.7 mg/dl
P	1.7	2.5–4.5 mg/dl
TSH	0.83	0.3–3.6 μU/ml
Cortisol	19.7	6.2–19.4 μg/dl
Osmolality	226	275–285 mOsm/kg
Urine		
Na	75	40–220 mEq/L
K	90	25–100 mEq/L
Osmolality	435	50–1200 mOsm/kg

DISCUSSION

In this patient, the clinical symptoms and the laboratory values were consistent with a SIADH diagnosis. Moreover, the absence of other causes of SIADH and the complete resolution of the hyponatremia in concomitance with the herpetic vesciculae healing, suggest a strict association between SIADH and VZV disease. Usually, psychotropic drugs are able to induce an inappropriate ADH release [3]. The patient was in treatment with some psychotropic drugs but, in light of the considerable treatments length (12 months) before the SIADH onset and that normal Na serum levels were maintained after resuming the chronic therapy, we exclude any drug involvement. Furthermore, brivudine has never been described as a potential SIADH cause.

Searching in the Pubmed database, the association between SIADH and localized herpes zoster is not frequent, involving only twelve patients, including the present case report (Table 2).

The investigated patients, seven women and four men, were either elderly (10/11) and/or diabetics (4/11), well-known risk factors for VZV reactivation. The trigeminal dermatome was involved in six patients, cervical in one, thoracic in three and lumbar in one [4].

The underlying mechanism of SIADH associated with localized herpes zoster remains elusive. VZV infection may involve the regulatory pathway of antidiuretic hormone (ADH) secretion. Upon reactivation from dorsal-root ganglia, VZV spreads to the corresponding dermatome via axons of infected neurons

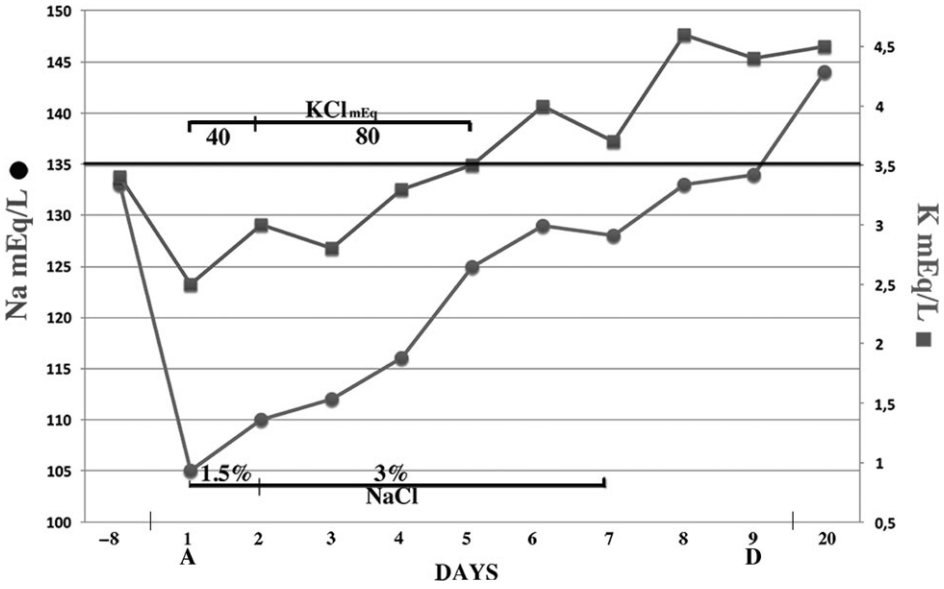

Figure 1: Serum Na and K values in the different days. NaCl and KCl treatment are indicated. A: admission; D: discharge.

Table 2: Publicated herpes zoster/SIADH case reports

Study*	Age/gender	dermatome	Latency	Natremia (mEq/L)	Conscious change	Duration	Complications
Maze (1983)	72/F	T2	6 days	95	+	14 days	PHN
Sato (1990)	67/F	T10	7 days	104	–	5 days	–
Furuta (1996)	70/F	C4-6	3 days	111	+	5 days	–
Calenda (1996)	78/M	V1	n.a.	108	+	n.a.	Death
Han (1996)	77/M	V1	5 days	115	+	n.a.	–
O'Rourke (2006)	86/F	T9/10	7 days	122	–	4	–
Dhawan (2007)	71/F	V1	4 days	120	–	9	–
Kucukardali (2008)	76/F	V1	15 days	112	+	7	–
Osinga (2009)	84/F	L1-2	n.a.	117	+	n. a.	–
Wang (2011)	58/M	V1	4 days	114	–	4 months	PHN
Wang (2011)	38/M	V1	7 days	116	–	3 months	PHN
Our patient	82/F	T10	4 days	102	+	20 days	Hypokalemia

Latency: time span from the diagnosis of herpes zoster and onset of hyponatremia; n.a.: not available; duration: time span for hyponatremia resolution; PHN: postherpetic neuralgia.
*Reported in the reference section of Wang *et al.* (2010).

and centripetally to the dorsal columns of the spinal cord [5]. Peripheral osmoreceptors also route a portion of their signals through the dorsal-root ganglia before reaching the spinal cord and CNS, suggesting a possible interaction [6].

The association of hyponatremia/hypokalemia could suggests the use of diuretics, diarrhea, vomiting or the presence of a third space sequestration. In our patient, the anamnesis, the clinical evaluation and the laboratory values seem to exclude these situations. FeUA with a cut-off >12% has demonstrated to be a very good marker (positive predictive value of 100%) to confirm the SIADH diagnosis [7, 8]. Liamis *et al.* [9] described different electrolytes imbalance in SIADH patients and hypokalemia association was present only in a minority of patients (5.4%). The hyponatremia/hypokalemia association could be explained by a transient increased aldosterone secretion, due to the frank hyposmolality (usually hyperaldosteronism is induced by values lower than 240 mOsm/kg, in our patient the value was 226 mOsm/kg), which counterbalances the inhibitory influence of the normal/expanded ECF on the renin–aldosterone axis in SIADH patients [10]. The observed hypokalemia, the relative high urinary potassium, an increased transtubular K gradient and the metabolic alkalosis suggest this evenience.

In conclusion, herpes zoster infection is a not a frequent cause of SIADH, but in these patients the presence of mental confusion induces to consider the possibility of hyponatremic encephalopathy vs. VZV encephalitis.

CONFLICT OF INTEREST STATEMENT

None declared.

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