CASE REPORT

Rhabdomyolysis in hyponatremia and paraneoplastic syndrome of inappropriate antidiuresis

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We report a 26-year-old woman admitted to our hospital for generalized tonic seizure. Laboratory investigations revealed severe hyponatremia possibly triggered by vomiting and diarrhea. 24 hours after correction of hyponatremia she developed diffuse myalgias and marked hyperCKemia. Syndrome of inappropriate antidiuresis (SIAD) was suspected as cause of hyponatremia. Abnormal vaginal bleeding prompts gynecological evaluation and a small-cell carcinoma of uterine cervix was detected.

Key words: rhabdomyolisis, hyponatriemia, syndrome of inappropriate antidiuresis, small cell neuroendocrine carcinoma

Case report

A 26-year-old woman was admitted to our hospital after generalized tonic seizure. There was no family history of epilepsy, psychiatric disease, neuropathy and myopathy. She smoked 10 cigarettes a day and was taking oral contraceptive therapy. No other medications, alcohol consume, drug abuse or allergies were reported nor trauma. Medical history was irrelevant, physical and neurological examination were normal. At the admission, laboratory investigations revealed severe euvolemic hypotonic hyponatremia (107 mEq/l) possibly triggered by vomiting and diarrhea occurred in the previous 3 days. Twenty-four hours after the correction of hyponatremia by the intravenous administration of normal saline solution (NaCl 0.9% saline) she developed diffuse myalgias associated with laboratory evidence of marked elevation of creatine kinase (CK) level (Table 1).

There was no evidence of muscle trauma, stiffness or swelling and a preserved renal function and diuresis were observed throughout the evolution. An extensive diagnostic workup (Table 2) excluded other presumed causes for rhabdomyolysis, so a diagnosis of rhabdomyolysis secondary to hyponatremia and/or its correction was made. In particular a diagnosis of Syndrome of inappropriate antidiuresis (SIAD) was suspected as the cause of euvolemic hypotonic hyponatremia as confirmed by diagnostic criteria of decreased serum osmolality (225mOsm/kg) and elevated urine osmolality (475 mOsm/kg) in the absence of renal, adrenal and thyroid insufficiency. Oral fluid restriction (1.5 lt/day) and salt tabs supplementation (200 mEq/day) maintained serum sodium level in a non-critical range (122 mEq/l). Abnormal vaginal bleeding prompted a gynecological evaluation that revealed a small-cell carcinoma of uterine cervix. Surgical treatment followed by chemoteraphy and radiotherapy resulted in the resolution of paraneoplastic SIAD and normalization of hyponatremia.

Discussion

Seizure and rhabdomyolysis are uncommon serious complications of severe acute hyponatremia and / or its correction (1, 2). Rhabdomyolisis is a potentially lifethreatening syndrome resulting from lyisis of skeletal muscle fibres with release of intracellular product into systemic circulation (3). It may be due to failure in cell volume regulation and ionic balance ultimately affecting membrane homeostasis and cell integrity (4). Syndrome of inappropriate antidiuresis (SIAD) is a disorder

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	Na	K	СК	AST	ALT	LDH	crea	POsm		UNa
	(mEq/l)	(mEq/l)	(IU/I)	(IU/I)	(IU/I)	(IU/I)	(mg/dl)	(mOsm/kg)	UOsm	(mEq/24h)
Time(h)	(134-146)	(3.6-5.4)	(90-205)	(5-37)	(5-40)	(125-243)	(0.4-1.2)	(280-300)	(mOsm/kg)	(50-200)
Admission (0)	107	3.9		37	22	274	0.69	225		
2	108									
28	122	3.9	26535	168	42	772	0.70	255	475	258
100	119		39561	476	372					
124	113		22508	157	166					
148	112									
194	110		1653							
Dimission	114	4.5	314							

Table 1. Laboratory data trends.

Table 2. Laboratory and instrumental investigations.

Standard hematological and byochemisty:	Normal
fT3-fT4-TSH, ACTH, cortisolemia, cortosoluria/24 h:	Normal
Clino/orthostatism plasma renin activity:	Low
Aldoserone:	Normal
Neoplastic markers:	Negative
Infections (VDRL, HBV, HCV, EBV, CMV, HSV1-2, VZV abs):	Negative
Stool colture: negative for Salmonelle, Shigelle, Campylobacter Rotavirus,	
Adenovirus, Norovirus Ag:	Negative
ECG:	Normal
EEG:	Normal
Brain CT and MRI:	Normal
EMG/ENG:	Mild myopathic pattern
Chest XR:	Normal
Abdomen/pelvic echography:	Normal

of sodium and water balance and is a major cause of euvolemic hypotonic hyponatremia (5). Ectopic production of antidiuretic hormone (ADH) by tumor, mainly small-cell neuroendocrine carcinoma (SNEC), is one of the most common causes of SIAD (6-8) and is exceptionally described in small-cell carcinoma of uterine cervix (9). We describe the case of a patient with a small-cell neuroendocrine carcinoma of uterine cervix presenting with generalized seizure and rhabdomyolysis related to severe hyponatremia, secondary to paraneoplastic SIAD. The case here reported suggests that an aggressive treatment to correct hyponatremia should be avoided. Furthermore, a careful monitoring for rhabdomyolysis is necessary to prevent and treat the possible complications. Paraneoplastic SIAD is one of the most common cause of euvolemic hypotonic hyponatremia and should be thoroughly investigated in particular for small-cell neuroendocrine carcinoma often difficult to detect. Small cell carcinoma of the uterine cervix is a rare variant of SNEC taking up only 0.5% to 5% of the type of cervical cancer and is rarely associated with SI-AD as in our case (9). Extensive evaluation of SIAD has great implication on the diagnosis, treatment, follow-up and prognosis of this extremely aggressive tumor.

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