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Letter to the Editor

Chronic Hyponatriemia Associated With Rett Syndrome

To the Editor:

Rett syndrome is a monogenic X-linked dominant neurodevelopmental disorder related to mutation in the *MECP2* gene[1] and characterized by early neurological regression that severely affects motor, cognitive, and communication skills.

A 13-year-old girl with Rett syndrome was evaluated in our center for persistent hyponatremia. When the girl was 8 years of age, during a hospital admission for severe abdominal pain, she had severe hyponatremia (sodium 124 mEq/L) that responded to sodium supplementation. Since then she has had several episodes of symptomatic hyponatremia especially during infections (pneumonia, vasculitis), and for that reason she has been supplemented with 240 mEq of sodium twice daily via gastrointestinal tube.

The patient was admitted to our pediatric ward for further investigation during a controlled withdrawal from the sodium supplementation. After 12 hours of sodium supplementation withdrawal, she became lethargic and testing revealed severe hyponatremia (sodium 120 mEq/L) with normal potassium (5.73 mEq/L). We stored blood and urine samples for analysis before starting intravenous hypertonic saline solution 3% (0.5 mL/kg/hr) supplementation. She was discharged 2 days later in good clinical condition after reestablishment of the sodium supplementation and 800 mL/day fluid restriction.

The results of our blood tests revealed a blood osmolarity of 257 mOsm/kg. The 24-hour urine collection done during the sodium withdrawal showed an increased sodium excretion (urinary sodium 51 mEq/L) and an osmolality of 373 mOsm/kg.

From our investigation and the child's response to withdrawal of sodium supplementation (no edema and normal blood pressure), we could establish the diagnosis of hypotonic euvolemic hyponatremia with high urine sodium level.[2,3] The main causes of hyponatremia are renal disorders, endocrine deficiencies, reset osmostat syndrome, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and drugs. Normal urine excretion and normal urea and creatinine levels excluded renal dysfunctions.[4] Her normal thyrotropin and cortisol levels and the lack of associated hyperkalemia and hypoglycemia excluded hypothyroidism and adrenal insufficiency. The medications used do not cause hyponatremia as a possible adverse effect. The diagnostic criteria for reset osmostat syndrome requires normal urinary diluting capacity (urine osmolality<100 mOsm/L) and lack of improvement on sodium supplementation and fluid restriction. At this point we could make a diagnosis of exclusion of chronic SIADH supported by the fact that our patient met all the diagnostic criteria (Table).[5] We could not evaluate whether the association between Rett syndrome and chronic SIADH was casual. However, the known link between many pathologies of the nervous system, including epilepsy, multiple sclerosis, Guillain-Barré syndrome, Shy-Drager syndrome, and SIADH, could suggest that this case was not an accidental finding. The screening of the electrolytes level may be important in the routinely workup of children with Rett syndrome because it can eventually lead to an early diagnosis and treatment of SIADH.

Table. Criteria for Syndrome of Inappropriate Antidiuretic Hormone Secretion Diagnosis

Criteria
• Lack of evidence for volume overload (e.g., edema)
• Hyponatremia
• Hypotonicity (plasma osmolality<270 mOsm/kg)
• Inappropriately concentrated urine (urine osmolality>150 mOsm/kg)
• Urine sodium level>20 mEq/L
• Sodium corrects with fluid restriction but not with 0.9% (normal) saline infusion

From Smith et al.[5]

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