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X-Linked Nephrogenic Syndrome of Inappropriate Antidiuresis Secondary to Vasopressin Receptor 2 Mutation

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X-Linked Nephrogenic Syndrome of Inappropriate Antidiuresis Secondary to Vasopressin Receptor 2 Mutation: A Case Report

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Background

X-linked nephrogenic syndrome of inappropriate antidiuresis (NSIAD) is a rare cause of hyponatremia biochemically similar to the syndrome of inappropriate antidiuretic hormone secretion but with suppressed vasopressin (AVP) levels. We present a case of hyponatremia due to NSIAD.

Case History

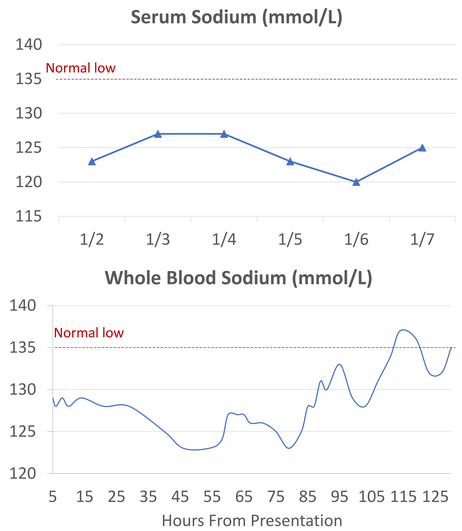
A 25-month-old male with developmental delay became unresponsive 30 minutes after falling off a couch onto a hardwood floor. He presented with tonic-clonic movements and eye deviation requiring anti-epileptics. He was clinically euvolemic. Physical exam and vital signs unremarkable except for mild tachycardia while upset. Laboratory data included in Table 1. Head imaging normal. He required several 3% saline boluses for persistent hyponatremia <130 mmol/L. Sodium levels shown in Figure 1. Further studies showed hypoaldosteronism (<0.4 ng/dL), hyporeninemia (<0.6 ng/mL/hr), and low AVP (<0.5 pg/mL). He had a mildly elevated thyroid stimulating hormone (6.71 mcIU/mL) with normal free thyroxine; repeat was normal. AM cortisol level was 2.5 mcg/dL; family declined ACTH stimulation testing due to family history. He required oral sodium chloride (NaCl) treatment of 12 mEq/kg/day and fluid restriction to maintain serum sodium >130 mmol/L. Patient had fluctuating hyponatremia outpatient that responded to resumption of strict fluid restriction and NaCl supplementation, though management was complicated by sensory issues contributing to a very selective diet. Remarkably, his verbal and ambulatory skills improved with normalized sodium.

Laboratory Data

Table 1: Laboratory values on admission and repeat after 48 hours of Na repletion

Lab	Admission	After NaCl replacement therapy	Normal Range
Serum sodium	123 mmol/L	123 mmol/L	135-145
Serum potassium	4.2 mmol/L	4.2 mmol/L	3.5-5.2
Serum chloride	90 mmol/L	94 mmol/L	99-112
Serum carbon dioxide	23 mmol/L	25 mmol/L	20-30
Serum calcium	9.3 mg/dL	8.5 mg/dL	8.6-10.5
Serum glucose	154 mg/dL	97 mg/dL	65-110
Serum urea nitrogen	10 mg/dL	12 mg/dL	5-20
Serum creatinine	<0.15 mg/dL	<0.15 mg/dL	0.26-0.64
Serum osmolality	262 mOsm/kg	268 mOsm/kg	275-296
Urine specific gravity	1.004		1.005-1.035
Urine osmolality	160 mOsm/kg	623 mOsm/kg	98-960
Urine creatinine	5.4 mg/dL	15.2 mg/dL	
Urine sodium	11 mmol/L	157 mmol/L	
FeNa	0.2%	1.3%	

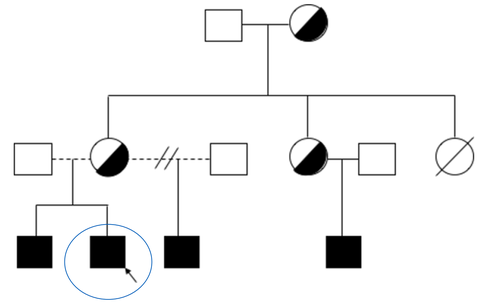
Figure 1: Serum and whole blood sodium levels during hospitalization



Family History and Genetics

Family history included a full biological brother, maternal half-brother, and maternal cousin with hyponatremia requiring oral NaCl from 2 to 5 years of age. Family members were evaluated at a different institution with no genetic diagnosis identified. Family pedigree in Figure 2. Patient's Next Generation Sequencing showed a hemizygous p.Arg137Cys variant in AVPR2 leading to a constitutively active renal AVP V2 receptor consistent with X-linked NSIAD. Mutation was also detected in patient's maternal grandmother.

Figure 2: Pedigree



Conclusions

Hypoosmolar hyponatremia with suppressed AVP and renin should raise concern for NSIAD. Given X-linked inheritance, family history may aid in the diagnosis. Maintaining eunatremia helps prevent seizures and promote normal development. Our patient was successfully treated with fluid restriction and sodium supplementation. The literature also describes use of urea to normalize sodium levels with fluid liberalization. Family declined this intervention.

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