Research Days

May 2nd, 11:30 AM - 1:30 PM

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

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☐ **Medical Student**

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X Fellow

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IRB Number: N/A

Describe role of Submitting/Presenting Trainee in this project (limit 150 words): I, the submitting/presenting trainee, am a current Pediatric Endocrinology Fellow. I was the fellow on the Endocrine consult service for Children's Mercy Hospital when this patient presented to the Emergency Room and throughout his hospitalization admission. The Endocrine attending, resident physician rotating with Endocrine, and myself were primarily involved in the diagnostic evaluation and treatment of this patient. I continued to follow him in Endocrine Clinic. We have submitted this abstract to the Pediatric Endocrine Society in the hopes of presenting at the annual conference.

Background, Objectives/Goal, Methods/Design, Results, Conclusions limited to 500 words

Background: X-linked nephrogenic syndrome of inappropriate antidiuresis (NSIAD) is a rare cause of hyponatremia with a similar biochemical evaluation to the syndrome of inappropriate antidiuretic hormone secretion but with suppressed vasopressin (AVP) levels.

Objectives: We present a case of hyponatremia due to NSIAD.

Results: 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. Serum laboratories noted hyponatremia (123 mmol/L), hypoosmolality (262 mOsm/kg) and hypochloremia (90 mmol/L) prompting endocrine consult. Head imaging normal. Urine dilute with specific gravity 1.004, osmolality 160 mOsm/kg, and fractional excretion of sodium 0.2%. He was clinically euvolemic.

He required several 3% saline boluses for hyponatremia <130 mmol/L. 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 TSH (6.71 mcIU/mL) with normal free thyroxine; repeat normal. He required oral sodium chloride (NaCl) treatment of 12 mEq/kg/day and fluid restriction to keep serum sodium >130 mmol/L. 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. 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. 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.

Conclusions: Hyponatremia is a common endocrine consult. 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.