Pediatric Endocrinology

PMON316

Novel Mutation Causing Pseudohypoaldosteronism Type 1 and Transient Hypercalcemia: A Patient Report

Vickie Wu, MD, Robert Rapaport, MD, Cassie Mintz, MD, and Mabel Yau, MD

Background: Autosomal dominant pseudohypoaldosteronism Type 1 (PHA-1) is a salt-wasting syndrome due to mutation in the renal mineralocorticoid receptor. Here, we report an infant with a novel mutation in NR3C2 causing PHA and associated with transient hypercalcemia.

Clinical Case: An ex-28 weeks (birth weight 1.35 kg) male infant admitted to the NICU had increased urine output of 6 mL/kg/hr on days of life (DOL) 9-10. Initial laboratory tests showed hyponatremia (121-127 mEq/L), hyperkalemia (5.4-8.4 mEq/L), hypochloremia (89-94 mEq/L), and hypercalcemia (11.2-11.6 mg/dL). Weight had decreased 4% from birth. On exam he was normotensive with no midline defect or hyperpigmentation; he had palpable testes bilaterally and 2 cm penile length. Sodium chloride (NaCl) supplementation 2.5 mEq/day was started on DOL 10. State newborn screen 17-OHP levels were normal. His family history was unremarkable.

To further investigate the hyponatremia and hyperkalemia, serum ACTH, cortisol, aldosterone, and renin were obtained. ACTH and cortisol were 33 pg/mL and 11.4 mcg/dL, respectively. While awaiting the results of the aldosterone and renin assays, fludrocortisone was started with minimal improvement in serum sodium and hypercalcemia worsening to 12.0 mg/dL. Laboratory tests obtained to investigate the hypercalcemia included phosphorus 5.5 mg/dL, hypercalciuria (urine calcium to creatinine ratio 0.4), 25-OH vitamin D 21.0 ng/mL (normal 30-100 ng/mL), and PTH 29 pg/mL (normal 10-65 pg/mL). PTH was inappropriately normal, concerning for primary hyperparathyroidism. While awaiting the aldosterone level, it was therefore recommended to decrease fludrocortisone dose.

Plasma renin activity resulted at 319 ng/mL/hr (normal 2-37 ng/mL/hr) and aldosterone at 612 ng/dL (normal 5-90 ng/dL), suggesting a diagnosis of PHA. Fludrocortisone was discontinued and NaCl supplementation was increased. A heterozygous pathogenic variant, c.2457C>A (p.Tyr819Ter), was identified in the mineralocorticoid receptor gene, NR3C2, confirming the diagnosis of autosomal dominant PHA-1. This variant has not been previously reported but meets the American College of Medical Genetics and Genomics and the Association for Molecular Pathology’s criteria for pathogenicity. At his outpatient follow up at 4 months, sodium was 134 mEq/L and calcium was 10.5 mg/dL. He was continued on 1.5 grams NaCl supplementation.

Conclusion: We report a patient with a novel mutation in the NR3C2 gene resulting in autosomal dominant PHA-1 and associated with transient hypercalcemia. Further exacerbation of hypercalcemia was seen with addition of fludrocortisone. We suspect the etiology of the transient hypercalcemia to be secondary to excess mineralocorticoids (exogenous or endogenous) that drives PTH to increase serum calcium levels, as previously described by Vaidya et al. (1)


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