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Case Reports

PSEUDOHYPOALDOSTERONISM: A CASE REPORT

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ABSTRACT

A four day old female infant was admitted because of poor feeding, vomiting and jaundice. Laboratory examination showed hyperkalemia, mild hyponatremia and renal tubular acidosis type 4. Serum aldosterone and plasma renin activity were elevated but serum cortisol, 17 -hydroxyprogesterone, ACTH, 24 hour urinary 17-ketosteroid, pregnanetriol, renal function and sonogram were normal and hence pseudohypoaldosteronism type 1 (pHA 1) was differentiated from congenital adrenal hyperplasia (CAH) and other metabolic disorders. These abnormalities were corrected with sodium chloride supplementation.
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INTRODUCTION

PHA type1 was reported by Cheek and Perry in 1958. They proposed that the condition was the result of renal tubular unresponsiveness to mineralocorticoids.[7] Rampini et al. reviewed 38 cases in 1978,[5] and after that a few more cases have been reported.

It seems that pHA is more common than expected and it's prevalence is underestimated because of asymptomatic cases and the diversified clinical presentation of this disorder.[6]

Case report

A four day old infant was admitted because of feeding problems coupled with vomiting and jaundice. She was born to a gravida 1, para 0, preeclamptic mother after a full term pregnancy. Labor and delivery were normal. The pedigree showed no consanguinity. The growth indices were on the 10th percentile on physical examination. The infant was normal except for a poor sucking reflex. Laboratory examination demonstrated mild hyponatremia (128-131 mEq/L, normal: 135-145 mEq/L), hyperkalemia (6.5-7.8 mEq/L, normal: 3.5-6.3 mEq/L), and metabolic acidosis. Serum bicarbonate was 9.7 mmol/L which appeared exceedingly low compared to its normal level of 21.4 mmol/L.

Hyperbilirubinemia was also apparent and serum bilirubin had reached 15.8 mg/dL, quite above its normal range of up to 12 mg/dL. Serum glucose, calcium, ammonia, chloride and sweat sodium were within normal limits.

Due to a low serum sodium and high serum potassium, hypoaldosteronism and RTA type 4 were suspected. Renal function tests, serum urea nitrogen, serum creatinine, renal sonogram, 24-hr urinary 17 -KS, pregnanetriol, serum 17-hydroxyprogesterone and cortisol concentrations were all normal.

Plasma aldosterone reached a limit of 98.2 ng/dL, far above its normal range of 4-31 ng/dL, whereas plasma renin activity (PRA) showed a similar elevation to 13.9 ng/mL/hr (normal range: 0.2-2.5 ng/mL/hr), compatible with hyperreninemic hyperaldosteronism.

Urinary sodium concentration was 60 mEq/L (normal: up to 20 mEq/L), urine pH was 5, and negative for glucose/ketone, reducing substance and aminoacid chromatography.

PHA type 1 was thus confirmed.

DISCUSSION

PHA type 1 is a hereditary salt-wasting syndrome which usually starts in early infancy and is characterized by a diminished renal tubular responsiveness to aldosterone, resulting in hyponatremia, hyperkalemia, metabolic acidosis,[11-13,15,18] markedly elevated plasma aldosterone and high plasma renin activity.[5,12,13]

The clinical presentation and natural history are variable from asymptomatic cases in adults to the fulminant form in premature infants. In other infants, the symptoms are chronic failure to thrive, lethargy, vomiting and poor feeding. In older children, the history may be limited to growth failure and ultimate short stature.[5] This type (pHA 1) has two distinctive forms, renal and multiple target organ involving colonic mucosa, sweat and salivary glands.[1,3,13] Isolated salivary gland involvement was reported in one case.[17] In spite of a slight male preponderance of 58%,[5] this uncommon disease appears to be inherited as an autosomal dominant trait in the renal form and autosomal recessive in the multiorgan system type.[3-4] The human mineralocorticoid receptor gene is located on chromosome 4.[10] A decrease in mineralocorticoid receptors has been reported in the mononuclear leukocytes of both forms.[2,21] Mineralocorticoid receptors were also found in cells from extrarenal tissues such as spleen, hippocampus, smooth muscle, heart, pituitary and mammary gland.[21]

In our case, we examined the parents and found an increased amount of plasma aldosterone (66 ng/mL) in the mother. In this case, the mode of transmission seemed to be autosomal dominant and sodium sweat concentration was normal, so the renal type was proposed.

There is an overlapping between pHA and childhood type 4 RTA. The latter is not characteristically associated with overt salt wasting, but exhibits reduced tubular responsiveness to aldosterone. Children with type 4 RTA have retarded growth and exhibit frequent bouts of vomiting. In light of this it seems likely that pHA and early childhood type 4 RTA are similar disorders with varying degrees of salt wasting.[5]

In the pathogenesis of pHA type 1, several factors including deficient renal Na-K ATPase activity,[5] and a reduced number of mineralocorticoid receptors have been implicated.[21]

Diagnosis is established on the finding of high levels of plasma aldosterone metabolites, high plasma renin activity, normal serum ACTH, 17-OH progesterone and cortisol levels, normal 24 hr. urinary 17-KS and pregnanetriol, and normal renal histology and function.[3,5,11,13,19]

PHA type 1 is treated with sodium chloride supplementation, which expands the extracellular fluid volume. Tubular flow and delivery of solute to the distal part of the nephron increases, thereby creating a favorable gradient for potassium secretion. In one child with pHA, treatment with indomethacin was successful. The drug appears to act by decreasing proximal renal tubular perfusion and improving reabsorption at this site, hence compensating for more distal losses.[5]

Typically, the disorder disappears or declines sufficiently after infancy[3,5,13] such that continuation of salt supplements is not a necessity, but can recur if salt is restricted.[13]

PHA type 1 can masquerade as CAH, especially in boys. This may result in the unnecessary utilization of glucocorticoids which may consequently increase the risk of growth retardation.[5]

In our case, hyperkalemia and metabolic acidosis suggested RTA type 4 and subsequent evaluations showed pHA type 1. This disorder was differentiated from CAH, organic acid disorders and urological disorders. Preeclampsia could not be attributed to the infant's aldosterone because this hormone does not cross the placental barrier.[8,9] PHA type II (Gordon syndrome) occurs in older children or adults and is easily distinguished from type 1 by the association of hypertension, volume expansion and low to normal plasma aldosterone and plasma renin activity. Increased NaCl avidity in the distal nephron is the cause, which results in volume overexpansion. Salt restricting diuretics such as the thiazides can bring about an improvement in the disorder.[12,16,20]

Salt-losing nephropathy occurring predominantly in male infants has been reported in association with a spectrum of urological diseases such as obstructive uropathy and massive infected vesicoureteral reflux. This has been called pseudohypoaldosteronism (pHA) or alternatively pseudosalt-losing congenital adrenal hyperplasia. Ultrasonography is the most useful tool in the evaluation of these infants with signs and symptoms of salt wasting.[14]

We conclude that pHA type 1 should be differentiated and individualized from CAH, organic acid disorders and salt-losing nephropathy because an incorrect diagnosis would entail the unnecessary use of glucocorticoids. Correct differentiation would further pave the strategy to correct the urological and organic acid disorders promptly.

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