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Case Report

Neonatal Pseudohypoaldosteronism-Case Series

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Abstract

Pseudohypoaldosteronism is a condition mimicking hypoaldosteronism but main pathology is due to end organ resistance or unresponsiveness of renal tubules to aldosterone. The condition is characterized by severe electrolytes disturbances and can be fatal if the condition is not recognized and managed promptly.

Primary pseudohypoaldosteronism is an autosomal dominant variety due to a mutation of the mineral corticoid receptor (MR) and a severe systemic one of autosomal recessive variety due to a mutation of the epithelial sodium channel (ENaC) gene. Urinary tract malformations and acute pyelonephritis usually leads to secondary pseudohypoaldosteronism.

We report two cases of neonatal pseudohypoaldosteronism. Patients present with severe electrolytes disturbances including hyperkalemia, hyponatremia, metabolic acidosis, and dehydration, without evidence of primary renal or gastrointestinal disease. Endocrine studies show high serum aldosterone, high renin activity and normal adrenal function.

Key Words: *Hyperkalemia, newborn, pseudohypoaldosteronism.*

Introduction

Pseudohypoaldosteronism (PHA) is a rare disorder of electrolyte metabolism due to renal tubular unresponsiveness or resistance to the action of aldosterone. The condition is characterized by hyperkalemia, hyponatremia, metabolic acidosis, with normal glomerular filtration rate (GFR). Patient can present with or without salt wasting crises; hypotension or hypertension; and elevated, normal, or low levels of renin and aldosterone. More than 70 cases have been reported in the literature since its first description in 1958**[**1**]**. A United Kingdom based study has reported an incidence of 1/2000**[**2**]**. The electrolyte abnormalities remain refractory to standard therapy but respond to high dose of dietary sodium supplements along with potassium binding resins. With appropriate treatment some children may outgrow the illness by 1-2years of age**[**3**]**.

Newborn can present with hyponatremia and hyperkalemia due to variety of renal and genetic disorders with significant long term health implications if not treated and diagnosed aggressively. We report two cases of severe hyperkalemia and hyponatremia from PHA requiring aggressive therapy. Our goal is to increase the exposure to this rare life threatening disease.

Case 1

A previously healthy six day old female infant, born at term to non-consanguineous parents, presented with irritability, poor feeding of one day duration. She had 15% postnatal weight loss and arrhythmia. Laboratory investigations showed serum potassium of 11.6 mmol/l, serum sodium of 128 mmol/l and metabolic acidosis. Urea, creatinine, complete blood count, C reactive protein and blood culture were normal. Urine output was adequate, fractional excretion of sodium (FENa) = 17.8%. ECG findings were consistent with hyperkalemia.

As congenital adrenal hyperplasia with salt-losing type was suspected, hydrocortisone and 9-α fludrocortisone acetate (9 FC) were commenced. Hyperkalemia was poorly controlled in spite of intensive anti-hyperkalemia measures. The condition stabilized after increasing sodium intake to 30 mmol/kg/day.

The persistent hyperkalemia with normal pigmentation and absence of ambiguous genitalia and the lack of response to mineral corticosteroid replacement were suggestive of PHA. High levels of plasma aldosterone (53,732 pmol/l) and active renin (1.4 mcg/l) and an aldesterone/renin ratio of 13.4 were found while androstendione, 17-hydroxyprogesterone, Deoxycorticosteroid, and ACTH stimulation test were normal, thus confirming the diagnosis of PHA. Hydrocortisone and 9FC were stopped and sodium supplementation was gradually increased.

The infant was discharged on Na bicarbonate and NaCl supplementation of human milk at 25 mmol/kg/day along with kayexalate enemas. She has normal weight gain and stable serum potassium levels at the age of 5 months.

Case 2

A previously healthy 5 day old term male newborn, first child of non-consanguineous parents presented with septic skin rash and was started on antibiotics. At 9 days of age he became lethargic, refused to feed, had apneic episodes and ectopic heart beats. Laboratory investigations showed serum Na of 117 mmol/l, serum K of 10.5 mmol/l, BUN > 25 mmol/L and metabolic acidosis. He was given fluid resuscitation and started on mechanical ventilation. Anti-hyperkalemia measures included peritoneal dialysis. Hydrocortisone and 9FC were started assuming salt losing congenital adrenal hyperplasia.

Endocrine studies showed elevated plasma renin activity of > 75 mcg/l/h and aldosterone level (>6660 pmol/l). Adrenal function tests and metabolic screen were normal. Fractional excretion of sodium was 10.3%. Based on the above findings, the diagnosis of PHA was made. Kayexalate enemas and Na supplement up to 20-30 mmol/kg/day were started. At 3 months of age, Indomethacin was introduced. A decrease in the need for Na supplementation was noted but the patient still required Kayexalate regularly in order to prevent hyperkalemia.

Approaching one year of age, he was readmitted with frequent vomiting and severe dehydration. Serum K and Na levels were 10.8 and 130 mmol/l respectively. Base excess was -10 and BUN > 20 mmol/l. In spite of high Na and fluid intake and intensive antihyperkalemia measures, the patient succumbed due to ventricular fibrillation.

Discussion

Neonatal PHA is a rare life-threatening disease, usually presenting with hyponatremia, dehydration and pronounced hyperkalemia as in our cases. PHA refers to a heterogeneous group of disorders characterized by end-organ resistance to aldosterone inducing hyperkalemia and metabolic acidosis. **[**4,5**]** It may be primary or secondary. Primary PHA is subdivided into PHA type I (PHA-I) with high renin, high aldosterone and often salt wasting and PHA type II (PHA-II) with normal to low renin and aldosterone levels and without salt wasting **[**5**]**.

Primary PHA1 is the most common form of neonatal PHA. The disease is usually limited to the kidney, rarely other organs are involved (multiple target organ defect = MTOD PHA-I) **[**5**]**. Primary PHA-I is either sporadic or familial with autosomal dominant or recessive inheritance of a variable degree of penetrance and different severity at presentation even among the members of the same family. Autosomal dominant and sporadic forms are caused by mutations in the mineral corticosteroid receptor gene. They manifest with anorexia, vomiting, polyuria and mild salt wasting that may start at birth and remits with age. **[**4,5**]** MTOD PHA-I also occurs in newborns and infants but persists into adulthood. In this variant, other organ; such as sweat glands, salivary glands, colon and lungs are involved **[**5**]**. The fundamental defect involves the epithelial Na channel resulting in a defect of Na transport. As a result, this variant carries the risk of potentially lethal respiratory complications mimicking cystic fibrosis **[**4,6**]**. Secondary PHA was also described in neonates but is presumed to be the result of renal tubular injury **[**5**]**.

The aim of treatment is to decrease hyperkalemic episodes and to prevent electrolyte disturbance. Na+ supplement up to 50 mmol/kg/day is required to promote K+ shift into cells and increase urinary excretion of K+ via Na-K ion exchange pump **[**4**]**. Although Indomethacin inhibits prostaglandin E and decreases Na+ loss, its use is controversial because of associated decrease in urine output and K+ loss **[**8**]**. Hydrochlorothiazide may increase K+ loss **[**7**]**. Early hospitalisation is needed in case of insufficient intake of fluid and medications, especially in children below 1 year of age.

Although unusual, pseudohypoaldosteronism should always be considered in the differential diagnosis of any infant with hyponatremic dehydration, hyperkalemia and acidosis refractory to mineralocorticoid replacement therapy. These patients require very high intake of sodium chloride supplementation along with potassium binding resins to correct the electrolyte imbalance.

Close follow up must be ensured with an emphasis on monitoring growth, blood pressure and electrolytes.

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