

## Life threatening hyperkalemia in a neonate with Pseudo-hypoaldosteronism

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### Abstract

Pseudohypoaldosteronism type 1 is a rare disorder characterized by renal resistance to aldosterone which may present with a salt wasting crisis in infancy. We report a neonate with hyponatremia, severe dehydration and refractory life threatening hyperkalemia who was treated with dietary sodium chloride supplementation, potassium binding resins and fluid replacement therapy which proved to be lifesaving.

**Keywords:** Pseudohypoaldosteronism, Hyponatremia, Hyperkalemia, Neonatal.

### Introduction

Pseudohypoaldosteronism type 1 (PHA-1) results from renal resistance to aldosterone which may present in infancy with severe life threatening hyperkalemia, hyponatremia, metabolic acidosis and dehydration. More than 70 cases have been reported in the literature since its first description in 1958.<sup>1</sup> A UK based study has reported an incidence of 1/ 20000.<sup>2</sup> The electrolyte abnormalities remain refractory to standard therapy but may respond to high dose dietary sodium chloride supplementation along with potassium binding resins. With appropriate therapy, some children may outgrow the illness by 1-2 years of age.<sup>3</sup>

### Case Report

A thirteen days old baby boy presented with vomiting, lethargy and poor feeding. There was no history of loose motions, fever or seizures. He was born at term by spontaneous vertex delivery, had no perinatal complications and was breast fed. He was the seventh issue of a consanguineous marriage. Two elder siblings with a similar presentation had unexplained early neonatal deaths.

On admission to NICU, the baby was lethargic, severely dehydrated with acidotic breathing. There was no hepato-splenomegaly and rest of the systemic examination was normal. He was managed with fluid resuscitation, broad spectrum antibiotics and supportive care.

Blood chemistry revealed hyponatraemia (117 mEq/l), hyperkalemia (9.7 mEq/l), metabolic acidosis (Serum bicarbonate 9 mEq/l, anion gap 10) and serum calcium of 10.2 mg/dl. Blood glucose was normal. Urinary electrolytes showed markedly decreased urine potassium (5.7 mEq/l,

normal value 20-80 mEq/l) and an increased urine sodium excretion (107 mEq/l, normal value 40-90 mEq/l). There was no hypercalciuria (5.3 mg/dl, normal value 6.7-21.3 mg/dl). His electrocardiogram had tall peak T waves and broad complex QRS pattern. Haematological values were normal and blood culture was later reported as negative. Considering the possibility of congenital adrenal hyperplasia, stress dose hydrocortisone (100mg/ m<sup>2</sup>/day) and fludrocortisone (0.3mg/day) was started. Sodium resonium was administered and bicarbonate was replaced.

Baby continued to manifest refractory hyponatraemia with hyperkalemia (max value 11.2 mEq/l) despite increasing glucocorticoid, mineralocorticoid, sodium chloride (NaCl) and fluid replacement with no improvement in urinary electrolytes. When ACTH, 17-hydroxyprogesterone and dihydroandrostenedione levels returned as normal, we considered the possibility of pseudohypoaldosteronism. This was confirmed with high level of aldosterone (139 ng/dl, normal value 2-16 ng/dl) and plasma renin activity (> 26.4 ng/ml/h, normal value 0.15-2.33 ng/ml/h).

Based on this diagnosis he was managed with oral sodium chloride supplementation of 35 mEq/kg/day, sodium resonium 4g/ kg/day and sodium bicarbonate supplementation of 4.4 mEq/kg/day in four divided doses. Fludrocortisone was increased to 0.8 mg/day and hydrocortisone was gradually tapered. Serum electrolytes gradually returned to normal but he continued to have natriuresis and decreased urine potassium excretion. At discharge after 20 days of hospitalization, baby had stable vital signs, good hydration and normal systemic examination. He was feeding well and had gained 800 grams body weight. The serum electrolytes were within normal limits (Serum sodium 135mEq/l, serum potassium 4.1 mEq/l).

### Discussion

PHA-I is a rare genetic disease where inactivating mutations of NR3C2 gene coding for mineralocorticoid receptor may lead to a dysfunction of ion channels resulting in salt wasting crisis and life threatening hyperkalemia in the early neonatal period.<sup>4</sup>

Renal PHA-I is the most common form. It is autosomal dominant in inheritance, presenting in the first few weeks of life with vomiting, lethargy and reluctance to feed. The autosomal recessive multiple target organ defect

(MTOD) PHA-I results from renal as well as systemic resistance to aldosterone. Hence, in addition to kidneys, salt wasting may also occur from the salivary glands, sweat glands and colon. These patients are at increased risk of lower respiratory tract involvement due to impaired bacterial killing resulting from increased sodium chloride concentration in airway fluid mimicking cystic fibrosis.<sup>5</sup>

Our patient presented in second week with life threatening salt wasting crisis and no evidence of salt wasting from other target organs or recurrent respiratory infections. Our provisional diagnosis, based on the above was renal type PHA-1.

Biochemically both the forms are characterized by severe hyponatraemia, hyperkalaemia, non-anion gap metabolic acidosis associated with high levels of plasma renin and aldosterone. Diagnosis is made by demonstrating inappropriately high urinary sodium and low urinary potassium excretion in the presence of hyponatraemia refractory to mineralocorticoid replacement. Our patient characteristically demonstrated all these biochemical abnormalities despite getting stress dose glucocorticoids and high replacement dose of mineralocorticoid. Plasma potassium concentration may vary from moderate to greatly increased values and can be life threatening or even fatal. The maximum value of serum potassium recorded in our patient was 9.7 mEq/dl. Two siblings had unexplained early neonatal deaths with a somewhat similar presentation. We feel that the coexistent hypercalcaemia along with other unknown non aldosterone based mechanisms may have played a protective role from the effects of life threatening hyperkalaemia in our case. Geibel et al have reported angiotensin II to play an independent role in Na<sup>+</sup> / H<sup>+</sup> exchange at the proximal tubule level in an animal model.<sup>6</sup> Hypercalciuria and nephrocalcinosis though absent in our baby may be present in some cases.

Since patients are refractory to large doses of mineralocorticoid, therapy primarily consists of oral fluid and sodium supplementation (10-15 mEq/kg/d) along with potassium chelation. Our patient required higher sodium supplementation (35 mEq/kg/day) about three times the normal requirement. Large doses of dietary sodium chloride (NaCl) can make food quite unpalatable. We experienced no

such problem as our baby tolerated the large NaCl supplementation to his feed quite well. We expect that after infancy sodium chloride supplementation in feeds could gradually be decreased as the child develops an appetite for salt rich food.

Indomethacin, a prostaglandin inhibitor has been used in selected cases of MTOD PHA 1 to decrease urinary sodium excretion.<sup>7</sup> Thiazide diuretics have also been used to correct hyperkalaemia and hypercalciuria. Response however is variable. Our patient did not require these drugs as the patient responded well to salt supplementation and oral potassium chelation. Close follow up will be required with an emphasis on monitoring his growth, blood pressure and electrolytes in the future.

## Conclusion

Pseudohypoaldosteronism type 1 should be considered in the differential diagnosis of an infant who presents with salt wasting crisis, refractory to mineralocorticoid replacement therapy. These patients require very high sodium chloride supplementation along with potassium binding resins to correct the electrolyte imbalance and achieve normal growth and development.

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