

# Transient Pseudohypoaldosteronism in Childrens Secondary to Urinary Tract Infection: Literature Review and Report of 2 Cases

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## Abstract

Pseudohypoaldosteronism (PHA) types I and II share hyperkalemia as a predominant finding. PHA is a heterogeneous syndrome characterized by a lack of response of the organs to the mineralocorticoid, and therefore there is loss of salts. Heredity can be autosomal dominant or recessive. It is very rare for other mutations to occur.

Autosomal dominant PHA-I is characterized by mutations in the mineralocorticoid receptor, while Autosomal recessive PHA-I results from mutations in the epithelial sodium channel (ENaC). Clinical expression of renal PHA-I is variable: patients present with salt loss in the neonatal period, failure to thrive, vomiting, and dehydration. Symptoms of renal PHA-I often improve in early childhood and older children.

PHA-II is the result of mutations in a family of serine-threonine kinases called with- no-lysine kinases (WNK) 1 and WNK4. The predominant role of WNK1 is the regulation of cation-Cl<sup>-</sup> cotransporters (CCCs) such as the sodium chloride cotransporter (NCC), basolateral Na-K-Cl symporter (NKCC1), and potassium chloride cotransporter (KCC1) located within the kidney. WNK4, its primary role in renal physiology, is as a molecular switch between the angiotensin II-aldosterone mediated volume retention and the aldosterone mediated potassium wasting. It also regulates the (NCC) and regulates the function of renal outer medullary potassium (ROMK) channels and ENaCs. Aldosterone inactivates WNK1 and WNK4 activity.

A typical picture of congenital adrenal hyperplasia (CAH) is hyponatremia with hyperkalemia; However, in the presence of pyelonephritis, the same biochemical manifestation can occur with transient PHA-I also known as type 4 renal tubular acidosis. We report two cases that present hyponatremia accompanied by urinary tract infection, leading to the diagnosis of transient pseudohypoaldosteronism.

The two cases support the idea that the renal tubular resistance to aldosterone is due to urinary tract infection. The two cases are presenting hyperkalemia with hyponatremia, and in whom a diagnosis of congenital adrenal hyperplasia was excluded. It is essential to know that serum aldosterone, urine sodium, and urine cultures may be obtained immediately.

**Keywords:** Pseudohypoaldosteronism; Congenital adrenal hyperplasia; Urinary tract infection; Hyperkalemia; Hyponatremia

## Introduction

Primary pseudohypoaldosteronism (PHA-I) is considered a heterogeneous syndrome and characterized by salt loss due to non-response to target organs for mineralocorticoids. Heredity is usually autosomal dominant, and in some cases is also recessive or sometimes mutated [1,2]. Since primary pseudohypoaldosteronism type 1 (PHA-1) was first described, which is the classic form, and PHA type II (PHA-II), which is also referred to as Gordon syndrome or chloride shunt syndrome.

PHA-I is a condition characterized by a defect in regulating the amount of sodium in the body. Sodium regulation, which is significant for fluid balance and blood pressure, primarily occurs in the kidneys. However, sodium can also be removed from the body through other tissues, such as the colon and sweat glands. People with PHA-I have high levels of aldosterone. However, pseudohypoaldosteronism type I is named for its characteristic signs and symptoms, which mimic (pseudo) low levels (hypo) of a hormone called aldosterone that helps regulate sodium levels [3].

Pseudohypoaldosteronism type II (PHA-II) is caused by problems that affect the regulation of the amount of sodium and potassium in the body. Sodium and potassium are essential in the control of blood pressure, and their regulation occurs primarily in the kidneys [4,5].

People with PHA-II have high blood pressure (hypertension) and high levels of potassium in their blood (hyperkalemia) despite having normal kidney function. Hyperkalemia usually occurs first, and hypertension develops later in life. Affected individuals also have high levels of chloride (hyperchloremia) and acid (metabolic acidosis) in their blood (together, referred to as hyperchloremic metabolic acidosis). In all children with dehydration and salt loss, the differential diagnosis includes congenital adrenal hyperplasia and pseudohypoaldosteronism. These two conditions are characterized by laboratory findings of hyponatremia, hypercalcemia, and acute metabolic acidosis with urinary Anomaly. Hyponatremia with hyperkalemia can be a manifestation of congenital adrenal hyperplasia (CAH). However, In the presence of pyelonephritis, the same biochemical event can occur

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with transient pseudohypoaldosteronism type 1 (PHA-I), also known as type 4 renal tubular acidosis.

However, it is essential to know that many pediatric specialists remain unfamiliar with this condition and its natural history. We report two cases of hyponatremia and UTI, recently diagnosed with PHA at our institution. Moreover, in each, the diagnosis of PHA was not immediately suspected. We present these cases to emphasize that the determination of transient pseudohypoaldosteronism should be seriously considered in the dehydrated, febrile, or failing to thrive infant with hyponatremia.

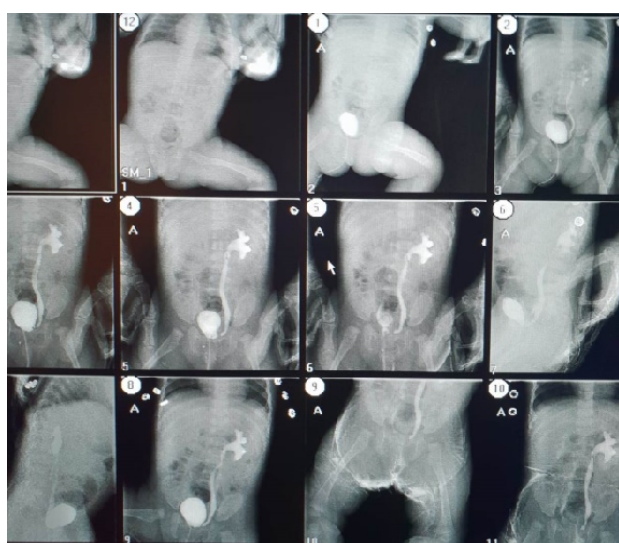
## Case Reports

### Patient 1

A 5-year-old girl presented with fever, vomiting, and severe dehydration. Physical examination showed an ill-appearing child with pale skin, fever, sunken eyes, and poor perfusion. The girl presented a picture of pyelonephritis. The laboratory results revealed hyperkalemia 7.5 mmol/L, with hyponatremia 125 mmol/L, and metabolic acidosis PH 7.25, in urine cultures *E-Coli* was found. Transient pseudohypoaldosteronism was diagnosed following elevated serum aldosterone and normal 17-hydroxyprogesterone level. Adequate replacement with intravenous saline and antibiotic therapy was given, hyperkalemia was treated with calcium gluconate, glucose-insulin, and beta-agonist inhalation. With antibiotic treatment and normal saline, the clinical and laboratory picture of hyperkalemia and hyponatremia was corrected.

### Patient 2

Preterm baby born at week 29, suffered from two events of urinary tract infection. In these events, the child was afebrile. However, urinalysis was positive for white blood cells and red blood cells, and urine culture subsequently grew *E. coli*, there was a picture of severe hyperkalemia 6.6 mmol/L and hyponatremia 128 mmol/L with metabolic acidosis PH 7.22. Cystography showing reflux (Figure 1), besides, renal ultrasound was performed, and moderate hydronephrosis was seen (Figure 2). Antibiotics and normal saline were provided.



**Figure 1:** Cystography of preterm baby showing reflux.



**Figure 2:** Ultrasound showing hydronephrosis of left kidney.

## Discussion

Transient pseudohypoaldosteronism is strongly related to urinary tract infections and structural urinary tract anomalies. Renal tubular resistance to aldosterone has been previously described in patients with a variety of urinary tract malformations [6,7].

The diagnosis of PHA facilitates appropriate renal investigations to reduce long-term morbidity. Urine analysis should be performed in infants with hyponatremia.

Hyponatremia with hyperkalemia and dehydration may be seen with congenital adrenal hypoplasia, congenital adrenal hyperplasia (CAH), hypoadrenalism, isolated aldosterone deficiency, or pseudohypoaldosteronism. The most typical cause of hypoaldosteronism is an adrenal failure due to CAH as a result of 21-hydroxylase deficiency. Measuring cortisol, 17OHP (17 $\alpha$ -hydroxyprogesterone), aldosterone, and renin levels are necessary, CAH is confirmed by low cortisol and high 17OHP, management is then directed towards CAH [8]. Normal ACTH, 17OHP, and cortisol values, high values of renin and aldosterone are essential for the determination of pseudohypoaldosteronism (PHA).

In our two cases, CAH and adrenal failure were excluded by the appropriate serum cortisol and normal 17OHP. The high aldosterone and the high renin levels were diagnostic of type I PHA, the two cases were presented with events of recurrent UTI, and imaging with ultrasound showed hydronephrosis in both cases, which supported the idea that the renal tubular resistance to aldosterone is due to urinary tract infection. And it's important to know that structural urinary tract abnormalities may be a predisposition to the development of PHA [9,10].

Type I pseudohypoaldosteronism (PHA) is a rare heterogeneous group of disorders characterized by resistance to aldosterone action. PHA-I can be divided into primary and secondary, primary PHA-I is a form of mineralocorticoid resistance presenting in the newborn with renal salt wasting, failure to thrive and dehydration, secondary PHA can be due to drugs.

The underlying pathology leading to mineralocorticoid resistance remains unknown. However, the two cases support the idea that renal tubular resistance to aldosterone is due to urinary tract infection, and that structural urinary tract abnormalities may be causes to the development of PHA.

## Conclusion

In all children with salt loss and failure to thrive, a distinction

should be made between pseudohypoaldosteronism and CAH. In a situation of hyperkalemia and hyponatremia and metabolic acidosis, there is a room to rule out a urinary obstruction with urinary tract infection.

The management of type I PHA then involves continuing salt and water replacement, and treatment of the precipitating cause (e.g. antibiotics for an UTI) and exclusion of urinary tract structural abnormalities. Appropriate treatment rapidly corrects the associated metabolic abnormalities.

An ultrasound of the urinary tract is recommended in all children under six months with an atypical UTI irrespective of type 1 PHA. We also, however, suggest that any child over the age of six months with a UTI and type 1 PHA should have imaging studies of the urinary tract.

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