

CASE REPORT

Diagnostic Predicament of Persistent Electrolyte Imbalance in a Neonate, Pseudo-hypoaldosteronism (PHA)Ahsan Ahmad Ghauri^{1*}, Muhammad Usman Munir², Zujaja Hina Haroon², Muhammad Younas²**ABSTRACT**

Pseudohypoaldosteronism (PHA) type 1 is a heterogeneous group of disorder of electrolyte metabolism characterized by apparent renal tubular unresponsiveness to aldosterone action. PHA-1 is manifested by hyponatremia, hyperkalemia, metabolic acidosis and may present as salt wasting crisis with elevated levels of renin and aldosterone. PHA-1 is subdivided into two types with varying degree of severity. The earliest sign of both type of PHA-1 is poor weight gain due to dehydration and failure to thrive during infancy. Here, we report a case of renal PHA-1 in a 30 days old female infant who presented with hyponatremia, mild dehydration and hyperkalemia and was treated with dietary sodium chloride supplementation, potassium binding resin and fluid replacement therapy which proved to be lifesaving.

Keywords: *Hyponatremia, Hyperkalemia, Mineralocorticoid Resistance, Pseudohypoaldosteronism*

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Introduction

Electrolyte imbalance can develop in various renal and genetic disorders with significant long-term health consequences.¹ Pseudohypoaldosteronism type 1 is among these disorders and characterized by mineralocorticoid receptor resistance to aldosterone action.² It is characterized by renal salt wasting, moderate to severe dehydration and failure to thrive. The chief biochemical features are clinically and genetically distinct, renal PHA-1 and systemic PHA-1. Renal PHA-1 is autosomal dominant disorder characterized by aldosterone resistance restricted to kidneys. On the contrary systemic PHA-1 is autosomal recessive disorder characterized by

severe resistance to aldosterone action in multiple organs including the kidneys, salivary glands, sweat glands and colon. Both forms share the same biochemical picture of hyperkalemia, hyponatremia and metabolic acidosis with elevated plasma renin activity and aldosterone levels. Both types may present with poor weight gain and failure to thrive during early infancy or may be asymptomatic at all as in cases of renal PHA-1. Clinical manifestations of this condition can vary widely whereas the treatment is often straightforward with oral salt supplementation. A differentiation between renal and systemic PHA may be made on the basis of response to oral salt supplementation therapy, ease of management to electrolyte disturbances, sweat test results and definitive diagnosis can be made on the basis of genetic testing. More than 100 cases have been reported in the literature since its first description in 1958.³ A study conducted in United Kingdom has reported an incidence of 1/47000.² Here we report a case of 30-day-old female infant who presented with decreased oral intake, lethargy, vomiting and poor weight gain at the time of admission.

¹Department of Chemical Pathology
Combined Military Hospital (CMH), Multan, Pakistan

²Department of Chemical Pathology
Armed Forces Institute of Pathology (AFIP), Rawalpindi,
Pakistan

Correspondence:

Dr. Ahsan Ahmad Ghauri

Department of Chemical Pathology
Combined Military Hospital (CMH), Multan, Pakistan
E-mail: aag00788@gmail.com

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Case Report

A thirty days old baby girl was brought to the Pediatric department of Combined Military Hospital Rawalpindi by her parents on 22nd Nov 2021 as a referred case with complaints of lethargy, decreased oral intake, poor weight gain and 2 episodes of vomiting for last 5 days. There was no history of associated fever, flu, cough, loose stools and seizures. We received the blood samples of this baby girl at Department of Chemical Pathology at Armed Forces Institute of Pathology, Rawalpindi for the detailed biochemical work-up of persistent electrolyte imbalance. She was born at full term by lower segment cesarean section (LSCS) with APGAR (Activity, Pulse, Grimace, Appearance, Respiration) score 9/10 and immediate cry. She had no perinatal complication and was on mother feed only. She was the third issue of a non-consanguineous marriage, had two elder siblings alive and healthy.

The baby was lethargic with normal vital signs at the time of admission to Neonatal Intensive Care Unit (NICU). She was mildly dehydrated with reduced skin turgor. Anterior fontanelle was flat. There were no dysmorphic features and no pigmentation noted. She had normal female genitalia with patent anal opening. She was passing urine and stools with 4 - 5 wet diapers daily. Her weight was 2300 grams which was below the 3rd percentile for her age. Upon examining the Central nervous system, she was hypotonic with depressed neonatal reflexes. There was no hepato-splenomegaly. Rest of the systemic examination was unremarkable. She was managed with fluid resuscitation, broad spectrum antibiotics and supportive measures.

Blood chemistry revealed raised serum reagent (8.4 mmol/L), creatinine (48 μ mol/L), potassium (6.6 mmol/L) and decreased sodium levels (129 mmol/L). Liver Function Tests and C-reactive protein were within the reference interval. Urine routine examination was unremarkable. There was no growth of microorganisms noted on blood culture. Radiological findings on ultrasound kidney ureter bladder revealed bilateral medullary nephrocalcinosis. Two dimensional echocardiography was unremarkable. Biochemical analysis of Arterial Blood Gases was suggestive of Normal Anion Gap Metabolic Acidosis with Partial

Respiratory Compensation (pH: 7.27; HCO₃: 18.7 mmol/l; pCO₂: 32.3 mmHg). Extended serum electrolyte profile showed hyperchloremia (109 mmol/l). Urine biochemical analysis indicated increased urinary sodium excretion (73 mmol/l), decreased urinary potassium (14 mmol/l) and creatinine excretion which was further augmented by fractional excretion of electrolytes. Thyroid profile, cortisol and 17-hydroxyprogesterone were within reference interval, whereas intact parathyroid hormone (0.32 pmol/l) was below the reference limit. Analysis of Plasma Amino Acids was performed using Ion exchange chromatography technique on Biochrome 30 which yield no significant elevation of amino acids.

Blood complete picture revealed decreased Haemoglobin levels (8.9 g/dl), rest of the Haematological values (WBCs: 8.1x 10⁹/L; Plt: 396 x 10⁹/L) were within reference range and blood culture was later reported as negative. At this point we considered the possibility of PHA-1 which was confirmed by elevated levels of plasma aldosterone (68650 pmol/l) along with raised plasma renin activity (271120 mIU/l).

Based on this diagnosis she was managed with oral sodium chloride supplementation of 30 mmol/kg/day, sodium bicarbonate of 4.5 g/kg/day in three divided doses. Serum electrolytes gradually returned to normal but she continued to have natriuresis and decreased urinary potassium excretion. At discharge after 15 days of hospitalization baby had stable vital signs, good hydration and normal systemic examination. She was tolerating oral feed well gained weight. The serum electrolytes were within the reference limits.

On follow-up investigations carried out after 6 months she was found to have significant improvement in her biochemical profile including serum electrolytes (Na: 141 mmol/l; K: 5.0 mmol/l), plasma aldosterone (3839 pmol/l), plasma renin activity (125 mIU/l) and arterial blood gases (pH: 7.38; HCO₃: 22.6 mmol/l; pCO₂: 40.4 mmHg).

Discussion

A renal form with autosomal dominant inheritance exhibiting salt loss mainly from the kidneys and a multi-system form with autosomal recessive form exhibiting salt loss from kidney, lung, sweat and

salivary glands.⁴

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 hyperkalaemia in the early neonatal period.⁵ 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.⁶

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 (>20 mmol/l Renal cause) and low urinary potassium excretion in the presence of hyponatraemia. Our patient characteristically demonstrated all these biochemical abnormalities. Plasma potassium concentration may vary from moderate to greatly increased values and can be life threatening or even fatal. Therapy primarily consists of oral fluid and sodium supplementation (20 – 40 mEq/kg/d) along with potassium chelation.⁷

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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