ONLINE FIRST

CASE REPORT

A Salty Mystery and Silent Storm: Neonatal Shock Revealing Pseudohypoaldosteronism: A Case Study

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ABSTRACT
Pseudohypoaldosteronism (PHA) is a rare but serious condition in neonates, often mimicking congenital adrenal hyperplasia (CAH). We present a case of a 16-day-old female neonate with a 10-day history of persistent vomiting, poor feeding, lethargy, and severe dehydration. Laboratory findings revealed hyponatremia, hyperkalemia, and metabolic acidosis. Initial suspicion of CAH prompted steroid therapy, but hormone profiles showed normal cortisol, Adrenocorticotropic hormone (ACTH), and 17-hydroxyprogesterone levels with markedly elevated renin and aldosterone levels, confirming PHA. The infant responded to fluid resuscitation, sodium supplementation, and potassium-binding therapy. This case highlights the importance of early differentiation between CAH and PHA to guide appropriate management and avoid unnecessary corticosteroid therapy.

Keywords: Pseudohypoaldosteronism, Aldosterone Resistance, Neonate, Hyperkalemia, Hyponatremia, Salt-Wasting.

INTRODUCTION

Pseudohypoaldosteronism (PHA) is a rare condition characterized by resistance to the action of aldosterone, leading to impaired sodium reabsorption and potassium excretion, which in turn results in hyponatremia, hyperkalemia, and metabolic acidosis, especially in neonates and infants[1]. It is classified into Type 1 and Type 2 variants. Type 1 PHA includes the renal (autosomal dominant) and systemic (autosomal recessive) forms. The renal form is milder and limited to the kidneys, often resolving with age. In contrast, the systemic form affects multiple organs, including the lungs, sweat glands, and colon, and persists throughout life [2,3].

In most neonatal cases, PHA presents with features mimicking congenital adrenal hyperplasia (CAH), such as salt-wasting, poor feeding, and vomiting. However, unlike CAH, PHA is marked by elevated levels of renin and aldosterone with normal 17-hydroxyprogesterone and cortisol levels, and does not respond to steroid therapy[4,5]. Accurate differentiation between PHA and CAH is essential as treatment strategies differ significantly.

Recent advances have identified mutations in genes encoding the epithelial sodium channel (ENaC) subunits (SCNN1A, SCNN1B, SCNN1G) as the genetic basis for systemic PHA1[6]. Genetic testing and counselling are increasingly becoming standard in managing confirmed cases[7].

In resource-limited settings without newborn screening, early identification of PHA remains a diagnostic challenge. Misdiagnosis can lead to inappropriate management and increased morbidity due to prolonged electrolyte imbalance and life-threatening arrhythmias[8,9]. Management is mainly supportive and includes fluid resuscitation, sodium supplementation, potassium chelation, and dietary potassium restriction[3].

This case report highlights a neonatal presentation of systemic PHA, initially misdiagnosed as CAH, and underscores the importance of endocrine evaluation and early differentiation in guiding appropriate care.

CASE PRESENTATION

A 16-day-old female neonate was admitted with a 10-day history of non-bilious, non-projectile vomiting occurring 10–15 times daily, refusal to feed, and progressive lethargy. She was born full-term (38 weeks) via elective cesarean section, weighed 2.4 kg, and was exclusively breastfed. Her birth and immediate postnatal period were unremarkable.

The parents sought medical attention on multiple occasions, receiving symptomatic treatment without improvement. There was no fever, diarrhea, abdominal distension, polyuria, seizures, or hyperpigmentation. Notably, there were no signs of ambiguous genitalia, and vaginal opening was normal.

On Examination, the neonate appeared lethargic, cyanosed, and severely dehydrated, which can be seen in **Figure 1.**

Figure 1: Severe Dehydration.
(Skin stays pinched for a long time, indicating severe dehydration)

Blood pressure was 52/20 mmHg, heart rate 187 bpm, respiratory rate 20 bpm, and oxygen saturation 91% on room air. She had sunken eyes, a depressed anterior fontanelle, delayed capillary refill (4 seconds), and hypotonia. No polyuria was observed. On Examination, there was a normal anal and vaginal opening, no ambiguous genitalia and clitoromegaly was seen. Initial management included oxygen, IV fluids, NPO status, and empirical antibiotics. Given the biochemical findings and presentation, congenital adrenal hyperplasia (CAH) was initially suspected. Hydrocortisone and fludrocortisone were started while awaiting endocrine tests.

Table I: Outcomes of Test Result

Laboratory Test	Results	Reference Range	Interpretation
Serum Sodium (Na^+)	124 mmol/L	135–145 mmol/L	Hyponatremia
Serum Potassium (K^+)	7.7 mmol/L	3.5–5.5 mmol/L	Severe Hyperkalemia
Bicarbonate (HCO_3^-)	13.05 mmol/L	22–28 mmol/L	Metabolic Acidosis
Anion Gap	23.68	8–16	Elevated
Random Blood Sugar (RBS)	75 mg/dL	70–140 mg/dL (random)	Normal
Serum Urea	Normal	7–20 mg/dL	Normal
Serum Creatinine	Normal	0.3–1.0 mg/dL (infant)	Normal
Urinalysis	Normal		No signs of UTI
Complete Blood Count (CBC)	Normal		No signs of infection
17-Hydroxyprogesterone	Slightly elevated	Age-appropriate range	Rules out CAH
Serum Cortisol	Normal	Age-appropriate range	Normal adrenal function
Plasma Renin	Elevated	Age-specific reference	Suggests Aldosterone Resistance
Plasma Aldosterone	Normal	Age-specific reference	Suggests Aldosterone Resistance

Diagnosis & Management:
Endocrine workup ruled out CAH due to normal cortisol, ACTH, and 17-OHP levels. Elevated aldosterone and renin confirmed Type 1 Pseudohypoaldosteronism, likely the systemic autosomal recessive form, given the severity and absence of renal anomalies or UTI. Steroid therapy was discontinued. The patient received IV fluids, sodium supplementation, kayexalate (1 g/kg 6-hourly), and potassium restriction. Electrolytes were monitored closely. Ultrasound of the abdomen ruled out structural abnormalities, such as pyloric stenosis, as shown in **Figure II.**

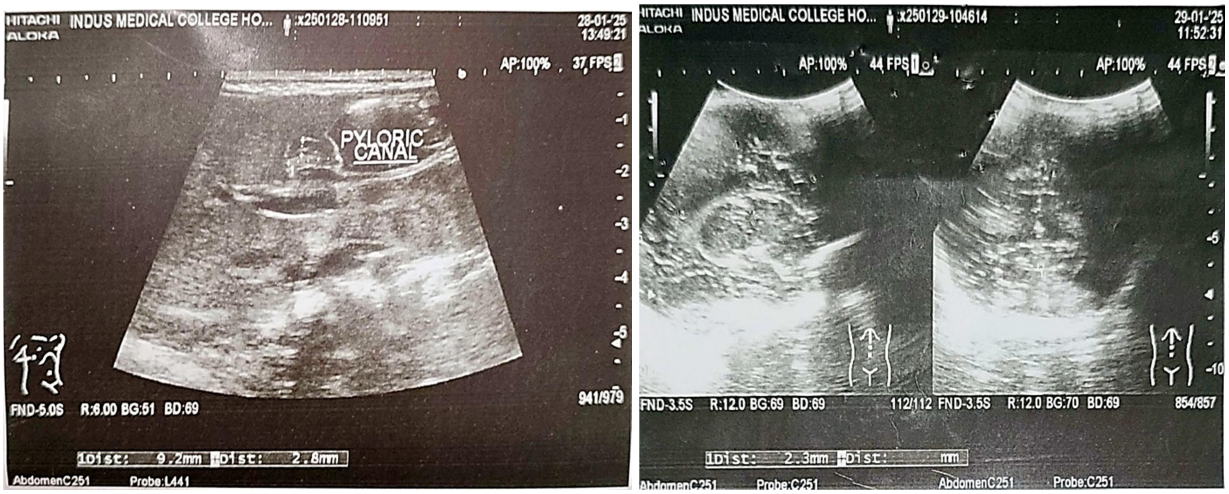

Figure 2: Ultrasound of Abdomen.

DISCUSSION

Pseudohypoaldosteronism Type 1 (PHA1) is a rare disorder characterized by aldosterone resistance at the renal tubular or systemic level, leading to impaired sodium reabsorption and potassium excretion. The systemic form, as seen in our case, is caused by mutations in genes encoding epithelial sodium channel (ENaC) subunits - SCNN1A, SCNN1B, or SCNN1G - resulting in multisystem involvement including kidneys, lungs, colon, salivary glands, and sweat glands[6,7]. The autosomal recessive inheritance pattern of the systemic type accounts for the severity of symptoms and their neonatal onset.

Our neonate presented with vomiting, dehydration, hyponatremia, hyperkalaemia, and metabolic acidosis - mimicking congenital adrenal hyperplasia (CAH), a common diagnostic pitfall. However, endocrine evaluation revealed normal 17-hydroxyprogesterone and cortisol levels, along with elevated renin and aldosterone, supporting the diagnosis of PHA1 rather than CAH[4,5]. Recent reports emphasize the critical need to distinguish PHA1 from CAH early, as the former does not respond to corticosteroids, and misdiagnosis may lead to unnecessary exposure and delayed management[4,5,7].

Studies from the last two years have highlighted the clinical variability and genetic underpinnings of PHA1. **Joshi K 2022**[2] reported a systemic form of PHA1 due to a novel SCNN1B mutation, reinforcing the importance of genetic testing in diagnosis and family counselling. Likewise, **Efthymiadou A et al.** [9] described a mild transient form of autosomal recessive PHA1 caused by a novel SCNN1A mutation, indicating that disease severity can range from self-limiting to life-threatening. In another recent case, **Tauber KA 2024**[4] described a neonatal cardiac arrest due to unrecognized PHA1, underscoring the urgency of timely diagnosis and electrolyte management.

Management remains supportive, mainly focusing on fluid resuscitation, sodium supplementation, potassium chelation, and dietary potassium restriction[3,6]. Our patient responded favorably to this approach, avoiding further complications. Although genetic testing was not performed due to resource limitations, it remains a valuable diagnostic and prognostic tool, particularly in systemic PHA1 cases with recurrent symptoms or family history[6,7.]

This case emphasizes that prompt recognition of PHA1 - particularly its systemic form is vital for guiding appropriate therapy, avoiding misdiagnosis, and reducing morbidity. In resource-constrained settings, a strong clinical suspicion, targeted endocrine evaluation, and multidisciplinary collaboration remain key to optimal patient outcomes.

CONCLUSION

This case emphasizes the importance of considering PHA in neonates with severe dehydration, vomiting, and electrolyte imbalance. Normal 17-OHP and cortisol with elevated aldosterone and renin levels confirm the diagnosis. Timely identification can guide correct treatment and prevent complications.

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AUTHOR CONTRIBUTION

Kanwal N: Analyzed and interpreted the data.
Bhatti A: Conceptualized and compiled the data for a case study.
Kumri R: Organized the article writing
Kumr R: Edited the original draft
Shaikh I: Edited the pictures according to the guidelines
Bai M: Rephrased the manuscript.

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