

Pseudohypoaldosteronism Type-I; a rare cause of hyperkalemia in neonates

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Abstract

Pseudohypoaldosteronism type I (PHA-I) is a rare disorder with only a few cases reported worldwide. It appears early in life with salt-wasting, failure to thrive, dehydration, hypotension, hyperkalemia and metabolic acidosis. There is a resistance to aldosterone by the mineralocorticoid receptors. We describe one such case of a 14-day-old female neonate who presented with frequent episodes of dehydration, hyperkalemia and hyponatremia. On further workup, she proved to be a case of PHA-I. The aim of this report is to discuss the evaluation and to highlight the difficulties associated with the management of this rare disorder.

Keywords: Pseudohypoaldosteronism Type-I, Hyperkalemia, Neonates, Case report, Hyponatremia, Neonatal.

Introduction

Pseudohypoaldosteronism (PHA) refers to a heterogeneous group of disorders of electrolyte metabolism characterised by an apparent state of renal tubular unresponsiveness or resistance to the action of aldosterone.¹ There are two types of familial disorders in this disease. PHA-I is a rare genetic disorder first described in 1958 by Cheek and Perry.² It is a disorder of early infancy characterised by severe salt and water depletion and other signs of aldosterone deficiency, although aldosterone secretion is normal or increased; causes include the defect in the maturation of aldosterone receptors.³ We would like to share our experience regarding the diagnosis and management of this rare disease.

Case Report

A 14-day-old female neonate was admitted from a peripheral hospital for further evaluation of persistent electrolyte imbalance i.e. hyperkalemia, hyponatremia and metabolic acidosis.

The neonate was a product of second-degree consanguineous marriage, born at term through a normal

vaginal delivery. Her birth weight was 2.1kg with a good Apgar (Appearance, Pulse, Grimace, Activity, Respiration) score. On the second day of life, she developed excessive crying and vomiting with reluctance to feed. She was immediately taken to a tertiary care unit where she was found to have severe dehydration, metabolic acidosis, hyperkalemia and hyponatremia (Serum Sodium = 115 meq/L, Serum Potassium = 11 meq/L, Bicarbonate=9.2 meq/L). Following the aforementioned clinical features, a provisional diagnosis of Congenital Adrenal Hyperplasia (CAH) was made and mineralocorticoid treatment was started after sending the work-up for CAH.

The baby was referred to our unit for further care and management. At the time of examination, the neonate was found to be sick looking, irritable and moderately dehydrated with signs of respiratory distress. She was hypotensive (35/20 mmHg).¹ Her systemic examination was unremarkable and external genitalia were normal.

Initial laboratory evaluation revealed a high Total Leucocyte Count (TLC) of 47000 cells/mm³, with raised Neutrophil count of 72% and raised C-reactive protein levels of 44.72mg/L; suggestive of sepsis. However, the blood and urine cultures were found to be negative. After giving intravenous (IV) antibiotics, her subsequent work-up was negative for sepsis. The electrolytes were deranged (Sodium (Na)=129 meq/L, Potassium (K)=7.0 meq/L, Bicarbonate (HCO₃)=13 meq/L, Chloride (CL)=93 meq/L), chest X-ray and Random Blood Sugar (RBS) levels were normal. The urinalysis, renal function tests and abdominal ultrasound showed no abnormalities with normal female internal organs. Despite the mineralocorticoid treatment, electrolyte correction and aggressive rehydration therapy there were still repeated episodes of dehydration, electrolyte imbalance and metabolic acidosis. Adrenal work-up showed serum cortisol 37 ug/dl (normal), 17 hydroxy progesterone (OHP) 0.99 ng/dl (normal) , plasma renin 33.3ng/ml/hr. (high), serum aldosterone >177 ng/dl (high), urinary sodium 200meQ/L (High)and adrenocorticotrophic hormone (ACTH)12.08 pg/ml (low).

Finally, on the basis of the normal genitalia, normal cortisol

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and 17 hydroxy progesterone level, markedly raised aldosterone and renin level and unresponsiveness to mineral corticoid therapy, the diagnosis of PHA-I was made.

Based on this diagnosis, the infant was managed with high sodium chloride supplements along with potassium exchange resin and oral sodium bicarbonate. She responded well to this treatment and was discharged after two weeks.

Discussion

PHA-I is a rare hereditary condition, which can be isolated to the kidney (i.e. autosomal dominant form/or adPHA-I) or may be systemic, autosomal recessive (arPHA-I). Autosomal dominant PHA-I has been linked to mutations in the mineralocorticoid receptors (MR).⁴ A mild disease responds to sodium supplementation and improves with time probably due to the maturation of renal sodium or enhanced proximal re-absorption of sodium.⁵ The autosomal recessive PHA-I (arPHA-I) was reported in 1996 to be caused by mutations in the ENaC.⁶ As compared to adPHA-I, it has a much severe clinical presentation and has been associated with systemic manifestations, such as recurrent pulmonary infections and fatal hyperkalaemia.⁷

PHA-II (Gordon's syndrome) is a rare cause of hyperkalaemia, hyperchloraemic metabolic acidosis, volume expansion and hypertension, which was not present in our patient.⁸

Secondary PHA has been reported in infants secondary to urinary tract infection, obstructive uropathy, reflux nephropathy, renal dysplasia and small bowel resection. In this end organ, responsiveness to aldosterone may normalise with appropriate treatment of the underlying cause.⁵

Early in infancy, patients with adPHA-I present with dehydration and failure to thrive associated with salt-wasting, hypotension, hyperkalaemia, and metabolic acidosis, despite increased plasma aldosterone levels.⁹ These patients can improve with age, and some adult patients are usually asymptomatic and have fewer abnormal biochemical findings (e.g., only lifelong increases in aldosterone or hyperkalaemia).¹⁰ To date, approximately 50 distinct mutations in the human MR gene and approximately 20 mutations in ENaC genes responsible for PHA-I have been described.¹¹ However, some patients, especially those with sporadic PHA-I, do not have genetic abnormalities in MR or ENaC.¹²

In this case the child presented early in life and required high dose of sodium supplementation to compensate salt-wasting, but there was no multi-organ involvement

and there was no secondary cause detected for unresponsiveness to aldosterone, so we considered our case as PHA-I.

Initially the child was managed in the neonatal intensive care unit (ICU) with continuous IV fluid administration, correction of electrolytes and metabolic acidosis. For hyperkalaemia, we started potassium exchange resin at a dose of 1gm/kg divided in 2 doses. Despite our efforts, potassium remained high and on several occasions it reached 10-11 meq/l (electrocardiogram [ECG] showed tall T waves), so we increased the dose up to 2gm/kg/dose every 6 hour per rectal at which it was controlled. We also faced difficulty in the management of hyponatraemia for which we went up to 20meq/kg/day initially as IV, and then shifted her to oral 20% sodium chloride (NaCl) solution. For metabolic acidosis, we started her with IV sodium bicarbonate (NaHCO₃), and increased the dose up to 7meq/kg/day to achieve control. After 2 weeks of aggressive management, her biochemical parameters came under control. The baby was discharged on oral hypertonic saline (20meq/kg/day of 20% NaCl solution), oral NaHCO₃ (7meq/kg/day) and potassium ion exchange resin (1.5gm/kg/dose 6 hourly). On follow-up after 2 weeks, the child was looking well, active with appropriate weight-gain and normal biochemical parameters (Na: 144meq/l, K: 3.6 meq/l, HCO₃: 22). The definitive diagnosis of PHA-I depends on genetic analysis, which can be done if facilities are available.

The mainstay of the treatment in PHA-I should include high sodium chloride supplements, potassium exchange resin and NaHCO₃. In subsequent follow-ups close serum electrolyte monitoring is needed. Oral NaCl supplementation is difficult because babies dislike the salty taste, but this can be overcome by feeding the baby upright and giving it at a time when they appear to be most hungry.

Outpatient follow-up of such patients involve close contact with family for monitoring of general health, electrolytes and weight-gain.

Conclusion

PHA-I (renal type) is a rare disorder. It should be considered in the differential diagnosis of an infant presenting with severe hyponatraemia and hypokalaemia, which is refractory to the mineralocorticoid therapy. The infants outgrow this problem by the age of 1 or 2 years. They should be treated with high sodium chloride supplements along with potassium binding resins to keep the electrolyte normal, thus ensuring the normal growth and development of the infant.

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