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Case Report

Pseudohypoaldosteronism in a Neonate Presenting as Life-Threatening Ventricular Tachycardia

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Abstract

Neonatal electrolyte disturbances, mainly the hyperkalemia and hyponatremia, medical conditions that require an emergent diagnosis and treatment to avoid morbidity and mortality. Here, we describe the case of an 11-day-old male baby presented with life-threatening ventricular tachycardia, hyperkalemia, hyponatremia, and metabolic acidosis diagnosed as autosomal recessive pseudohypoaldosteronism type 1 (PHA1).

This report aims to recognize that PHA1 may present with a life-threatening ventricular tachycardia due to severe hyperkalemia and describes the management of such cases in neonates.

Keywords: *Pseudohypoaldosteronism; Hyperkalemia; Hyponatremia; Metabolic Acidosis, Ventricular Tachycardia*

Introduction

Aldosterone is the primary hormone responsible for the regulation of sodium and potassium in blood. Aldosterone acts on the mineralocorticoid receptors (MR) which are situated in the distal tubules intracellularly. Upon cell diffusion, aldosterone mineralocorticoid receptor complex leads to activation of a transcription machine. As result, the transcription of the DNA sequence into mRNA in the activated gene regulates sodium reabsorption and potassium excretion [1]. In infancy, hyperkalemia may be caused due to acute hemolysis, kidney disorders, and hormonal disorders. Congenital adrenal hyperplasia (CAH) and adrenal insufficiency are common hormonal disorders leading to hyperkalemia in neonates and infants, while pseudohypoaldosteronism (PHA) remains a rare cause. PHA can result in neonatal mortality due to severe hyponatremia, hyperkalemia, and metabolic acidosis, if remained undetected and thus untreated [2]. Most patients with PHA1 have identifiable mutations, but pathogenesis of PHA1 still remains challenging [3].

Case Report

11-day-old male, product of full term pregnancy, born by elective C-section, to G2 P2 A0 mother; whose course of pregnancy was smooth. The birth weight was 3710 grams. His post-natal course was complicated with NICU admission for suspected early neonatal sepsis, received antibiotics (Amoxicillin and Gentamicin), and discharged home at day 3 of life against medical advice. The infant was on breast feeding every 2 - 3 hours, and was doing well until few hours prior to presentation (day of life 11) when the mother noticed pallor, hypoactivity, and poor feeding.

Upon presentation to ER, the patient was pale and hypoactive with scaly skin, perioral cyanosis, in respiratory distress. Vital signs were: T = 36.2 c, HR = 245 b/min, RR = 60b/min, BP and O2 saturation were undetectable. He was found to have ventricular tachycardia confirmed by ECG that returned to spontaneous rhythm spontaneously. The patient experienced difficulty in breathing associated with severe lethargy. He had generalized maculopapular skin rash, poor perfusion and normal external genitalia on physical examination With regard to his family history, it was unremarkable.

Electrolytes showed serum potassium 9.4 mEq/dl, sodium 124 mEq/l, bicarbonate 11 mEq/dl, BUN 29 mg/dl, and creatinine 0.72 mg/dl.

The patient was given calcium gluconate, started on continuous IV Insulin, Glucose, sodium bicarbonate ($NaHCO_3$), Fludrocortisone, and hydrocortisone. His Potassium level decreased to 6.5 mEq/dl, but after stopping insulin, potassium level increased again to 10mEq/dl and didn't decrease despite insulin IV drip and kayexalate per rectum, so peritoneal dialysis started. On same day, he developed ventricular tachycardia not responsive to medication so he was intubated and D/C shock done that reverted to sinus rhythm. 48 hours after starting the peritoneal dialysis, potassium level decreased to 4.5 mEq/dl, and then he was extubated.

Laboratory data revealed normal level of cortisol (30 mg/dL), and newborn screening for congenital adrenal hyperplasia (CAH) was done and was negative, with normal renal and pelvic ultrasound. So CAH was ruled out.

Aldosterone level was found to be more than 45000 pmol/L (N = 832 - 5272 pmol/L), with high renin level 2723 mui/L (N = up to 46 mui/L), with normal urine osmolarity indicating aldosterone resistance.

Fludrocortisone and hydrocortisone were tapered and stopped. The patient was discharged at 55 days of life on the following medications: 2 ml NaCl 20% (2 mEq/kg per day), 15g kayexalate per day (4g per kg per day), and 4 ml NaHCO3 8.4% (1 mEq/kg per day).

The patient was followed-up by electrolytes level twice weekly, and potassium level ranged between 4 - 4.5 mEq/dl.

Genetic studies were done and showed the presence of mutation at the level of *SCNN1B* (c.1542+1G > A) in homozygous state.

Discussion and Conclusion

Hyperkalemia can cause fatal cardiac arrhythmia [4]. Early recognition and forceful management are life saving. The picture of adrenal insufficiency is usually expected when hyperkalemia, hyponatremia and metabolic acidosis coexist, and hydrocortisone therapy gives excellent response. However, resistance to aldosterone should be always considered when the response to corticosteroids is poor, or if the clinical picture is atypical [5,6].

PHA is defined as the presence of an apparent unresponsiveness of the renal tubules to the action of aldosterone. PHA type 1 can be presented in two forms, the renal and the generalized type [7]. The two forms differ genetically, clinically and phenotypically. The renal form (ad-PHA1) can be asymptomatic diagnosed by elevated aldosterone level, besides that it can present with more severe symptoms related to salt losing nephropathy, it is the result of a heterozygous mutation (autosomal dominant) of mineralocorticoid receptor gene NR3C2 located at 4q31.1. Clinical presentation in early infancy usually includes failure to thrive, vomiting, and dehydration. In this form, hyperkalemia is usually mild, and management includes only sodium supplementation. Ad-PHA1 could be potentially lethal in neonates although it is comparatively milder, as suggested by Geller., *et al.* [8] and carries a good prognosis.

Multiple type 1 PHA (ar-PHA1) is inherited as autosomal recessive trait due to mutations of epithelial sodium channel (ENaC) subunit genes *SCNN1A* situated in 12p13.31, *SCNN1B*, and *SCNN1G*, both located in the locus 16p12.2 [7]. It has an early presentation with severe dehydration, profound electrolyte disturbances, and even cardiac arrhythmia. In contrast to the renal form, aldosterone resistance is not limited only to kidneys, it affects many organs containing the ENaC, including lungs, colon, salivary and sweat glands, as well it can present with chronic recurrent chest infections and wheezing, and can be confused with cystic fibrosis due to sodium loss through sweat and salivary glands. Moreover, skin manifestations present as milia rubra like, similar to the generalized scaly skin rash in our case, and recurrent skin infections. In general, patients affected with this generalized type suffer from recurrent life threatening episodes of salt loss, and carries a very bad prognosis.

Furthermore, a transient form of PHA exists named PHA type 3, occurs secondary to urinary tract infections or obstruction in urinary tract [7,9,10].

Considering the presentation of our case, the severity of hyperkalemia, the difficulty of its management, and the generalized skin rash, along with the elevated aldosterone, plasma renin activity and normal cortisol level indicate the multiple type 1 PHA (ar PHA1).

A homozygous or compound heterozygous mutations in *SCNN1A*, *SCNN1B*, or *SCNN1G* genes lead to systemic autosomal recessive form. The α, β, and the γ subunits are the protein complex of epithelial sodium channel (ENaC) that are essential for sodium and potassium transport and encoded by the above three genes.

Thus, the genetic analysis was done and confirmed the diagnosis, it showed presence of mutation at the level of *SCNN1B* (c.1542+1G>A) in homozygous state. This mutation was already detected in the study of Saxena., *et al* [11].

Treatment of PHA type 1 comprises adequate hydration, sodium supplementations, correction of hyperkalemia and acidosis. Renal form (ad PHA1) may need treatment till two years of age, after that it usually improves contrary to multiple type 1 PHA (ar PHA1), therapy is very challenging and needs to be lifelong.

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