



## A Newborn with Type 1 Pseudohypoaldosteronism: Case Report

Terek D<sup>1</sup>, Ergin F<sup>1</sup>, Uygur O<sup>1</sup>, Yalaz M<sup>1</sup>, Akisu M<sup>1</sup>, Koroğlu OA<sup>1</sup>, Darcan S<sup>2</sup>, Ozkinay F<sup>3</sup> and Kultursay N<sup>1\*</sup>

<sup>1</sup>Department of Neonatology, Ege University, Turkey

<sup>2</sup>Department of Endocrinology, Ege University, Turkey

<sup>3</sup>Department of Genetics, Ege University, Turkey

### Abstract

Pseudohypoaldosteronism (PHA) is a rare disease developing as a result of peripheral resistance to aldosterone and is characterized by salt loss. We present a 6-day-old newborn who was admitted to emergency care with poor enteral feeding and vomiting, with hyponatremia, hyperkalemia and elevated plasma aldosterone levels. Type 1 PHA was diagnosed due to resistance to the fluid replacement and steroid treatment. Genetic analysis showed homozygous SCNN1A mutation.

**Keywords:** New born; Hyperpotassemia; Hyponatremia; Pseudohypoaldosteronism

### Introduction

Pseudohypoaldosteronism (PHA) is a rare disease developing as a result of peripheral resistance to aldosterone and is characterized by salt loss. PHA may be primary due to a genetic mutation in the mineralocorticoid receptor or epithelial sodium channel, or secondary as a result of infection, uropathy or drugs. Characteristic findings are hyponatremia, hyperkalemia, metabolic acidosis and elevated plasma aldosterone levels. PHA has three types, while type 1 and 3 are characterized by salt loss; type 2 results with salt-hold. Type 1 PHA is divided into two types as renal and systemic. The systemic type has autosomal recessive transition and develops due to a genetic mutation in the epithelial sodium channel. On the other hand, renal type has autosomal dominant transition and is secondary to a mutation in the mineralocorticoid receptor [1-3]. In this case report, a 6-day-old girl registering to the emergency care with poor enteral feeding and vomiting, diagnosed with PHA1 is presented and this rare disease is discussed in the light of the literature.

### OPEN ACCESS

#### \*Correspondence:

Nilgun Kultursay, Head, Division of Neonatology, Ege University Childrens Hospital, 35100, Bornova, Izmir, Turkey, Tel: +90 5326082890; E-mail: nilgunkultursay@gmail.com

Received Date: 02 Jan 2017

Accepted Date: 01 Mar 2017

Published Date: 03 Mar 2017

#### Citation:

Terek D, Ergin F, Uygur O, Yalaz M, Akisu M, Koroğlu OA, et al. A Newborn with Type 1 Pseudohypoaldosteronism: Case Report. *Ann Clin Case Rep.* 2017; 2: 1285.

**Copyright** © 2017 Kultursay N. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

### Case Presentation

The patient was delivered to a 19-year-old primigravid healthy mother by cesarean section at the 41<sup>st</sup> gestational age. No clinical or laboratory abnormality was reported for the pregnancy period. There was no structural defect that was identified during the fetal anomaly sonographic screening such as oligohydramnios and polyhydramnios or any structural anomalies of the urinary tract of the fetus.

The birth weight of the fetus was 3200 grams. 6-day-old female infant was admitted to our emergency department with poor enteral feeding and vomiting. In her physical examination, a weight loss of 13.7% was detected and the baby was hospitalized in the neonatal intensive care unit (NICU).

There was a first degree cousin marriage between the parents.

In admission to NICU, her weight was 2750 gm (25-50P), height was 51 cm (75-90P) and the head circumference was 34 cm (50 P). A 13.7% of weight loss was present compared to birth weight. Her general condition was poor, she was pale and her capillary refill time was prolonged. Blood pressure measurements (72/56/60) were within normal limits according to post conceptional week. Her turgor, tonus and subcutaneous fat tissue were decreased. The newborn reflexes were weak. The genitourinary system showed a female-compatible appearance. In order to rule out sepsis, complete blood count, serum C reactive protein, urine and blood cultures were obtained. Leukocyte and platelet counts were 15.000/ml and 205.000/ml; hemoglobin level was 17.8 g/d. Serum C reactive protein and urine analysis were normal. Urine and blood cultures were negative.

In her biochemical examination; plasma glucose level was 75 mg/dl, sodium was 122 meq/l, and potassium was 8 meq/l and in blood gas analysis bicarbonate level and base excess were 11 and 11.8 in order. Since high blood potassium result may be due to a hemolytic blood sample, potassium level was re-evaluated and was found high again.

Congenital heart disease was ruled out with normal preductal and postductal oxygen saturations and echocardiography. Abdominal and cranial ultrasounds were revealed no pathologies.

Spot urine examination was performed in the differential diagnosis of salt-wasting diseases in newborn. The spot urine analysis showed high sodium excretion (156 meq/l, FeNa%7.8) and normal potassium excretion (3.5 meq/l, FEK%2.9). Hormone profile was obtained during the hyponatremic and hypovolemic period for evaluation of metabolic acidosis, hyponatremia, hyperpotassemia and high sodium excretion in urine that might be indicative of adrenal insufficiency. Adrenal ultrasound did not show any evidence of bleeding or hyperplasia.

During clinical follow up, seizures which did not resolve with 3% NaCl bolus treatment developed and intravenous levitracetam loading dose was administered. In order to rule out central etiology of adrenal insufficiency cranial computed tomography imaging, cranial and hypophysial magnetic resonance imaging's were obtained and found normal. Sodium deficit treatment was given and intravenous sodium bicarbonate and insulin-dextrose fluid treatment were started for hyperpotassemia treatment. Oral calcium polystyrene sulphate (anti potassium granules) with a dosage of 1gr/kg was also added to the treatment. Intravenous calcium gluconate was administered for prevention of cardiac effects of hyperpotassemia. Hyperpotassemia and hyponatremia were treated first with hydrocortisone bolus and consequently with hydrocortisone infusion with a dosage of 25 mg/g. For mineralocorticoid replacement, oral 9 $\alpha$ -dihydrocortisone was also added to the treatment. Despite all this hydrocortisone and mineralocorticoid treatment, no improvement was observed in serum electrolyte levels.

Detailed hormone tests showed that 17-OH progesterone level was 5.1 ng/ml, ACTH level was 12.8 U/l and cortisol level was 47.08 mcg/dl, all within the normal range. Plasma aldosterone was elevated being 3560 ng/l. Plasma renin activity could not be analyzed in an outside private laboratory due to the poor economical status of the family. PHA was diagnosed due to elevated urinary sodium excretion, high plasma aldosterone level and normal blood pressure. Blood samples for genetic analysis were obtained.

During the follow-up, the unsuccessful steroid treatment was gradually decreased and finally stopped. Table salt was added to enteral feeding and oral potassium lowering treatment with anti-potassium granules was continued. Detailed urinary ultrasonography was found normal. All other secondary reasons for PHA were excluded.

Pseudohypoaldosteronism has to be taken into consideration in cases with salt-wasting and adrenal insufficiency findings who do not respond to medical therapy for adrenal insufficiency in the first weeks of life. In our patient, type 1 pseudohypoaldosteronism was diagnosed due to resistance to the fluid replacement and steroid treatment.

There was no familial history of salt-wasting disease. TruSight Inherited Disease<sup>®</sup> Panel Illumina was used to analyze the known genes (SCNN1A, SCNN1B and SCNN1G) responsible for PHA. A

homozygous c.1052+1G>A variant, which was previously reported (rs142439390), was detected in SCNN1A gene. The parents were found to be carrier for the variant following segregation analysis of the family.

## Discussion

Salt-wasting syndromes in the neonatal period may present with different clinical features. While the clinical symptoms may be nonspecific such as feeding intolerance, loss of weight gain, vomiting and weakness, patients may admit to the emergency departments with shock symptoms due to hypoglycemia and/or severe dehydration.

This clinical situation may happen due to many causes in the newborn period and may be fatal. The differential diagnosis of salt-wasting diseases includes primary and secondary causes. Primary adrenal insufficiencies include congenital adrenal hyperplasia, hypoplasia, adrenal bleeding, severe systemic infections and pseudohypoaldosteronism. Secondary adrenal insufficiencies, steroids passing from mother, hypothalamo-hypophysial defects, central nervous system tumors, trauma and associated bleeding. Other causes are renal sodium loss due to pyelonephritis, tubulopathy, inappropriate ADH secretion syndrome, central salt waste, pylor stenosis and congenital hypothyroidism [1,4].

Congenital adrenal hyperplasia must be considered in the first step in case of salt-loss clinical symptoms during the newborn period. The patients are generally admitted with salt-loss symptoms and sexual differentiation disorders. Although, salt-loss clinical symptoms may present early in the first week of life, generally the symptoms are expected to appear in the 2<sup>nd</sup>-3<sup>rd</sup> week of life. Therefore, the treatment should be aimed directly to correct the fluid and electrolyte imbalance, particularly hyperpotassemia. Clinical and laboratory findings of patients should be closely monitored and the underlying causes of treatment failure should be considered. Aldosterone resistance should be considered and therefore plasma renin and aldosterone levels should be determined in case of resistance to fluid-electrolyte treatment and steroid replacement in patients with hyponatremia, hyperpotassemia and metabolic acidosis [1,4].

Our patient was admitted with severe vomiting and pathological weight loss. Genital examination was normal. Laboratory analysis showed metabolic acidosis, hypernatremia, hyperpotassemia and increased sodium excretion in urine. There were no adrenal and intracranial bleeding, adrenal hyperplasia and renal structural anomaly on ultrasound. Infection criteria were negative. Cranial and hypophysial tomography and magnetic resonance imaging's were normal. Our patient was then diagnosed with pseudohypoaldosteronism with the resistance to fluid and steroid replacement treatment and the elevated plasma aldosterone level.

Aldosterone passively crosses the epithelial cell membrane and binds to the mineralocorticoid receptor. The ligand-bound receptor translocates into the nucleus and promotes or represses gene signaling. Transcription of signaling factors results in an accumulation of epithelial sodium channels at the plasma membrane and they increase sodium transport into the epithelial cell. Sodium is then actively given out of the cell by the sodium-potassium ATPase. Inactivating mutations in the mineralocorticoid receptor cause renal PHA type 1 whereas inactivating mutations in the epithelial sodium channel subunit genes cause the systemic form of the disease [1].

Pseudohypoaldosteronism may be primary due to a mutation

in the mineralocorticoid receptor or amiloride-dependent epithelial sodium channel, or secondary to infection, uropathy or drugs. Type 1 pseudoaldosteronism (PHA1) may be inherited either autosomal dominant and autosomal recessively. Renal type PHA1 is transmitted autosomal dominantly. It is usually mild and may resolve spontaneously. The systemic form PHA1 is transmitted autosomal recessively and may be persistent until adulthood. SCNN1A gene mutations leading to Type 1 autosomal recessive PHA have been reported in the literature [5-7]. Mutation in the subunit genes (SCNN1A, SCNN1B, SCNN1G) of epithelial sodium channel and the NR3C2 gene encoding the mineralocorticoid receptor, result in systemic PHA1 and renal PHA1, respectively [7]. In our case, gene mutation was detected and the diagnosis of type 1 PHA was confirmed.

In conclusion, although the most frequent and most important cause of life-threatening salt-loss syndromes in the first weeks of life is congenital adrenal hyperplasia, considering other causes and performing the necessary tests for differential diagnosis may be life saving. Pseudohypoaldosteronism should be considered in differential diagnosis in those cases where adequate response to treatment of congenital adrenal hyperplasia cannot be observed.

## References

1. Amin N, Alvi NS, Barth JH, Field HP, Finlay E, Tyerman K, et al. Pseudohypoaldosteronism type 1: clinical features and management in infancy. *Endocrinol Diabetes Metab Case Rep.* 2013; 2013: 130010.
2. Geller DS, Zhang J, Zennaro MC, Vallo-Boado A, Rodriguez-Soriano J, Furu L, et al. Autosomal dominant pseudohypoaldosteronism type 1: mechanisms, evidence for neonatal lethality, and phenotypic expression in adults. *J Am Soc Nephrol.* 2006; 17: 1429-1436.
3. Wang J, Yu T, Yin L, Li J, Yu L, Shen Y, et al. Novel mutations in the SCNN1A gene causing pseudohypoaldosteronism type 1. *Plos One.* 2013; 8: e65676.
4. Belot A, Ranchin B, Fichtner C, Pujo L, Rossier BC, Liutkus A, et al. Pseudohypoaldosteronisms, report on a 10-patient series. *Nehrol Dial Transplant.* 2008; 23: 1636-1641.
5. Riepe FG. Clinical and molecular features of type 1 pseudohypoaldosteronism. *Horm Res.* 2009; 72: 1-9.
6. Chang SS, Grunder S, Hanukoglu A, Rosler A, Mathew PM, Hanukoglu I, et al. Mutations in subunits of the epithelial sodium channel cause salt wasting with hyperkalaemic acidosis, pseudohypoaldosteronism type 1. *Nat Genet.* 1996; 12: 248-253.
7. Welzel M, Akin L, Buscher A, Guran T, Hauffa BP, Hogler W, et al. Five novel mutations in the SCNN1A gene causing autosomal recessive pseudohypoaldosteronism type 1. *Eur J Endocrinol.* 2013; 168: 707-715.