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Severe Systemic Pseudohypoaldosteronism Type 1 5 years of evolution

P2 Category
Perinatal endocrinology

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Introduction

Type 1 pseudohypoaldosteronism (PHA-1) is a rare syndrome of unresponsiveness to aldosterone, expressed in two forms: renal PHA-1 and systemic PHA-1. In renal PHA-1 the mineralocorticoid resistance is isolated to this organ, so the phenotype is milder and often improves spontaneously due to proximal nephron maturation. Systemic PHA-1 results from autosomal recessive mutations in the genes encoding α, β and γ subunit of epithelial sodium channel (ENaC) that exists in multiple organs (kidney, colon, lung, salivary and sweat glands), and therefore the phenotype is severe. The diagnosis is established by the presence of high levels of serum aldosterone and plasma renin activity associated with hyponatremia, hyperkalemia and metabolic acidosis. Symptoms manifest during the first week of life, requiring prolonged hospitalizations and often lifelong high-salt replacement therapy. The mortality rate is high, especially during the neonatal period.

Case Report

Presentation

Male; Born at full term; Birth weight of 3010g (10-25th percentile)
No parental consanguinity; 6-year-old sister with Chediak-Higashi syndrome

10th day
Hypovolemic shock
NICU

Dehydration
Hyponatremia: 125mEq/L; Hyperkalemia: >10mEq/L
Metabolic acidosis

Normal saline bolus → **To correct dehydration**

Calcium gluconate
Sodium bicarbonate
Nebulized salbutamol
Glucose infusion
Insulin infusion
Rectal cation-exchange resin
→ **To control hyperkalemia**

Numerous life-threatening crisis

Congenital Adrenal Hyperplasia was suspected and he started **hydrocortisone** (max 200 mg/kg/day) and **fludrocortisone** (max 1.5 mg/day)

Initial **17-OHP** was falsely raised (10.76 ng/mL)
In sick newborns a repeated assessment may be required for the diagnosis

Systemic PHA-1
homozygous mutation of intron 3 of the SCNN1A gene
c.1052 + 2dupT

Elevated

- **Serum aldosterone 1750 ng/dL** [reference range 7-184]
- **Plasma renin activity 70 ng/mL/h** [reference range 0.4-1.9]

5-months-old
Discharge

Fludrocortisone 1.5mg/day + 20% saline supplement 33mEq/kg/day + cation-exchange resin 1g/kg 6 times/day

Evolution

✓ **Recurrences of fluid and electrolyte imbalances**
- Requiring increase of cation-exchange resin and frequent nebulized salbutamol and calcium gluconate

✓ **Episodes that mimicked recurrent respiratory infections**
- Cough, tachypnea, fever and wheezing
- Defective Na+ dependent liquid absorption and mucociliary function

✓ **Atopic dermatitis-like rash**
- Result of increased salt-loss through the skin

✓ **Seizures**
- Single episode in apirexy and six simple febrile seizures
- Normal EEG and Brain MRI

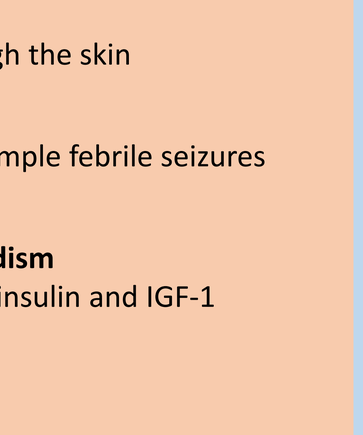
✓ **Transient subclinical hypothyroidism**
- Normal ACTH, cortisol, C-peptide, insulin and IGF-1
- Normal ACTH stimulation-test

✓ **Mild development delay**

✓ **Failure to thrive**

Medication by nasogastric tube until 2-years
✓ **Hydrochlorothiazide** from 1.5 to 4-years
✓ **Fludrocortisone** reduced from 1.5 to 3-years
✓ **Cation-exchange resin** reduced until 3.5-years
✓ **Oral 20% saline** ranged from 28 to 55mEq/kg/day

Currently with 5-years-old
✓ Failure to thrive (height -2.61SDS, weight -3.53SDS)
✓ Normal development
✓ Keeps only oral 20% saline supplement 43mEq/kg/day
✓ Symptoms became less severe and less frequent with increasing age



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Conclusions:

We report this severe PHA-1 case with poor initial prognosis but with favorable evolution.
Management of PHA-1 is challenging since there are no evidence-based recommendations.

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