New mutation causing systemic Pseudohypoaldosteronism

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Pseudohypoaldosteronism (PHA) is a rare heterogeneous syndrome of mineralocorticoid resistance.

**PHA type 1**
- neonatal salt loss
- failure to thrive
- dehydration
- circulatory shock

**Renal form**
- autosomal dominant
- due to mutations in mineralocorticoid receptor coding gene NR3C2

**Systemic form**
- autosomal recessive
- due to mutations in 1 of 3 subunit genes of the epithelial sodium channel (ENaC)

**SCNN1A gene**
chromosome 12p13.31
(alpha subunit)

**SCNN1B gene**
chromosome 16p12.1
(beta subunit)

**SCNN1G gene**
chromosome 16p12.1
(gamma subunit)

We report the case of a **12-months-old girl** with systemic form of PHA1, presented in the neonatal period with:
- dehydration
- weight loss
- feeding difficulties
- hyperkalemia (9.43mEq/L)
- hyponatremia (127 mEq/L)
- metabolic acidosis
- elevated plasma aldosterone levels (>22000 pg/mL).

Clinical conditions improved after **elevated sodium chloride and sodium bicarbonate supplementation** (total amount of sodium: 1-1.5 g/kg/die), administration of **ion exchange resins** and nutrition with milk formula low in protein and potassium.

**Percutaneous gastrostomy** was placed for nocturnal supplementation with sodium.

Nevertheless, frequent **life-threatening salt-losing crises** occurred, requiring recovery in Paediatric Intensive Care Unit and administration of higher doses of electrolytes and fluids intravenously. To ensure the prompt management of these episodes a **port-a-cath** was placed into internal jugular vein.

She also presented an **abnormal sweat test** with lung spiral TC showing **areas of altered ventilation** secondary to thick secretion (fig. 1). This condition (cystic fibrosis-like) required prophylactic antibiotic therapy and respiratory physiotherapy.

**Fig. 1 – Lung spiral TC, performed when the patient was 5 month-old**

So far, despite all these findings, the infant is **asymptomatic for lung disease**; she presents normal auxologic parameters and **neuro-psychomotor development**.

Genetic analysis showed a **compound heterozygosity in intron 8 of the SCNN1G gene**:
- c.1294+5G>A, inherited from the father
- c.1295-10T>A, transmitted by the mother.

Bioinformatics analysis shows that the **first variation abolishes the 5’ splice site** and is probably pathogenic; the **second variation is predicted to abolish the 3’ splice site** and to introduce a cryptic splice site of unknown significance.