



Isolated aldosterone deficiency due to an aldosterone synthase mutation: Report of the first Lebanese case

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INTRODUCTION

Isolated hypoaldosteronism is a rare cause of salt wasting in infancy caused by the loss of activity of aldosterone synthase, which is encoded by the CYP11B2 gene. This condition may be life-threatening, especially in newborns.

We are reporting the case of a newborn male born to consanguineous parents, who presented at the age of 1 month with severe dehydration, vomiting, and hypotonia.

CASE REPORT

The patient, a 1 month old male, was first seen at the clinic with symptoms of severe dehydration, vomiting and hypotonia. He was born full-term to consanguineous Lebanese parents, following an uneventful pregnancy and normal delivery. At birth, his weight was 3700 g, his length 52 cm, and his head circumference 36 cm; all measurement at the 50th percentile.

Upon admission to the emergency department, the patient was severely dehydrated with tachycardia to 170 beats/min, a normal blood pressure of 92/58 mmHg, abnormally prolonged capillary refill time, mottled extremities, and marked hypotonia. He demonstrated severe weight loss, presenting with a weight of only 3 kg (below fifth percentile). His genital exam was normal and he did not present with skin hyperpigmentation.

The patient received fluid replacement and was immediately admitted to the NICU. Initial blood investigations (Table 1) showed severe hyponatremia (Na 118mmol/l), hyperkalemia (7mmol/l) and metabolic acidosis (CO₂ 16 mmol/l). The patient's negative CRP and normal CBC ruled out an infectious cause of his presentation. The preliminary diagnosis was congenital adrenal hyperplasia, and the patient was treated with fluids and sodium without potassium. He was also started on a high dose of hydrocortisone and fludrocortisone.

Subsequent hormonal assessment showed a **very high level of renin (17260 mU/l)** and abnormally normal aldosterone level (Aldosterone 21 ng/l) with normal corticotrope axis (cortisol 169 nmol/l, ACTH 4.48 pg/ml) and normal androgen secretion (17OHP 2.7 ng/ml, delta4 androstenedione 0.5 ng/ml, total testosterone 2.8 ng/ml). These findings are summarized in Table 1.

	On the Admission	Normal Range
Blood Tests		
17 OHP	2.7 ng/ml	0-2.7 ng/ml
Cortisol	59 / 169 nmol/l	50 - 400 nmol/l
Renin	17260 mU/l	35 - 246 mU/l
Aldosterone	21 ng/l	20-900 ng/l
ACTH	4.48 pg/ml	10-60 pg/ml
Testosterone (total)	2.8 ng/ml	0.75-4 ng/ml
Delta 4 Androstenedione	0.5 ng/ml	<1.5 ng/ml

RESULTS

A genetic analysis of *CYP11B* revealed a homozygous likely pathogenic mutation in chromosome 8 ((grch 37) g.143996461C>A or NM_000498.3: c.595+1 G>T intron 3, highly conserved donor splice site of exon 3).

The *CYP11B2* variant c.595+1 G>T is predicted to disrupt the highly conserved donor splice site of exon 3. This mutation in the sequence should induce a truncated protein and an inactive form of aldosterone synthase. It is classified as likely pathogenic (class II) according to the recommendation of the American College of Medical Genetics.

CONCLUSION

Severe salt-wasting with hyponatremia is a known presentation of mineralocorticoid deficiency or complete adrenal insufficiency (both glucocorticoid and mineralocorticoid deficiency).

Affected infants by aldosterone synthase deficiency may develop symptoms of mineralocorticoid deficiency, including clinical presentation with frequent vomiting, a variable degree of hyponatremia, hyperkalemia, and metabolic acidosis combined with a severe failure to thrive.

In our patient, isolated aldosterone deficiency resulted from loss of activity of aldosterone synthase due to a homozygous pathogenic variant in the *CYP11B2* gene. In the neonatal period, the clinical presentation of hypoaldosteronism can be dramatic, with significant hemodynamic instability and life-threatening episodes of seizure and coma. Studies have shown that defects in the mineralocorticoid pathway present with more severe cases of hyponatremia than other etiologies. Typically, we observe a gradual improvement in the clinical presentation with age, and adults are frequently asymptomatic despite no mineralocorticoid therapy. This may be attributed to a steady decline in the patient's dependence on aldosterone for normal ionic imbalance over time, possibly due to extra-adrenal compensatory mechanisms and alternative ACTH-dependent pathway activation for mineralocorticoid biosynthesis.

CONTACT INFORMATION

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