Typical phenotype of isolated aldosterone synthetase (AS) deficiency in two infants with heterozygous AS gene mutation: Dilemma for diagnosis

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Introduction

Isolated hypoaldestronism is a rare endocrinopathy in a limited number of patients who secrete normal level of cortisol, due to mutation in CYP11B2. In some cases clinical diagnosis can be late and genetic analysis showed difficulties. There are some cases with clinically and biochemically appropriate AS deficiency but determiantion of mutation could bedifficult as our patients.

Case-I

- A 7 month-old girl infant ➡ womiting, failure to thrive and severe hyponatremia,
- Unexplained **neutropenia**
- Birth weight: 2440 gr.
- There was no consanguinity between parents.
- **Physical examination;**
  - Dehydration
  - She had atopic eczema.
  - Weihgt: 5100 gr (<-2SDS)
  - Height: 58,4 cm (<-2SDS)
  - Head circumtance: 43 cm (0 SDS).
- **laboratory evaluation;**
  - Na: 122 mmol/L (136-146)
  - Urine Na: 64mmol/L (<20)
  - Potassium: 5,9 mmol/L (3.8-5.5)
  - Ca: 11,7 ng/dl (9-11)
  - Plasma renin activity (PRA): 80,5 ng/ml/hours (0,48-4,88)
  - Aldosterone: 13,3 pg/ml(5,38-38)
- NaCl and fludrocortisone was initiated. LCMS profile was studied (Table 1).
- A heterozygous change in the CYP11B2 (c.554 C> T (p.T185I)) was detected. Advanced genetic analyses has not been completed.

Case-II

- A 2 month-old male infant ➡ severe hyponatremia with suspected diagnosis of congenital adrenal hyperplasia.
- Birth weight of 2700 gr.
- Parents were first degree cousin.
- **Physical examination**
  - Dehydration
  - Weihgt: 3190 gr (<-2SDS)
  - Height: 52 cm (<-2SDS)
  - Head circumtance 35.5 cm was (<-2SDS)
  - Severe eczema, protein-losing diarrhea, dissemine squamatos lession
  - Eosinophilia
- **laboratory evaluation:**
  - Na: 124 mmol/l (136-146)
  - Urine Na: 34 mmol/L(<20)
  - K: 6 mmol/L (3.8-5.5)
  - PRA: 100ng/ml/h (0,48-4,88)
  - Aldosterone: 5.4 pg/ml(5,38-38)

LCMS profile was studied (Table 2).

- A heterozygous change was detected in the CYP11B2 gene c.763 G> T (p.Glu255Ter)
- Advanced genetic analyses (Next Generation Array) determined a homozygous change on CYP11B2 gene

Table 1: LCMS Profile of case I

Aldosterone	0,326 ng/ml
Cortizol	82,806 ng/ml
Corticosterone	20,013 ng/ml
11deoxycortisole	2,985 ng/ml
11deoxycoticosterone	0,822 ng/ml
17 OH-pregnenolone	1,224 ng/ml
17 OH-progesterone	0,326 ng/ml
21deoxycortisol	0,211 ng/ml
Androstenedione	0,08 ng/ml
Testesterone	0,02 ng/ml
DHEAS	10,427 ng/ml
Progesterone	0,18 ng/ml
Cortizone	24,21 ng/ml

Table 2: LCMS Profile of case II

Aldosterone	0,292 ng/ml
Cortizol	209,077 ng/ml
Corticosterone	72,996 ng/ml
11deoxycortisole	2,985 ng/ml
11deoxycoticosterone	1,327ng/ml
17 OH-pregnenolone	2,476 ng/ml
17 OH-progesterone	1,075 ng/ml
21deoxycortisol	0,034 ng/ml
Androstenedione	1,152 ng/ml
Testesterone	2,02ng/ml
DHEAS	42,72 ng/ml
Progesterone	1,157 ng/ml
Cortizone	11,179 ng/ml

Discussion

- Aldosterone synthetase deficiency is a rare cause of persistant hyponatremia.
- Clinical findings vary with age.
- The association of eosinophilia and neutropenia has not been reported so far. In order to explain for these rare associations and make clear the heterozygous mutation an advanced genetic analyses is needed in rare cases such ours.