P2-D2-280

A 26-day-old Japanese girl with aldosterone synthase deficiency caused by a novel mutation in the CYP11B2 gene

Satomi Koyama1), Tatsuo Tsuboi1), Naoto Shimura1), Akie Nakamura2), Toshihiro Tajima2), Osamu Arisaka1)

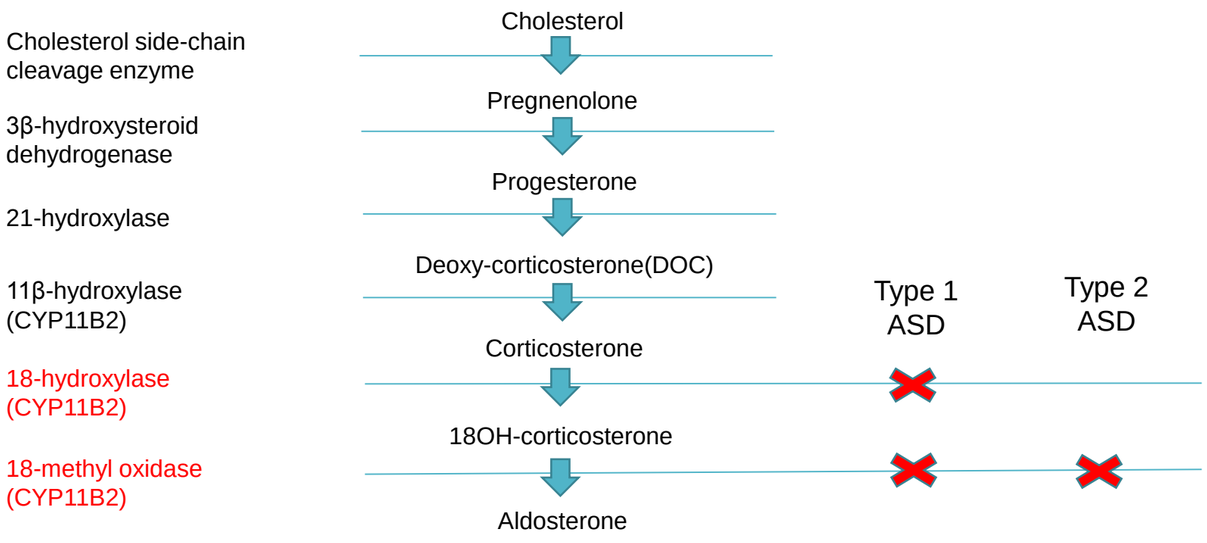
1)Department of Pediatrics, Dokkyo Medical University, 2)Department of Pediatrics, Hokkaido University

- We have no conflict of interest.

Background and Objective

1. Aldosterone synthase deficiency (ASD) is a rare autosomal recessive disease, presenting with salt wasting and failure to thrive in early infancy. It is caused by inactivating mutations of the CYP11B2 gene.
2. Our objective was to describe a Japanese patient with ASD, who presented with failure to thrive and salt wasting and investigate molecular analysis of CYP11B2 gene.

Aldosterone synthesis in the adrenal zona glomerulosa



Case：a 26-day-old Japanese girl

- Her length and weight at birth were 46.0cm and 2,820g with 39 weeks and 5 days gestation of unrelated parents.
- At 26 days of age she was admitted for poor weight gain, vomiting and dehydration. She drank formula milk only about 400ml/day and vomited once or twice a day.
- Her 17-OHP level at neonatal mass-screening was within normal limit.

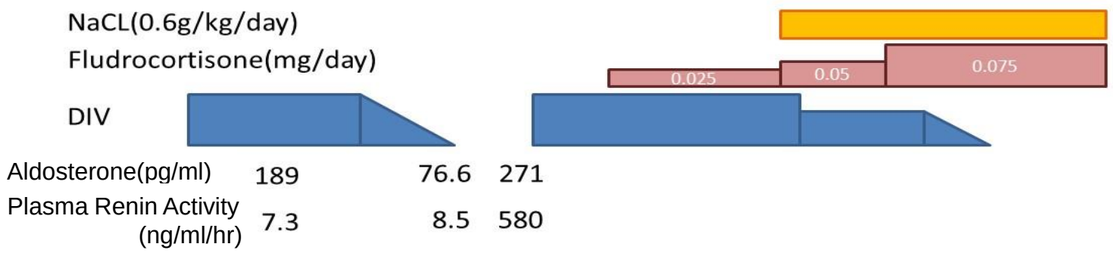
【Physical findings at admission】

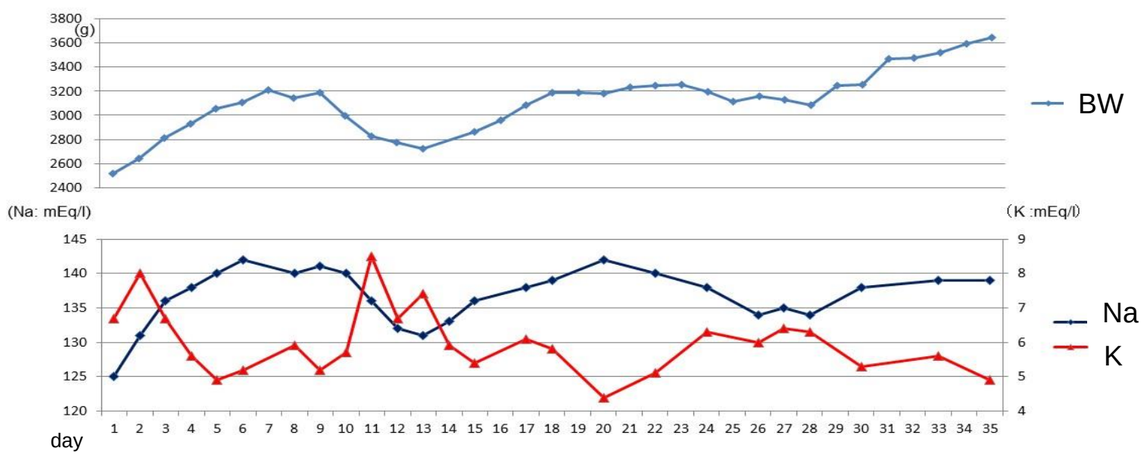
- Length 48.0cm (-1.9SD), Weight 2,515g (-2.4SD)
- Blood pressure 80/- mmHg
- normal female external genitalia

【Laboratory data】

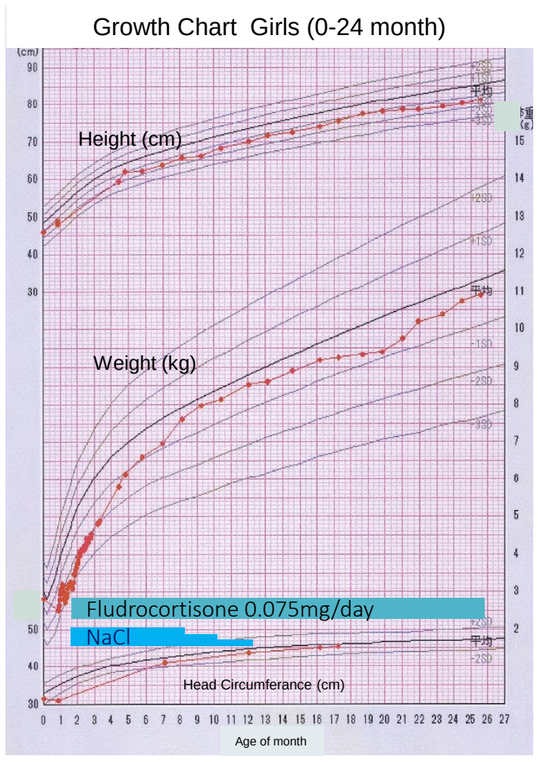
TP	7.6	g/dl	BUN	35	mg/dl	WBC	14.50	×10⁹/l
Alb	4.6	g/dl	Cre	0.51	mg/dl	Hb	16.7	g/dl
AST	34	U/l	Glu	70	mg/dl	Plt	51.1	×10⁴/μl
ALT	20	U/l	CRP	0.10	mg/dl以下			
LDH	239	U/l	Serum osmotic pressure			PH	7.306	
Na	125	mEq/l		266	mOsm/kg	PCO2	36.4	mmHg
K	6.7	mEq/l				PO2	36.7	mmHg
Cl	95	mEq/l	ACTH	35.7	pg/ml	BE	-7.6	mmol/l
			Cortisol	21.2	μg/dl	HCO3	17.6	mmol/l

Clinical course





Growth chart・development



Head control: 4 months
Sitting: 7 months
Walking: 10 months

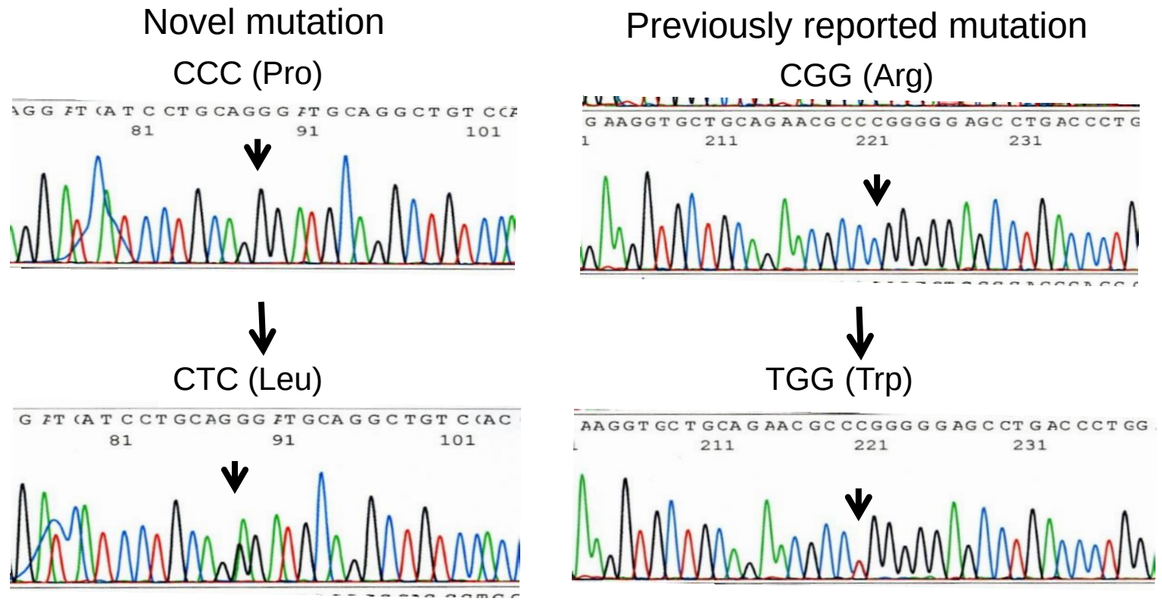
Speech:
1 word: 1 year
Sentence (2 words)
: 1 year and 10 months

Analysis of CYP11B2 gene

- CYP11B2 gene: 8q21-22, 9 exons
- Gene abnormality of CYP11B2 had been reported first in 1992 and over 30 mutations (nonsense, missense, frameshift) has been reported since then.

exon 2
P108L (c. 323 C >T)
Inherited from her father
Novel mutation

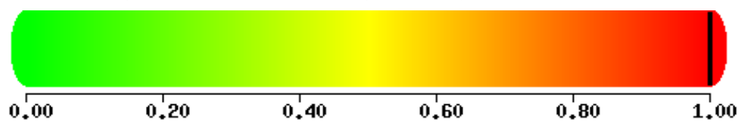
exon 3
R181W (c. 541 C >T)
Inherited from her mother
Previously reported mutation



【Analysis of protein function by Polyphen-2】

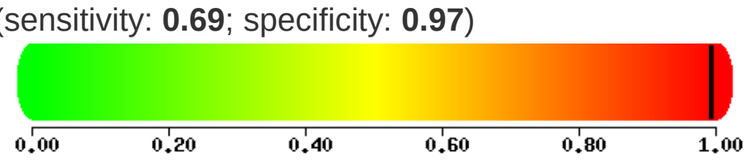
P108L : from CCC (Pro) to CTC (Leu)

This mutation is predicted to be **PROBABLY DAMAGING** with a score of **1.000** (sensitivity: **0.00**; specificity: **1.00**)



R181W : from CGG (Arg) to TGG (Trp)

This mutation is predicted to be **PROBABLY DAMAGING** with a score of **0.994** (sensitivity: **0.69**; specificity: **0.97**)



Conclusion

1. ASD is an important differential diagnosis of diseases associated with failure to thrive and salt wasting in early infants.
2. Urinary steroid analysis is one of the useful tools for the diagnosis of ASD.