Homozygous c.923 dupT combined with heterozygous c.334G>A CYP21A2 mutation- a case report from the Bulgarian CAH screening programme

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Perinatal history	**Screening results of 17-OHProgesterone (filter paper card)**		
First uneventful pregnancy, normal delivery, birth weight 3200 g, length 50 cm (50 percentile); intensive jaundice. Discharged on the 7th day, ***clinically healthy,*** weight 2970 g. Breastfed. From the 9th day on began to vomit a little after each feeding.	**Age (days)**	**17-OHP nmol/l**	**ISNS reference range**
	4	>285 (578.7)	20
	11	>285 (422)	20

Age: 11 days **Evaluation (University Pediatric Hospital - Sofia)**	**Laboratory results**							
Weight reduction- 200 g, jaundice, slightly decreased skin elasticity, hyperpigmented areoles and labia, clitoromegaly - virilisation grade 2 according to Prader.	HCT	Na mmol/l	K mmol/	pH	pCO2 mmHg	BE mmol/l	pO2 mmHg	HCO3
	64.3%	129	8.1 l	7.42	37	0	44	24
Clinical Diagnosis: CAH - salt-wasting form. Treatment start: iv. rehydration, Urbason 3x3 mg, Cortineff 2x 50 mcg/d								

Molecular genetic analysis	
Methods	MLPA; Gene sequencing
Results	Heterozygous missense c.334G>A, p.Asp112Asn; Homozygous frameshift c.923dupT, p.Leu308Phefs*6 (Fig. 1, 2, 3)

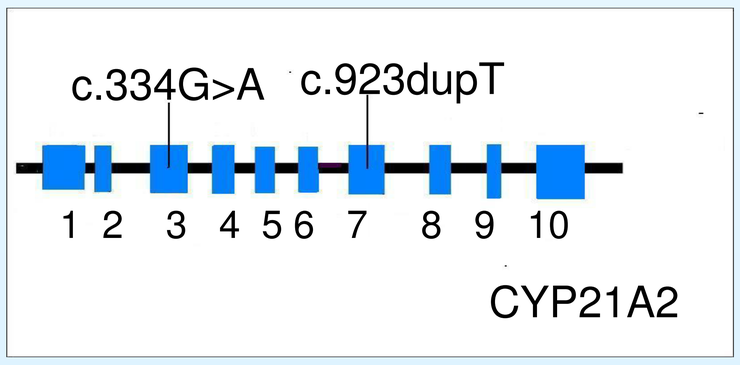

Fig. 1 Mutations of the CYP21A2 mutations in our patient

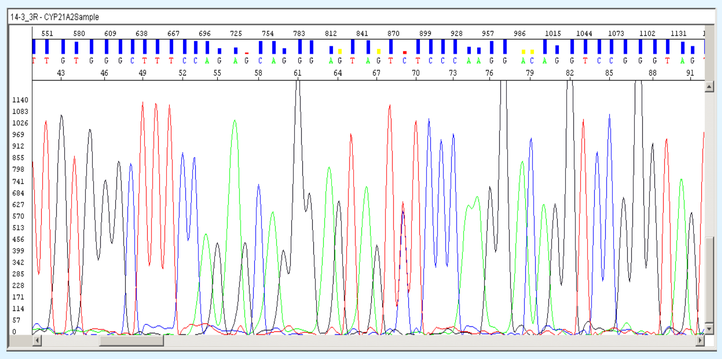

Fig. 2 Heterozygous missense c.334G>A, p.Asp112Asn;

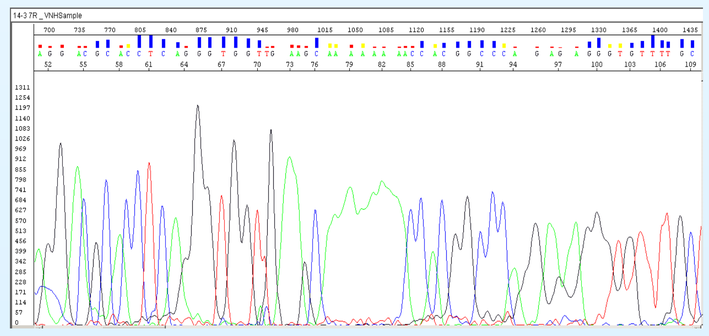

Fig. 3 Homozygous frameshift c.923dupT, p.Leu308Phefs*6

Monitoring of treatment based on: growth, bone age, blood pressure, profiles of the circadian variations of 17-OH-Progesteron, measured from FPC (Fig. 4, 5, 6, 7). She showed growth and development according to that of healthy children. Switch to hydrocortisone and gradual decrease of the daily requirements, followed by reduction of the mineralocorticoid dosages as well was performed early, without salt wasting episodes.

Treatment	
Hydro-cortisone	The dosage varies between 11 and 15 mg/m²
Cortineff tabl. 0.1 mg	Reduced from 0.1 to 0,75 mg (RR-110/60 mmHg, Na-128 mmol/l, K-5.8 mmol/l)
Salt	Irregular intake

Fig. 4 Supplementary treatment

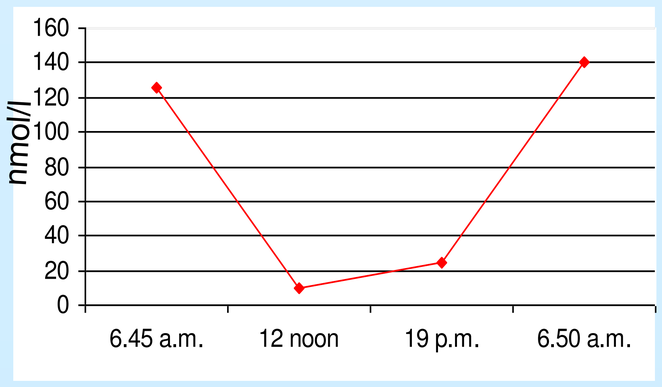

Fig. 5 Profile of 17-OH-Progesterone from FPC on Hydrocortisone 14 mg/m²

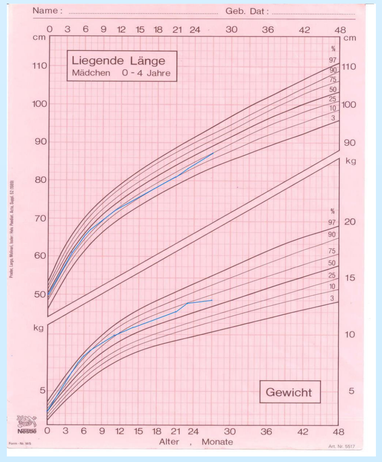

Fig.6 Growth curve

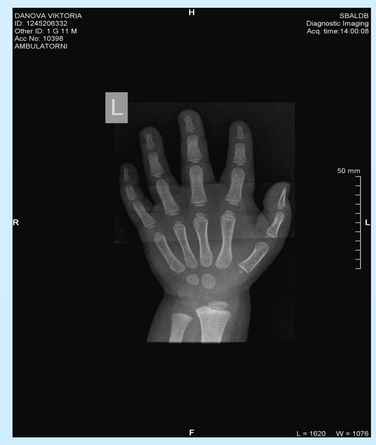

Fig. 7 Bone age at 2 years – corresponding to the chronological

Conclusions

The double mutated allele was inherited from the mother and it is most probably formed due to non-allelic homologous recombination between the CYP21A2 and the pseudo gene. The c.923 dupT mutation belongs to the group Null Cyp21A2 mutations, corresponding to salt-wasting forms of CAH. Future functional studies of Asp112Asn are needed.

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