# Homozygous c.2422delT hTPO mutation in three patients with congenital hypothyroidism followed over 20 years

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## INTRODUCTION

The homozygous deletion c. 2422delT in the carboxyl-terminal coding region of the hTPO gene results in a frameshift mutation and leads to an early stop codon in exon 14 of the gene (p.Cys808AlafsX24)[1,2]. Combination with double heterozygous DUOX2 mutations was also reported[3]. We present the data on the clinical course of CH in three patients with permanent congenital hypothyroidism (CH) harboring one and the same mutation.

## MATERIAL AND METHODS

After informed consent molecular analysis of the hTPO gene (Sanger sequencing) was performed in all three patients and the same homozygous previously described mutation c. 2422delT could be detected.

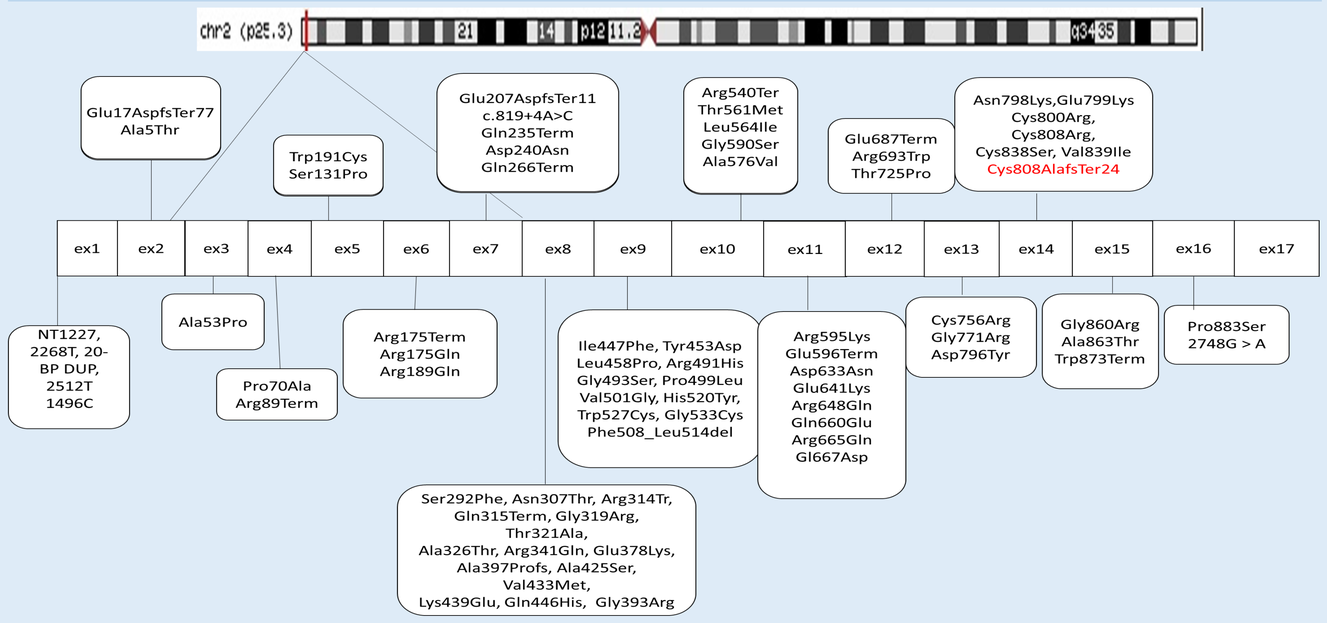
## Results

Two familial cases with rs76366277:c.2422delT p.(Cys808AlafsTer24), exon 14 were found by SANGER sequencing . The third patient was sporadic (Fig 1, 2)

### Case 1

Pat1 was followed 29 yrs; after an uneventful pregnancy (no consanguinity) and vaginal delivery she was diagnosed at 38d by clinical signs (severe prolonged jaundice, constipation, feeding difficulties, edema, delayed bone age, hoarse voice) before the screening introduction. She was started on L-thyroxin (25 mcg/d) on d36 (pretreatment TSH >43 mU/l, fT4 1.2 pmol/l), adjustments were performed, but TSH was often above 5 mU/l. The development milestones were normal, she had excellent marks during school attention, graduated and is working (HST169b).

Fig. 1 Schematic drawing of TPO gene mutations (in red exon 14)



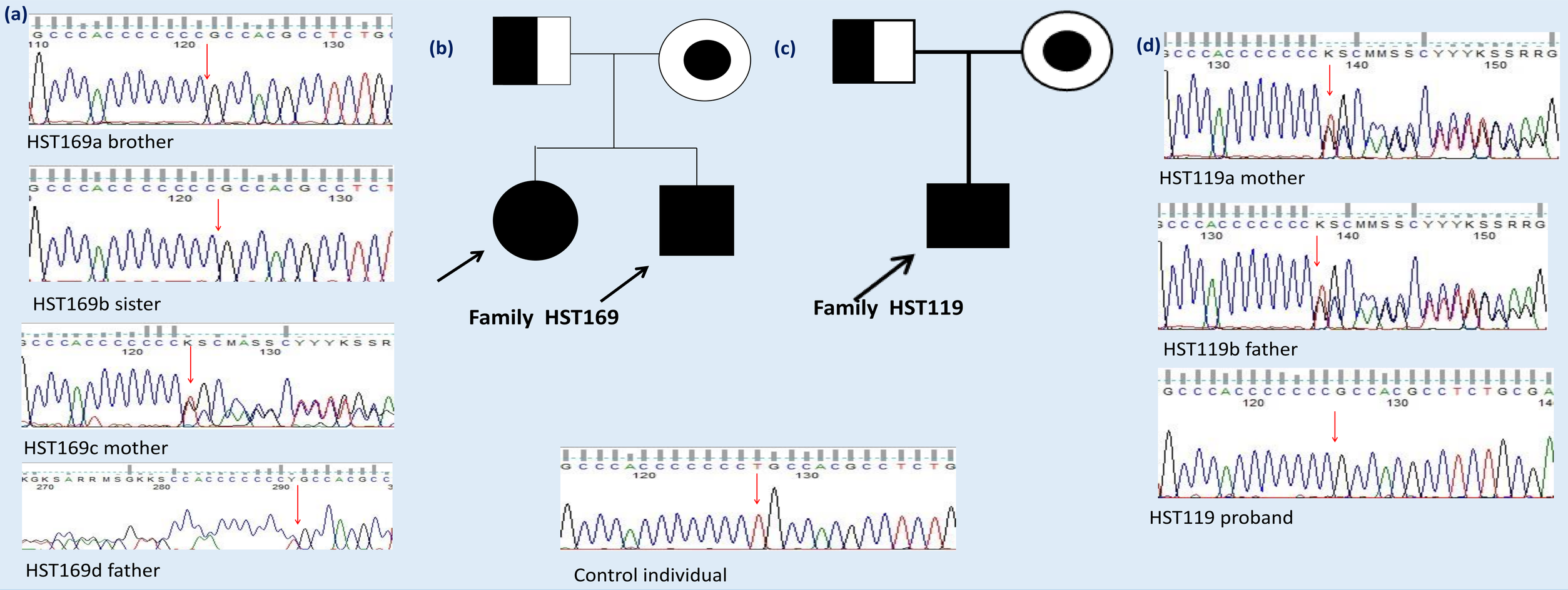

### Case 2

HST169b younger brother was diagnosed at d 10 (TSH 368 mU/l, fT4 0.7 pmol/l), L-T4 was given initially at a dosage of 25 mcg/d (10 days) and 50 mcg/d soon thereafter. Normal motoric and intellectual development were noticed, an eutopic thyroid as well (HST169a).

### Case 3

Pat.3 was picked up by TSH screening (NTSH 238 mU/l d3), the high CH suspicion was confirmed on d 22 (TSH>900 mU/l, T4 <20 nmol/l, Tg 490 ng/ml) and 50 mcg/d L-T4 were given. His thyroid volume increases with elevation of the TSH (several times) and multinodular goiter developed bilaterally, therefore the thyroid was extirpated at 19 yrs (HST119).

Fig. 2. Family trees b, c, and electrofotrgrams (a, d) of families HST 169 and HST 119




## CONCLUSIONS

Follow up data combined with molecular genetics could help in personalizing the treatment (no re evaluation needed) and facilitate the possibilities for genetic consultation. Regular thyroid US (start at diagnosis), in CH patients with eutopic glands combined with frequent hormonal controls as well are highly advisable.

**References**

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