Unusual Pattern of Thyroid Function Tests with DUOX2 mutation and Iodine deficiency

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Introduction

Dual oxidase 2 (DUOX2), a reduced NAD phosphate: O2 oxidoreductase flavoprotein, is a component of the thyrocyte which produce H2O2 required for thyroid hormone synthesis [1].DUOX2 mutations have been reported in association with a wide spectrum of congenital hypothyroid phenotypes, ranging from very mild to severe. [2,3]. In this case we report the a case of DUOX2 mutation and implications of environmental factors like iodine deficiency.

Case

History:

We report a case of 30 years old female presented with polyhydromnios in fourth pregnancy. She was feeling tired for several years and had a long standing goitre . Her menstrual cycle was regular and had normal previous three pregnancies with normal babies.
She was vegetarian and has been vegan for 13 years.
She delivered baby with a huge neonatal goitre and severe hypothyroidism of S.TSH >100 miu/L.

Investigations:

Mother's thyroid function test (TFTs) showed an unusual pattern of TSH being marginally elevated, 6.4 miu/L (0.35-4.5) with Free T3 in upper normal range, 6.8 pmol/L (range 3.9-6.8) and Low Free T4 4.8 pmol/L (10.5-26) Table1. Free T3/T4 ratio was elevated.
Similar pattern was seen when confirmed with another laboratory excluding assay interference. Random Cortisol was 579 nmol/L and being postpartum serum Prolactin was appropriately raised at 1268 mu/L.
24 hours urinary iodine measurement in mother showed profoundly low iodine level of 0.05 micromol (1-3micromol/L) suggesting severe iodine deficiency.
Gene sequencing showed a novel rare heterozygous DUOX2 missense mutation (c.3956C>G,pT1319R) in both mother and baby and the other 3 children showed wild-type for the variant.

Treatment:

She was commenced on iodine supplement (Sea Kelp Tablet) which improved Thyroid status (table 2).
The baby responded very well to Levothyroxine replacement which normalised his TFTs and resolved goitre.

Test	Result		Normal values
	On presentation	After Iodine replacement	
S.TSH	6.4 miu/L	0.3 miu/L	(0.35-4.5)
S.Free T4	4.8 pmol/L	12.2 pmol/L	(9-19)
S.Free T3	6.8 pmol/L	4.6 pmol/L	(3.9-6.8)
24 hours Urine Iodine	0.05 umol/L		(0.39-1.97)
TPO antibodies	Negative		

Table 1

Discussion and Conclusion

DUOX2 mutation being heterozygous is less likely to be pathogenic. However combined with environmental factor like maternal Iodine deficiency could explain overt dyshormogenesis in the baby and unusual thyroid function tests and longstanding goitre in the mother. This is further supported by the fact that three other siblings not carrying the mutation didn't develop hypothyroidism at the time of birth although they were exposed to presumably same maternal iodine level.

References

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