Resistance to thyroid hormone in a Southasian family

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Resistance to Thyroid Hormone (RTH) is a rare genetic disease due to thyroid hormone receptor defect and is usually inherited in an autosomal dominant fashion. We describe a case of RTH in a Southasian family of Bangladeshi extraction.

Presentation

A 32 year old female , normally fit and well, initially referred to ENT surgeon due to goitre. She was clinically euthyroid and not on any medications.

Investigations

Ultrasound thyroid: Multinodular goitre with benign features; THY2 on FNA
Thyroid function test:
TSH:1.35miu/l (normal range 0.4-4miu/l)
FT4: 29.2 pmol/l (12-22pmol/l)
FT3: T3 7.1 pmol/l (2.80 – 7 pmol/l)

Differential Diagnoses

1. TSHoma
2. RTH (resistance to thyroid hormone)
3. Assay interference

Further Investigations

Alpha subunit: <0.30 IU/L (0-1)
SHBG: 27nmol/l (20 – 130)
Anterior pituitary function: normal
Assay interference ruled out.

Family history

Her father and brother have similar thyroid function test results (normal TSH , raised FT4 and FT3).

Diagnosis

RTH confirmed by genetic analysis: heterozygous for thyroid hormone receptor beta mutation due to single base change at c.1378G>A in exon 10 of TRbeta gene resulting in abnormal TRbeta protein (p.Glu460Lys).

Management

1. Conservative management of goitre
2. Euthyroid clinically – no treatment
3. Further family screening and genetic testing underway

Parameter	RTH	TSHoma
Family history	Positive	Negative
SHBG and subunit	Normal	Increased
T3 suppression test	TSH suppressed	TSH not suppressed
TRH test	positive	Negative
Pituitary MRI	Negative	Positive(tumour)
Molecular study	TR mutation	No Mutation

Conclusion

1. RTH has been described in multiple ethnicities.
2. It is rare but important diagnosis to make
3. Wrong diagnosis can have significant repercussions.
4. TSHoma is an important differential diagnosis(see table above).
5. Family screening and genetic testing is vital.
6. It has implications for inheritance.
7. Management of RTH in pregnancy can be challenging.

References:

1. Refetoff S, Weiss RE, Usala SJ. The syndromes of resistance to thyroid hormone. Endocr Rev 1993; 14:348.
2. Sakurai A, Takeda K, Ain K, et al. Generalized resistance to thyroid hormone associated with a mutation in the ligand-binding domain of the human thyroid hormone receptor beta. Proc Natl Acad Sci U S A 1989; 86:8977.
3. Lafranchi SH, Snyder DB, Sesser DE, et al. Follow-up of newborns with elevated screening T4 concentrations. J Pediatr 2003; 143:296.

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