THE CHALLENGES TO DIAGNOSE AND DIFFERENTIATE TSHoma FROM THYROID HORMONE RESISTANCE (THR): a case report

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BACKGROUND:

TSHoma and Thyroid Hormone Resistance (THR) can both present with symptoms and signs of hyperthyroidism. Both conditions are rare and differentiating the two can be difficult. Correct diagnosis is crucial in ensuring appropriate treatment. The objectives of this presentation are to share our experience in diagnosing a TSHoma, to appreciate the complexity and requirement of specialised investigations to make a diagnosis, and to learn about the treatment for TSHoma.

THE CASE:

A 39 year old lady who was referred to the endocrine clinic in 2006 with excessive lethargy, recurrent palpitation and abnormal TFT (fT4: 41.6pmol/l, TSH 4.6 mU/l). The TFT's were noted to have been abnormal since 2000. She was diagnosed to have THR initially (despite no abnormalities of thyroid hormone receptor β-gene). She was also diagnosed to have Diabetes Insipidus in 2007. She suffers from subfertility, having failed several IVF treatments in the past.

EXPLORING AN ALTERNATIVE DIAGNOSIS: TSHoma

In 2013, she presented with worsening symptoms of polydipsia, polyuria, lethargy, abnormal TFT's and raised serum prolactin.

REPEAT INVESTIGATIONS	
Thyroid hormone receptor β-gene	no abnormalities
Serum prolactin	893 mU/l (100-500)
Serum osmolality	300mmol/kg (275-295)
fT4	37.2 pmol/l (11-25)
fT3	10.9 pmol/l (3.1-6.8)
TSH	2.04 mU/l (0.27-2.20)
SHBG	147 nmol/l (25-122)
A.M. Cortisol	225 nmol/l (171-536)
α-subunit level	< 0.3 IU/l (normal <1 IU/l)
MRI pituitary with contrast	2 small focal enhancing lesions within the pituitary measuring less than 3 mm in diameter, consistent with microadenoma

TRH stimulation test (Protirelin 200mcg IV bolus)

	Prolactin mU/l	TSH mU/l
O min	433	1.59
20 mins	678	3.05
60 mins	482	2.54

*Interpretation: peak rise at 20 mins, If TSH < 3.5 : likely TSHoma. If TSH > 4.5: likely THR

Octreotide suppression test (100mcg Octreotide s/c)

	fT3 pmol/l	fT4 pmol/l	TSH mU/l
0 min	10.6	36.2	1.89
60 mins	10.6	37.6	1.55
120 mins	10.4	37.3	1.23
180 mins	9.9	36.2	1.05
240 mins	9.7	35.0	0.98
300 mins	10.0	34.2	0.93

FURTHER INVESTIGATIONS:

-Methionine-PET scan: 'Hot spots in the pituitary' (Protocol as (2))

-Trials of Sandostatin LAR 20mg IM (see box below)

Administration dates	fT3 pmol/l	fT4 pmol/l	TSH mU/l
21/4/15	11.9	42.4	2.03
18/5/15	4.5	17.0	0.03
15/6/15	4.8	16.7	0.01
15/7/15	5.1	18.3	0.02
12/8/15	8.4	22.7	0.01
8/9/15	6.2	21.4	0.02

Transphenoidal pituitary adenectomy

- Performed in University Hospital of Wales in October 2015
- Tissue immunohistochemistry: possible minor focal tumoural reactivity for TSH
- Post-op issues: Hypoadrenalism (on Hydrocortisone 10mg BD), Persistent DI (on DDAVP)
- Most recent TFT (Oct 2016): fT3 2.7, fT4 10.5, TSH 0.7. Prolactin: 16

DISCUSSION / CONCLUSION:

TSHoma is rare, reported to be 1% of all pituitary adenomas. Our patient underwent series of tests, and we explain why she was subsequently diagnosed with TSHoma, in a table below:

Investigations	Explanation /Caveat
High fT3 and fT4 with unsuppressed TSH	Can also be biochemical features of THR, but presence of hyperthyroid and neurological symptoms (SOL) are suggestive of TSHoma
High SHBG	Higher level observed in TSHoma (1) (can also be high in liver disease and oral contraceptive pills)
High Prolactin/presence of DI	Suggestive of TSHoma
Thyroid hormone receptor β-gene mutations NOT detected	Positive mutation tend to occur in THR (but up to 15% THR cases have no mutation identified)
Blunted TSH response to TRH	Blunted response is observed in 90% of TSHoma (1) as opposed to peak response in THR
Abnormal MRI pituitary	Presence of pituitary adenoma is suggestive of TSHoma (1)
Reduction of TSH and fT4 level with octreotide supporession test	Observed in both TSHoma and THR (3)
Normalisation of fT3 and fT4 following chronic administration of Sandostatin LAR	Normalisation tend to occur in TSHoma, but not in THR (3)
Methionine PET scan	'Hot spots' in the pituitary, that tend to disappear following a chronic administration of somatostatin analogue (2)

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