J Triay, N Thorogood, D Wynick, KJ Bradley.
Department of Endocrinology, Bristol Royal Infirmary

TSH-Secreting Pituitary Adenoma Identified in Pregnancy: Management of an Unusual Case

Case History:

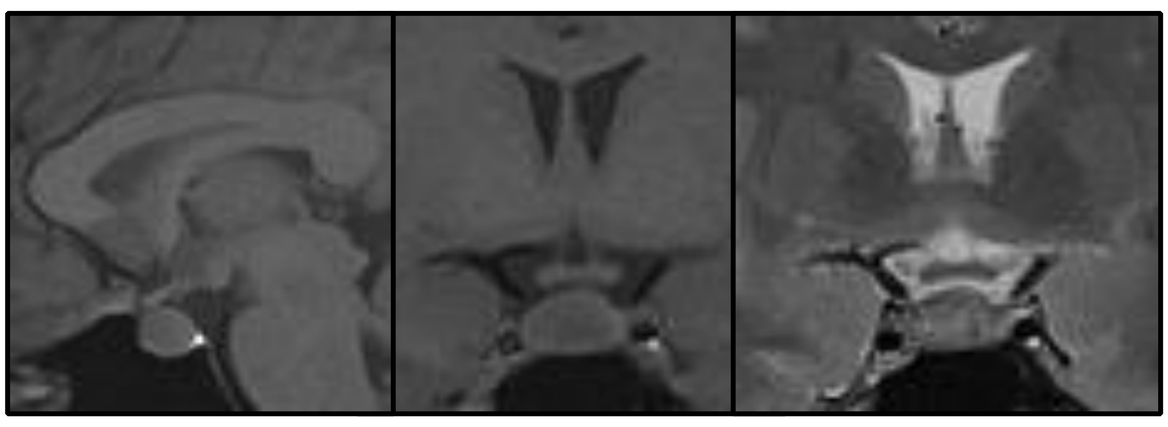
35 year old Columbian lady. Routine blood tests by GP due to impaired fertility showed hyperthyroidism with high TSH.

- At time of clinic appointment, 7/40 after natural conception
- Migrainous headaches in early pregnancy, and vague history of palpitations, but no clear symptoms of hyperthyroidism
- No personal/family Hx of thyroid/pituitary problems
- Ex: completely unremarkable
- 2 days before Christmas

Pre-conception:
free T4 **30.8 p**mol/L
free T3 **7.5** pmol/L
TSH **5.1** mIU/L

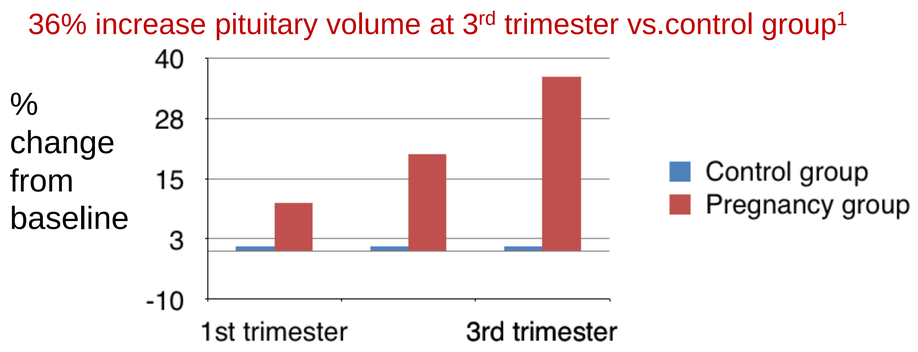
MRI Pituitary: Enlarged asymmetrical pituitary

(Performed on Christmas Eve, at 7/40 gestation)



MRI Limitations: Statistically significant increase in pituitary dimensions at all stages of pregnancy (p <0.001)

36% increase pituitary volume at 3rd trimester vs.control group[1]



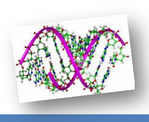
Gonzalez JG, et al. Pituitary gland growth during normal pregnancy: an in vivo study using magnetic resonance imaging. Am J Med. 1988 Aug;85(2):217-20.

Biochemistry:

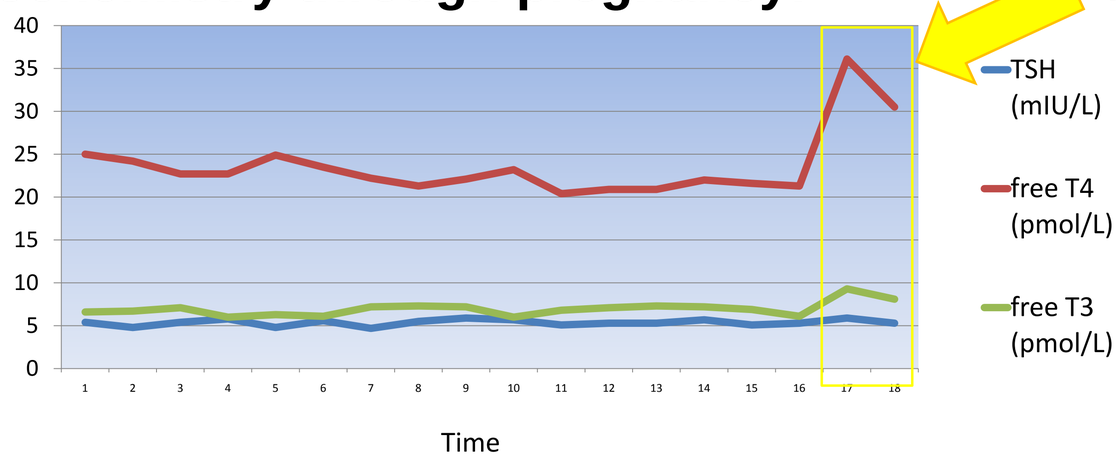
	2/11/11	23/12/2011	Ref. Lab 21/12/2011	3/01/2012
TSH	**5.1**	**5.7**	4.84 (0.35-5)	5.3
T4	**30.6**	**25.0**	**23.4 (9-19.1)**	**24.2**
T3	**7.5**	**6.6**	**6.4 (2.6-5.7)**	**6.7**
TRAb		<1		
Anti-TPO		**967**		
Heterophile Ab		Negative		

Results of investigations difficult to interpret due to pregnancy:

- Prolactin 722 mIU/L (normal range outside pregnancy<700)
- SHBG 209 nmol/L (normal range outside pregnancy 20-130)
- LH and FSH fully suppressed
- Alpha-subunit: >24 ug/L (normal range outside pregnancy<1)
- **Thryoid Hormone Resistance Syndrome: Negative** (but 15% have no detectable mutations)



Biochemistry through pregnancy:



Post partum results

Thyroid function monitored 2 weekly through pregnancy.

Biochemistry throughout pregnancy remained stable.

A healthy baby boy was delivered after a normal vaginal delivery. His thyroid function tests are all within the normal range

Our patient remained asymptomatic despite an elevation in her free thyroid hormones post partum

Past experience of management:

TSH secreting Pituitary Adenoma in Pregnancy

3 case reports (all diagnosed preconception). In all cases, pituitary enlargement associated with visual symptoms (3rd trimester). Different management pathways in each report:

1. Continuous subcutaneous octreotide 300mcg/day[2]
2. Intermittent subcutaneous octreotide[3]
3. PTU, bromocriptine and decompressive surgery[4]

Thyroid Hormone Resistance and Pregnancy

- Ideal management pathway remains unclear[1]
- Patients typically asymptomatic unless selective pituitary thyroid hormone resistance present
- Challenges surrounding how to manage the metabolic status of the fetus when it is at odds with maternal metabolic environment.
- Issues regarding frequency of fetal monitoring and intrauterine diagnosis.

Management of TSH Producing Pituitary Tumours Outside of Pregnancy[5]:

1. Anti-thyroid medications not considered effective:
unless concurrent autoimmune disease

2. Somatostatin analogues: most commonly used.
(cure possibly influenced by somatostatin receptor subtype[6])

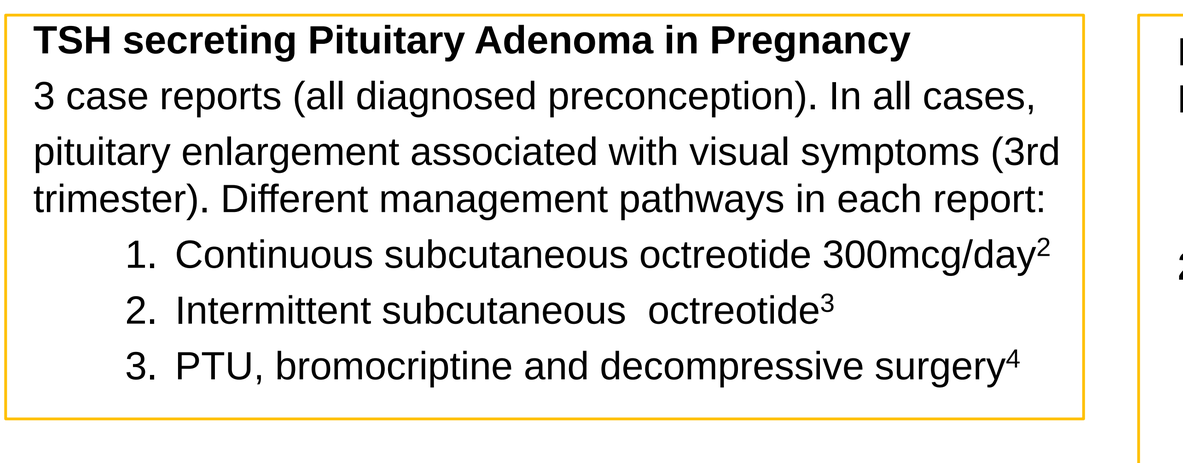
Biochemical cure (T4/T3 normalisation) in ~75%
TSH improvement in ~90%
Tumour shrinkage in ~33%

3. Dopamine agonists
less efficacious UNLESS mixed TSH/Prolactin secretion

4. Transphenoidal surgery:
Further surgery required in up to 20%

5. Alternative management:
Thyroid ablation (surgery/radioactive iodine; n=2),
no changes in pituitary size over 8 and 12 years of follow up[7]

MRI Pituitary Post Partum: Unchanged



Dimensions of the pituitary adenoma post partum are unchanged from the original MRI performed during the first trimester

Results additional investigations post-partum:

- Prolactin 545 mIU/L (normal)
- SHBG 120 nmol/L (normal)
- LH 8.1 and FSH 8.8 (normal)
- Alpha-subunit: 4.95 ug/L (elevated)

Ongoing Management Plan:

Our patient would like to have further pregnancies.

She is scheduled to have transphenoidal pituitary surgery for removal of the adenoma in March 2013.

References:
1. Gonzalez JG, et al. Pituitary gland growth during normal pregnancy: an in vivo study using magnetic resonance imaging. Am J Med. 1988 Aug;85(2):217-20.
2. Chaiamnuay S, Moster M, Katz MR, et al. Successful management of a pregnant woman with a TSH secreting pituitary adenoma with surgical and medical therapy.Pituitary. 2003 Sep;6(2):109-13.
3. Blackhurst G, Strachan MW, Collie D, et al. The treatment of a thyrotropin-secreting pituitary macroadenoma with octreotide in twin pregnancy. Clin Endocrinol (Oxf). 2002 Sep;57(3):401-4.
4. Caron P, Gerbeau C, Pradayrol L, et al. Successful pregnancy in an infertile woman with a thyrotropin-secreting macroadenoma treated with somatostatin analog (octreotide). JCEM. 1996 Mar;81(3):1164-8.
5. Socin HV, Chanson P, Delemer B, et al. The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. Eur J Endocrinol. 2003 Apr;148(4):433-42.
6. Yoshihara A, Isozaki O, Hizuka N, et al. Expression of type 5 somatostatin receptor in TSH-secreting pituitary adenomas: a possible marker for predicting long-term response to octreotide therapy. Endocr J. 2007 Feb;54(1):133-8.
7. Daousi C, Foy PM, Macfarlane IA. Ablative thyroid treatment for thyrotoxicosis due to thyrotropin-producing pituitary tumours. BMJ Case Rep. 2009;2009. pii: bcr07.2008.0541.