SOME COMPLEX (MAYBE NOT SO COMPLEX) THYROID CASES

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CASE ONE – MR SA, 33 INDIAN

Complex comorbidity:

- Asthma with mild airflow obstruction, gas trapping
- Mild OSA
- Dysfunctional breathing
- Lumbar spine stenosis
- Chronic tachycardia since 2017 (normal ECHO Dec 2017)
- GORD

❖ **Medications at initial clinic appt**

- Bisoprolol
- QVAR inhaler
- Symbicort 200/6 inhaler
- Ventolin inhaler

❖ Father has hypothyrodidism

❖ Thyroid US (May 19): solid small hypoechoic nodules, increased gland vascularity

TIMELINE – MR A

- ICU admission in Feb 2019 after respiratory arrest, short intubation & ventilation
- 7/2/19: T4 22, TSH 0.10 (new)
- 11/4/19: T4 29, TSH <0.01, T3 12
- Carbimazole 5mg BD started on 26/4/19
- 9/5/19: T4 39, T3 15 (Carbimazole increased to 10mg BD)
- 22/5/19: T4 35, T3 14.3 (Carbimazole increased to 15mg BD)
- Endocrine clinic on 28/5/19: Bisoprolol stop → Diltiazem CD 120mg daily started
- 28/5/19: T4 40, T3 15 (Carbimazole stayed at 15mg BD)
- 5/6/19: T4 29, T3 12 (Carbimazole 10mg BD continued), Diltiazem 180mg
- Positive TSH receptor antibody : **Graves' disease**

TIMELINE - GRAVES DISEASE

- Persistent tachycardia, palpitation, hand tremor persisted
- Weight stable, no dysthyroid eye disease

- 19/6/19: T4 37 (was 29), T3 10.3 (was 12) – (CBZ 15mg BD, Diltiazem ↑240mg)
- 3/7/19: T4 38, T3 11.7, GGT 160, ALP 168, ALT normal
- 18/7/19: T4 47, T3 16.6
- 31/7/19: T4 45, T3 19.5 (CBZ ↑20mg BD)
- 14/8/19: T4 53, T3 22.9, GGT 242, ALP 166

MR A'S PROBLEMS

- T4 and T3 continue to climb despite increment in carbimazole dose
- New liver derangement
- Persistent tachycardia despite diltiazem increased to 240mg (already seen Cardiologist, no heart issue)
- Compliant to treatment

ISSUES

- Severe Graves disease
- Persistent symptomatic tachycardia
- Asthma – beta blocker not advisable
- Risk of rate related cardiomyopathy

- What is next best management plan?

GRAVES' DISEASE - *MANAGEMENT*

- Thionamides = methimazole, carbimazole, prophythiouracil (PTU)
- Carbimazole preferred to PTU : can reverse the hyperthyroidism quicker, fewer side effects, less hepatotoxic
- Small goitre & mild hyperthyroidism (T4 1.0-1.5x ULN) 5-10mg daily
- Moderate to severe 10-40mg daily (divide into 2 doses if >20mg)
- Fewer patients need >40mg/day

SEVERE GRAVES' DISEASE

- Radioiodine – less expensive, lower complication rate
  - Non pregnant (except moderate to severe orbitopathy)
  - Usually needs pre treatment with thionamide (Except mild, well tolerated hyperthyroidism)

INFLUENCE OF RADIOIODINE ON TSH RECEPTOR ANTIBODY

- TRAb concentration initially rise, peaks at 3-5 months after treatment, then gradually decline
- This could explain transient initial worsening of orbitopathy
- TRAb may persist for many years after RAI

PRECIPITATING & PREDISPOSING FACTORS OF GRAVES' DISEASE

- Genetic susceptibility
- Infection (viral, hepatitis C when treated with interferon)
- Stress (negative life events)
- Gender – F:M 4:1
- Smoking
- Pregnancy – GD tends to improve during pregnancy (increase in regulatory T cells)
- Drugs (amiodarone, CT contrast, interferon alpha, alemtuzumab for MS)

MR A'S PROGRESS

- Received radioactive iodine on 4th September, with Prednisone cover for 15 days prior to his RAI
- On 4/9/19 (pre RAI) – T4 59 (↑), T3 23.2 (↑), GGT 159 (↓), ALP 144 (↓)
- Post RAI he was started on PTU 200mg BD (equivalent to CBZ 20mg BD)
- TFT 13/9/19: T4 35 (↓), T3 12.7 (↓), ALP 150 (slight ↑), GGT 155 (slight ↓)

LEARNING POINTS FROM CASE 1

- Management of severe Graves' disease could be complex, especially with other comorbidities
- Need to monitor LFT carefully
- Close TFT monitor is essential
- If not responding to carbimazole and continue to be symptomatic, refer for radioactive iodine

CASE 2: MRS N, 60 MAORI

- Referred to Thyroid clinic in May 2018
- Right sided neck lump x6 months
- Ex-smoker
- COPD
- Cervical CIN 3
- FH of T2D

- O/E: right sided thyroid nodule 2cm;
- Resting pulse 66 (regular)

- One sister had thyroid cancer with spine metastases, one sister had bowel ca, one sister had pancreatic cancer

MRS N

- Thyroid US 1 June 2018 – multinodular goitre, right central nodule 32 x 26 x 20mm with calcifications, TIRADS 4-5

- Thyroid nodule FNA 17July 2018 – Benign follicular nodule, Bethesda category 2

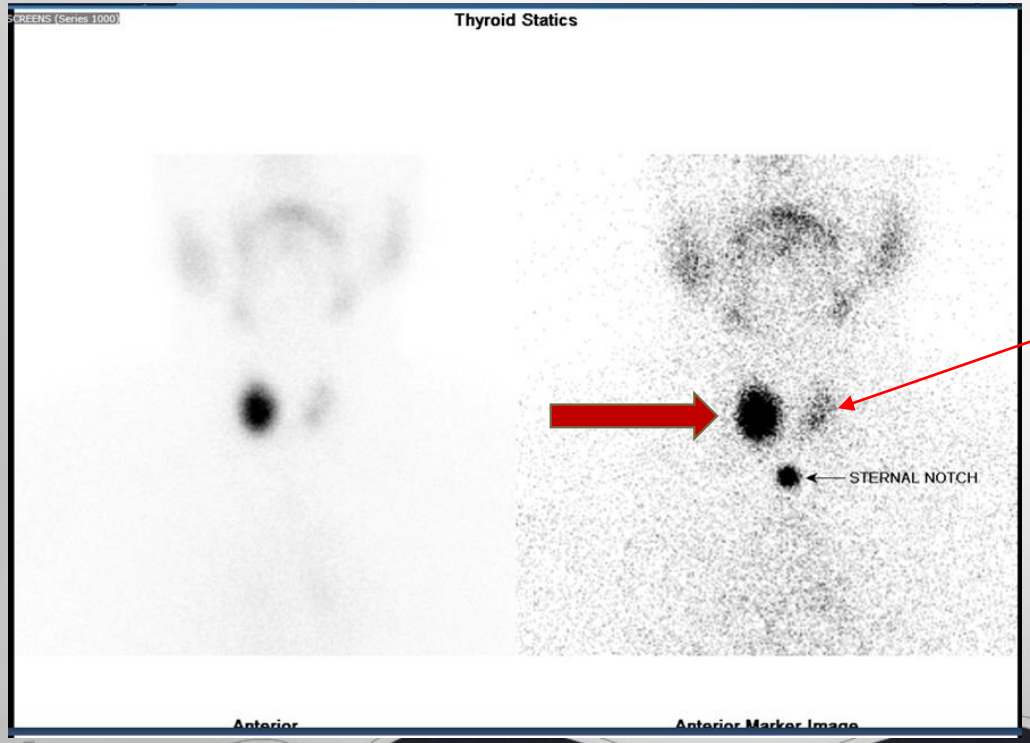
LONGSTANDING T3 TOXICOSIS

	Aug 19	June 19	Jan 19	Sep 18	May 18	Jan 18
T4	16	16	16	16	18	17
T3	**6.6**	**6.6**	6.2	6.0	**6.9**	**6.5**
TSH	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**

TRAb & TPO – negative

What's next?

THYROID SCINTIGRAPHY 28/8/19



Well defined hot area involving most of the <u>right</u> thyroid lobe with minimal tracer uptake in left thyroid. Overall uptake at 20 minutes upper normal at 1.8%

AUTONOMOUS TOXIC THYROID NODULE

- Second most common cause of hyperthyroidism (after Graves' disease)
- Prevalence increase with age, iodine deficiency
- Result of focal and/or diffuse hyperplasia of thyroid follicular cells whose functional capacity is independent of TSH regulation
- 20-80% of toxic adenoma and some nodules of MNG have somatic mutation of TSH receptor gene that confers autonomous hyperctivity

INDICATIONS FOR TREATMENT

- All overt hyperthyroidism (↑T4, ↑T3, ↓ TSH) due to toxic adenoma or toxic MNG require treatment

- If subclinical hyperthyroidism (as in Mrs N) – decision to treat is based upon the risk for developing complications (skeletal, cardiovascular) and degree of TSH suppression

THERAPEUTIC APPROACH

- Symptom control (Beta blocker – atenolol or propranolol)
- Decrease thyroid hormone synthesis
  - Surgery
  - Radioactive iodine
  - Thionamide (pretreatment before RAI or surgery, not long term)

- Toxic nodules and MNG rarely resolve spontaneously with prolonged thionamide therapy

THERAPEUTIC APPROACH

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RADIOACTIVE IODINE (RAI)

- Patients not candidate for surgery (obstructive goitre, goitre>80g, coexisting malignancy, needs rapid and definitive correction of hyperthyroidism)
- Widely used for therapy of toxic adenomas or MNGs
- Oral solution or 131-I capsule
- Induces extensive thyroid tissue damage and destruction of adenoma or autonomous foci within 6-18 weeks
- RAI reduces thyroid volume by ~35-45%

RADIOACTIVE IODINE (RAI)

- Thionamide should be discontinued three days before RAI is given
- TSH should be still below normal when RAI is given
- Thionamide can be restarted 3-7 days after RAI, and stopped on RAI is proven to be effective
- After RAI, patients require monitoring for hypothyroidism or persistent or recurrent hyperthyroidism – measure T4, T3, TSH 6-8 weeks after treatment, then at 4-8 weeks interval thereafter

LEARNING POINTS FROM CASE 2

- Toxic adenoma/nodules or autonomous toxic nodules are second most common cause of hyperthyroidism/subclinical hyperthyroidism
- Negative antibodies
- Older patients
- Radioactive iodine more effective than prolonged thionamide therapy
- Thyroid scintigraphy is the main imaging modality

CASE 3: MRS P (29YR INDIAN)

- Clinic 21 Dec 2018
- Incongruent TFT
- Marked raised (TSH), normal to raised T4
- Left thyroidectomy then completion total thyroidectomy Nov 2010 (large benign goitre)
- Current smoker
- Gained 20kg since thyroidectomy
- On Depo Provera so amenorrhoea

CONFUSING TFT

	13/12/18	16/11/18	29/9/18	May 18	Apr 18	2014-2017
T4 (10-20)	25	27	14	58	36	
TSH (0.3-4.0)	19	26	45	6.9	11	2.5-4.9
LT4 dose	100mcg/ day	stopped				400mcg/ day

BLOOD TEST 21/12/18

- T4 38, TSH **6.9** (both raised); TRAb negative
- Testosterone 0.6 nmol/L (normal)
- Prolactin **666** (<400)
- IGF-1 **750** ng/ml (94-324) {+5.7 SD}
- ACTH <1
- FSH 2, LH <1
- ***What's going on here?***

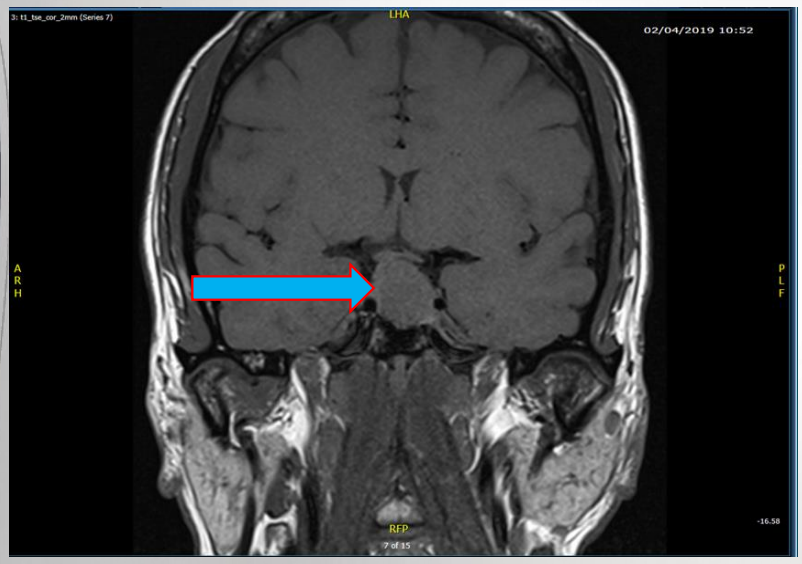
FOLLOW UP 29/3/19

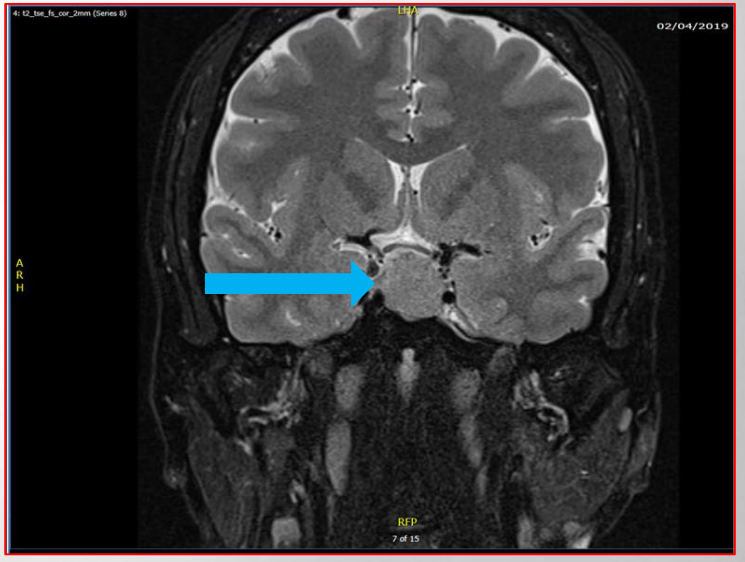
- Deepening of voice
- Facial acne flare up
- Some hair loss
- Ring gets tighter on finger
- Sore gum, ?widening of teeth
- Does not drive – missing road signs
- Headache

- BP 94/56, oily skin
- IGF-1 **692** (94-324; +5.7 SD); T4 27, TSH **27**

- MRI Pituitary not done yet!

MRI PITUITARY 2/4/19





DIAGNOSIS….

- Pituitary macroadenoma
- Functioning
- TSHoma
- Acromegaly

PLANS AFTER MRI PITUITARY

- Referred to Neurosurgeon at ADHB
- Perimetry referral for visual field testing
- Thyroxine dose reduced to 50mcg daily (T4-27)
- No medical treatment started for the acromegaly at that stage

PROGRESS

- Endonasal transphenoidal resection of pituitary adenoma on 15th July 2019 (7 months after diagnosis)
- Histology: adenoma producing both TSH and GH, positive for P1T1 and Somatostatin receptor
- Pre-op IGF-1 852, TSH 17.2, T4 30
- Day 2 post-op IGF-1 627, TSH 0.32, T4 19

POSTOPERATIVE COURSE

- **Rx**: Hydrocortisone 20mg mane, 10mg midi; thyroxine 50ug od
- 11/8/19: T4 15, TSH 1.2, Na 139, cortisol 376, IGF-1 482 (↑)
- Constant headache, no CSF leak
- BP 95/30, no postural drop; normal VF, some persistent acromegalic features
- To taper hydrocortisone - to drop 5mg each week
- Octreotide not to be started until a repeat IGF-1 in 3 months' time

ACROMEGALY

- Clinical syndrome results from GH excessive secretion
- Rare - annual incidence 6-8 per million people
- Mean age at diagnosis 40-45 years
- Most common cause is a somatotroph (GH-secreting) pituitary adenoma (1/3 of all hormone-secreting pit adenoma)
- Onset is insidious, diagnosis often delay (mean 12 years)

May 1998

June 1999

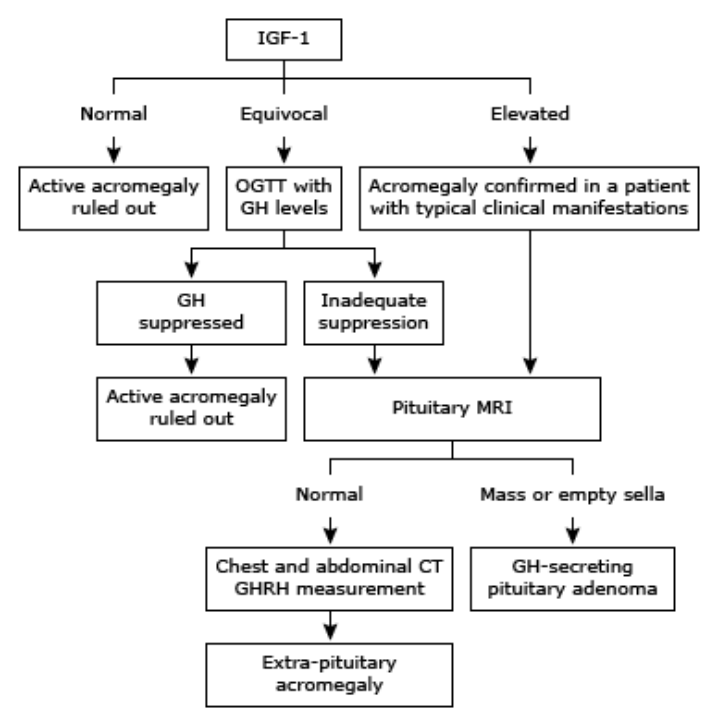
December 2001

June 2003

June 2005

June 2006
(15days before diagnosed)

ACROMEGALY DIAGNOSIS

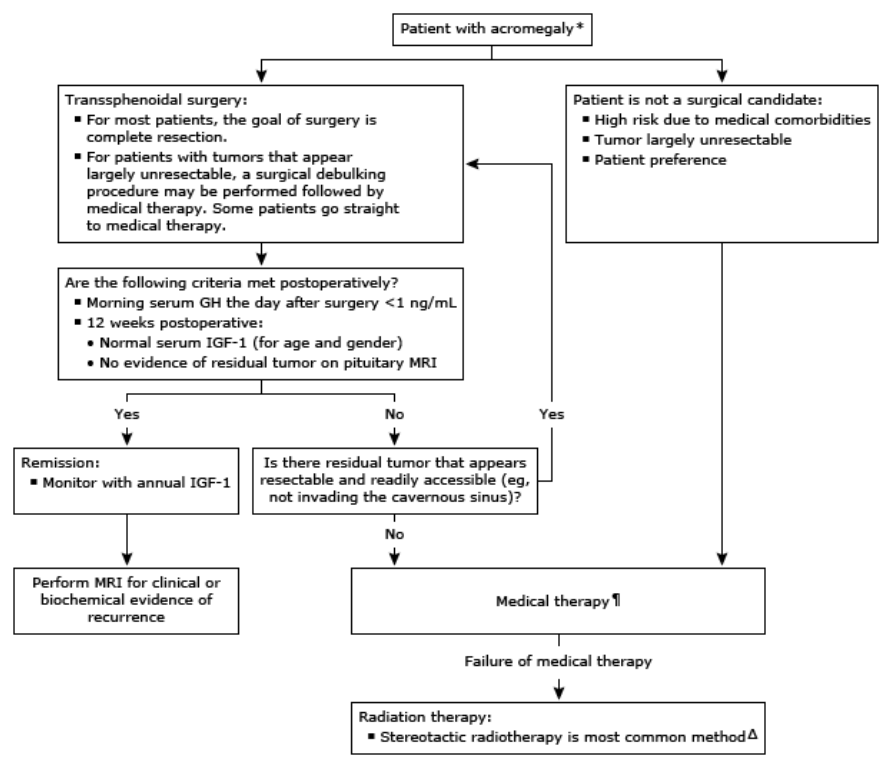


ACROMEGALY EFFECTS

- Somatic & metabolic effects + local compressive symptoms

- Skin thickening, enlarge jaw, enlarged hands/feet
- HTN, LVH, cardiomyopathy, insulin resistance, DM, increased risk of colon polyps/cancer, goitre, sleep apnoea, carpal tunnel syndrome

ACROMEGALY TREATMENT



LEARNING POINTS FROM CASE 3

- Index of suspicion should be raised if there is persistent incongruence in TFT (?TSHoma)
- Always test pituitary panel
- Raised prolactin – could be stalk effect
- Acromegaly features could be subtle, diagnosis is often delayed
- Treatment of acromegaly is essential in view of its metabolic and somatic effects