TOXIC GOITRES: unusual clinical encounters

- Department Of Endocrine Surgery
- Presenters:
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  - Dr. Sunil
  - Dr. Verma
OVERVIEW - WHAT ARE TOXIC GOITRES

• A goitre with the following one/more symptoms:
  • A. Anxiety, Tremors
  • B. Weight loss
  • C. Palpitations
  • D. Exopthalmos
  • E. irregular pulse
  • F. Diarrhoea
  • G. Visual disturbances
  • H. Heart failure
OVERVIEW- CLINICO-PATHOLOGICAL PRESENTATIONS

- **Common presentations:**
  - Graves’ Disease
  - Toxic Multi Nodular Goiter
  - Toxic nodule

- **Uncommon presentations:**
  - Graves’ with pregnancy
  - Graves’ with nodule
  - Graves’ with malignancy
  - Retrosternal goitre with toxicity
  - Hashimoto thyroiditis
  - Thyrotoxicosis facticia
OVERVIEW- SOME CLARIFICATIONS

- **Hyperthyroidism**: Thyrotoxicosis resulting from overproduction of thyroid hormones by the thyroid gland.
- **Graves’ disease**: An autoimmune clinical syndrome associated with hyperthyroidism, diffuse goitre often associated with eye involvement.
# Overview - Investigations

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Graves’</th>
<th>Toxic MNG</th>
<th>Toxic STN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid hormones</td>
<td>TSH↓ T₃↑ ±T₄↑</td>
<td>TSH↓ T₃↑ T₄↑</td>
<td>TSH↓ T₃↑ T₄↑</td>
</tr>
<tr>
<td>X-Ray Chest (Soft Tissues, trachea, Retrost. Extn.)</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>ECG (Tachy., arrhythmia)</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Ultrasound (about nodule, Cervical L. nodes, guided FNA)</td>
<td>±</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>FNA</td>
<td>±</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>RAI Scan</td>
<td>+</td>
<td>±</td>
<td>+</td>
</tr>
</tbody>
</table>

CT/MRI if indicated if indicated if indicated
(Roadmap for surgery, retrosternal extn., compression/displacement/invasion of vessels & structures, lymphatic spread to nodes etc.)
OVERVIEW-MANAGEMENT

- Anti thyroid drugs
- RAI ablation
- Surgery
## OVERVIEW- MANAGEMENT OPTIONS

<table>
<thead>
<tr>
<th></th>
<th>MEDICAL THERAPY</th>
<th>R.A.I. THERAPY</th>
<th>SURGERY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>Small goitres, mild disease, Pre-op. prep., recurrent disease, ophthalmopathy?</td>
<td>Adult Graves’, toxic adenoma, recurrence after partial thyroidectomy</td>
<td>Large goitres, Graves with ophthalmopathy, when quick control required</td>
</tr>
<tr>
<td><strong>Success rate</strong></td>
<td>about 40-60%</td>
<td>About 80%</td>
<td>&gt; 98%</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Usually minor, sometimes major, Rare-life threatening</td>
<td>Quite safe, &gt;one sitting may be needed, isolation required</td>
<td>Nerve palsy, hypoparathyroidism (&lt;1%)</td>
</tr>
<tr>
<td><strong>Relapse rate</strong></td>
<td>About 40-60%</td>
<td>About 20%</td>
<td>About 2%</td>
</tr>
<tr>
<td><strong>Other requirements</strong></td>
<td>Nothing special needed</td>
<td>Pre-thrapy euthyroidism preferred</td>
<td>Pre-op preparation required</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
a. Medical therapy: First line of action, Success rate = 40-60%, Average Duration = 18 months. Useful in all patients – RAI therapy/Surgery. & pre-therapy/ pre-op. preparation. Drugs: Carbimazol, methimazol Prpyl thouracil.

b. Radiolodine therapy:

Each one equally important in overall patient management.
ANTI THYROID DRUGS

- Do not cure graves’ hyperthyroidism: Control hyperthyroidism
- Immunosuppressive role

**Incidence of Relapse: 40%**
MEDICAL TREATMENT: INDICATION

- Mild disease
- Small goiters
- Negative / low-titer TrAb
- Elderly / Limited life expectancy
- Previously operated or irradiated necks
- Ophthalmopathy
SIDE EFFECTS - MINOR

- Rash
- Arthralgia
- Bad taste, Nausea
- Paresthesia
- Headache
- Skin pigmentation
- Alopecia/ graying of hair
- Drug fever
SIDE EFFECTS - MAJOR

Agranulocytosis
Hepatotoxicity
Vasculitis
Birth defects: aplasia cutis
<table>
<thead>
<tr>
<th></th>
<th>Agranulocytosis</th>
<th>Hepatotoxicity</th>
<th>Vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>0.1-5%</td>
<td>0.1-0.2%</td>
<td>0.1%</td>
</tr>
<tr>
<td><strong>Presenting features</strong></td>
<td>Fever, sore throat</td>
<td>Cholestatic jaundice, Hepatic necrosis</td>
<td>ANCA+ Anti MPOAb+ Arthritis, skin ulcers, rash Sinusitis, haemoptysis</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>▪ Broad spectrum antibiotics</td>
<td>▪ Withdraw drug</td>
<td>▪ Withdraw drugs</td>
</tr>
<tr>
<td></td>
<td>▪ Withdraw drugs</td>
<td></td>
<td>▪ Induction therapy (3months): Steroids Cyclophosphamid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Maintenance therapy steroid+ Azathioprine</td>
</tr>
<tr>
<td><strong>Serial monitoring</strong></td>
<td>Not required</td>
<td>Not required</td>
<td>Not required</td>
</tr>
</tbody>
</table>
ADVANTAGES OF SURGERY

- Immediate cure
- Tissues for histologic examination
- Absolute titration of Thyroid hormone replacement
- Avoids use of steroids in TAO (Thyroid associated Ophthalmopathy)
- Complication rates low in High Volume centers with experienced hands
- Safe in pregnancy & lactation
- RAI: increased risk of benign thyroid tumors & malignant transformation in young pts
RAI: INDICATIONS

INDICATIONS
- Small goiters < 80 gms
- Associated co-morbidities
- Previously operated neck
- Externally irradiated necks
- Contraindications to ATD use

**Incidence of Relapse: 21%**

CONTRA-INDICATIONS
- Pregnancy
- Lactation
- Suspicion of thyroid cancer
- Ophthalmopathy
INDICATIONS OF SURGERY

Absolute indications
- Symptomatic compression
- Thyroid malignancy
- Pregnancy
- Failure of medical/RAI treatment

Relative indications
- Large goiters (≥80 g)
- Ophthalmopathy
- Desirous of rapid control of symptoms

Incidence of Relapse: 5%
• Temporary hypocalcemia: 10-30%
• Permanent hypocalcemia: <2%
• Permanent recurrent laryngeal nerve injury: <1%
• Bleeding necessitating reoperation: 0.3%-0.7
• Mortality: 1 in 10,000 and 5 in 1,000,000
PRE OPERATIVE PREPARATION

- Antithyroid drugs for 6 weeks
  Starting dose of
  - Methimazole - 15–30 mg/day twice daily
  - Propylthiouracil - 100–200 mg every 6–8 h
  - Carbimazole - 10–20 mg every 8 or 12 h

- Resting PR > 90/min/ co-existing cardiac disease: beta-blockade.

- Iodine (as Lugol solution or saturated solution of potassium iodide to provide ≥30 mg of iodine/d) for 10 days before surgery: decrease thyroid gland vascularity, the rate of blood flow, and intraoperative blood loss during thyroidectomy
Rapid preparation of severe uncontrolled thyrotoxicosis due to Graves’ disease with Iopanoic acid - a case report

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rationale</th>
<th>Order of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbimazole (30–80 mg)</td>
<td>Antithyroid effects, converts hyperthyroid state to euthyroid</td>
<td>Initial drug of therapy</td>
</tr>
<tr>
<td>Propranolol (80–120 mg)</td>
<td>To inhibit the peripheral conversion of $T_4$ to $T_3$, control tachycardia and hypertension, block the peripheral effects of thyroid hormones</td>
<td>Along with carbimazole</td>
</tr>
<tr>
<td>Amlodipine (5 mg)</td>
<td>To control hypertension</td>
<td>Along with carbimazole and propranolol</td>
</tr>
<tr>
<td>Iopanoic acid (500 mg four times a day)</td>
<td>To inhibit the conversion of $T_4$ to $T_3$, reduce tissue uptake of thyroid hormones, decrease thyroid hormone synthesis, decrease thyroid response to TSH, and decrease the release of thyroid hormones from the thyroid gland</td>
<td>Added when above drugs could not control hyperthyroidism</td>
</tr>
<tr>
<td>Dexamethasone (0.5 mg four times a day)</td>
<td>To inhibit thyroid hormone secretion</td>
<td>Administered along with Iopanoic acid</td>
</tr>
</tbody>
</table>
• Investigations:

• Suppressed TSH
• Elevated Total T4 & or T3
• ECG Rhythm abnormalities
• I^{131} Scan High thyroid uptake
• Ultrasound Thyromegaly ± nodule
• Eye Vision abnormalities ±
• Skin Pre-tibial myxoedema
• Low BMD
ETIOLOGY

Increased formation
1. Graves (70%)
2. Toxic MNG (20%)
3. Toxic adenoma (5%)

Non thyroidal
1. Factitious
2. Struma ovary

Destruction of thyroid
1. Thyroiditis

Others
1. TSH secreting pituitary adenoma

THYROTOXICOSIS
PATHO-PHYSIOLOGY

• Increased β adrenergic activity

• Stimulate Na+ K+ATPase

• Increase oxygen consumption & BMR
CLINICAL FEATURES & INVESTIGATIONS
MRS SN 60/F: GRAVES DISEASE

Anterior neck swelling - 12 yrs

Anxiety, Palpitations, tremors, weight loss - 11 yrs

Protrusion both eyes - 10 years

Change in voice & dysphagia - 4 yrs

Diplopia, Photophobia - 1 year
CLINICAL EXAMINATION

PR: 106/min, irregular

Examination of neck:

- Diffuse symmetrical bilateral bosselated thyroid swelling 1
- Bruit +

Thyromegaly
CLINICAL EXAMINATION

- B/L Tremors
EYE EXAMINATION

B/L Proptosis (Rt-27 mm, Lt-26 mm)

conjunctival congestion

Eyelid edema
CLINICAL ACTIVITY SCORE

CAS: score items 1-7

1. Spontaneous orbital pain
2. Gaze evoked orbital pain
3. Eyelid swelling
4. Eyelid erythema
5. Conjunctival redness
6. Chemosis
7. Inflammation of caruncle or plica
SKIN CHANGES

Graves dermopathy

- Raised waxy pretibial lesions
- Hyperpigmentation
- Hyperkeratosis
- Non-pitting edema
INVESTIGATIONS:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT4</td>
<td>11.1 pmol/L</td>
<td>10.3-25.7</td>
</tr>
<tr>
<td>T3</td>
<td>4.88 nmol/L</td>
<td>1.3-2.8</td>
</tr>
<tr>
<td>TSH</td>
<td>0.02 mIU/L</td>
<td>0.3-5</td>
</tr>
</tbody>
</table>

ECG-irregular rhythm, no p wave
USG NECK

- For echotexture of thyroid
- Nodules
- Lymph nodes
- Planning a FNA
- Flow pattern on doppler
Thyroid nodules in Graves' disease: implications in an endemically iodine deficient area.

A Mishra, S Mishra

Table 1: Clinico-pathological details of the carcinoma patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age Yrs.</th>
<th>Sex</th>
<th>Scan</th>
<th>FNAC</th>
<th>Frozen section</th>
<th>Surgery</th>
<th>Histology</th>
<th>Tumour size (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63</td>
<td>F</td>
<td>Cold nodule</td>
<td>-</td>
<td>Adenomatous hyperplasia</td>
<td>Subtotal thyroidectomy</td>
<td>Follicular carcinoma</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>F</td>
<td>Diffuse</td>
<td>Hemorrhagic</td>
<td>-</td>
<td>Subtotal thyroidectomy</td>
<td>Papillary carcinoma</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>45</td>
<td>M</td>
<td>Cold nodule</td>
<td>-</td>
<td>Colloid goitre</td>
<td>Subtotal thyroidectomy</td>
<td>Papillary carcinoma</td>
<td>4.6</td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>F</td>
<td>Diffuse</td>
<td>Hyperplastic lesion</td>
<td>-</td>
<td>Total thyroidectomy</td>
<td>Papillary carcinoma</td>
<td>10</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>F</td>
<td>Diffuse</td>
<td>-</td>
<td>-</td>
<td>Total thyroidectomy</td>
<td>Papillary carcinoma</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>53</td>
<td>F</td>
<td>Cold nodule</td>
<td>Cellular colloid</td>
<td>-</td>
<td>Total thyroidectomy**</td>
<td>Papillary carcinoma</td>
<td>10</td>
</tr>
</tbody>
</table>

All cases were detected pre-operatively. * Later completion total thyroidectomy was performed. ** In addition modified radical neck dissection was performed as lymph nodes were involved. Case no. 3 and 6 had multicentric tumours.
Thyroid scan: Grossly enlarged thyroid left > right, diffuse increased uptake both lobes. T/P ratio 3.25
CECT NECK AND SUPERIOR MEDIASTINUM
CASE II /43/F: TOXIC MNG

- Neck Swelling: 6yrs
- h/o tremors, anxiety, sweating, palpitations, Wt loss: 6 years
- h/o diarrhoea: 4 years
- h/o decreased menstrual flow: 4 years
- Gradually increasing in size
- o/e: palpable nodular thyroid

18/02/2013
Endo-Radio-Nuclear Meet
INVESTIGATIONS

- USG neck
- Thyroid scan

Underwent Total Thyroidectomy
CASE III: 56/F

- h/o Anterior neck swelling: 10 years
- h/o heat intolerance: 2 years
- Sweating, palpitations: 2 years
- Dyspnea on exertion: 1 year
- o/e: Lt side thyroid nodule
INVESTIGATIONS

• USG Neck
• Thyroid scan

• Underwent Left Hemithyroidectomy
<table>
<thead>
<tr>
<th>Study ,Type &amp; (Evidence)</th>
<th>Total No of pts</th>
<th>TT (no)</th>
<th>Treatment, follow up</th>
<th>Recurrent disease( %)</th>
<th>Permanent RLN palsy (%)</th>
<th>Permanent HypoPT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ST</td>
<td>TT</td>
<td>ST</td>
<td>TT</td>
<td>ST</td>
</tr>
<tr>
<td>Palit , Meta analysis (I)</td>
<td>7241</td>
<td>538</td>
<td>TT vs ST, 5.6 yrs</td>
<td>7.9 0</td>
<td>0.7 0.9</td>
<td>1.0 0.9</td>
</tr>
<tr>
<td>Witte , PRCT (II)</td>
<td>150</td>
<td>50</td>
<td>TT vs ST, 18-58 mnths</td>
<td>NA 1.9 2.1</td>
<td>2.9 10.6</td>
<td></td>
</tr>
<tr>
<td>Winsa , RCS (IV)</td>
<td>173</td>
<td>19</td>
<td>TT vs ST, 0.17-23 yrs</td>
<td>20 0 1.3 2.0</td>
<td>0.6 0</td>
<td></td>
</tr>
<tr>
<td>Miccoli, RCS (IV)</td>
<td>140</td>
<td>60</td>
<td>TT vs ST, 6-48 mnths</td>
<td>5.0 0 2.5 1.6</td>
<td>3.8 3.3</td>
<td></td>
</tr>
<tr>
<td>Barakate, RCS (IV)</td>
<td>1365</td>
<td>119</td>
<td>TT vs ST, NA</td>
<td>NA 0.4 0.8</td>
<td>0.1 0.8</td>
<td></td>
</tr>
<tr>
<td>Ku, RCS (IV)</td>
<td>217</td>
<td>98</td>
<td>TT vs ST, 64 mnths</td>
<td>5.9 0 0 0</td>
<td>0.8 3.1</td>
<td></td>
</tr>
</tbody>
</table>
## OUR EXPERIENCE

Safety and Efficacy of Surgical Management of Hyperthyroidism: 15-year Experience from a Tertiary Care Center in a Developing Country

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Pre-1995</th>
<th>Post-1995</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematoma/seroma</td>
<td>5 (5%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Temporary hypocalcemia</td>
<td>9 (10%)</td>
<td>49 (24%)</td>
</tr>
<tr>
<td>Permanent hypocalcemia</td>
<td>2 (2%)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>Temporary VC palsy</td>
<td>4 (4%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Permanent VC palsy</td>
<td>1 (1%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Recurrence of thyrotoxicosis</td>
<td>4 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>24 (26%)</td>
<td>All</td>
</tr>
</tbody>
</table>

ATYPICAL PRESENTATION
UNUSUAL PRESENTATIONS

MJA, 30/M, GRAVES WITH PERIODIC PARALYSIS

h/o Sudden onset weakness B/L lower limbs with difficulty in standing

No h/o pain/numbness/sensory loss

No h/s/o cranial nerve/bladder/bowel involvement
CLINICAL EXAMINATION

O/E-HMF-WNL, cranial N intact

Hypotonia B/L lower limbs

Gr 4/5 power B/L lower limbs

Ankle, knee jerks depressed

Lower limb symptoms improved with iv KCl

Referred to Endocrinology and Neurology

Started on PTU
<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Units</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. Na⁺</td>
<td>133</td>
<td>mg/dl</td>
<td>135-147</td>
</tr>
<tr>
<td>S. K⁺</td>
<td>2.0 (↓)</td>
<td>mg/dl</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>T3</td>
<td></td>
<td>ng/dl</td>
<td></td>
</tr>
<tr>
<td>FT3</td>
<td>9.6 (3-6.5)</td>
<td>pmol/L</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td></td>
<td>µg/dl</td>
<td></td>
</tr>
<tr>
<td>FT4</td>
<td>35 (9-23)</td>
<td>ng/ll</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>0.4</td>
<td>µIU/mL</td>
<td>0.3-4.0</td>
</tr>
<tr>
<td>CPK</td>
<td></td>
<td>mcg/L</td>
<td>50-170</td>
</tr>
<tr>
<td>Urine K⁺</td>
<td>70.8</td>
<td>mmol/L</td>
<td>25-125</td>
</tr>
</tbody>
</table>

- RNST- non-decremental response
- CPK-55mcg/L
- Thyroid scan- increased uptake B/L lobes
TOTAL THYROIDECTOMY

Post operative smooth recovery
No further episodes of weakness
Doing well in FU on Thyroxine supplements
PERIODIC PARALYSIS

- Recurrent attacks of muscle weakness in the presence of hyperthyroidism
- Incidence: 0.1-0.2%
- Channelopathy: increased Na/K ATPase
- Respiratory failure, cardiac arrhythmias
- Potassium infusion
- β-blockers
- Definitive treatment
ATYPICAL MANAGEMENT
TAKE HOME MESSAGE

- Wt loss
- Anxiety
- Heat intolerance
- Amennorhoea
- Diarrhoea
- Cardiomyopathy
- periodic paralysis

SUSPECT THYROTOXICOSIS!
Prevent the morbidity of an easily curable disease
Thank you