Graves’ Disease
-Management and Surgical Indications-

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SUNY DOWNSTATE
52 year old male with a recent diagnosis of Graves’ and hypertension was referred from Thyroid clinic for thyroidectomy.

Chief complaints: The patient complained of neck swelling, difficulty breathing, and a choking sensation for two months. The patient also noted that his eyes were enlarged.

The patient was recently started on Methimazole for symptoms of anxiety, tremors, and nervousness.
Case Presentation

**History**

Medical:
- Graves’ Disease,
- Hypertension

Surgical: none

Allergies: NKDA

Medications:
- Methimazole
- Metoprolol
- Amlodipine
- Hydrochlorothiazide

**Exam**

Eyes: proptosis, periorbital edema, lid retraction

Neck: diffusely enlarged, nodular thyroid, non tender

Heart: RRR

Lungs: CTAB
Case Presentation

- Pre-Operative Studies
Thyroid Ultrasound: Right lobe of the thyroid is markedly enlarged 12 x5x5.6 cm, Left lobe 11x5x4.5 cm.
Pre-operative studies

CT Neck:
- Diffuse enlargement of thyroid gland.
- Right lobe: 
  12.3 x 5.2 x 6.3 cm
- Left lobe: 
  11.7 x 5.5 x 6.6 cm.
- Mild displacement of the trachea posterior and right
Case Presentation

- Pre-Op Thyroid Function tests:
  (patient’s Methimazole titrated until patient was euthyroid)
  - TSH 0.24
  - FT4 0.4
  - T4 1.8

- Pre-Op Preparation
  - Continued on Metoprolol
  - Prescribed Lugols Solution to start taking 10 days pre-operatively
Case Presentation

- Operation
  - Awake intubation using a bronchoscope
  - Total thyroidectomy
  - Nerve monitor used

- Pathology
  - Thyroid (400 G): Symmetrical enlargement, diffuse hypertrophy and hyperplasia of the follicular cells. Consistent with Graves’ Disease.
Post operative course:

- The patient was kept intubated post operatively and desaturated on POD #2, CXR demonstrated a right lower lobe pneumonia. Patient started on antibiotics.
- Respiratory failure did not improve and patient diagnosed with pulmonary embolism on CTA. Started on Lovenox.
- Required tracheostomy.
- Currently tracheostomy is capped and patient is eating.
Questions??
Outline

• Introduction
• Clinical Features
• Diagnosis
• Medical Management
• Radioactive Iodine
• Surgical Management
• Summary
• Questions
Introduction to Graves’ Disease

- Described by Robert Graves in the 1830’s as a diffuse toxic goiter associated with exophthalmos and palpitations
- Female predominance (5-7 x higher than men)
- Familial predisposition
- Peak incidence between age 40-60
Introduction to Graves Disease

- Autoimmune disease with unknown etiology

- Possible etiologies of the initiation of the immune process: postpartum state, iodine excess, lithium therapy, bacterial and viral infections

- Hyperthyroidism is caused by stimulatory autoantibodies to the TSH-R

- Thyroid stimulating antibodies stimulate the thyrocytes to grow and synthesize excessive thyroid hormone.
Clinical Features

Presentation of Graves’ Disease:

- Goiter
- Ophthalmopathy
- Dermopathy
- Symptoms of Hyperthyroidism
Goiter
- Thyroid gland 2-3 x larger
- Diffuse enlargement
- Smooth, firm, rubbery
- May have a bruit or thrill

Dermopathy (2%)
- Infiltrative skin manifestations
- Pretibial myxedema
- Deposition of glycosamines into the skin resulting in thickening
Clinical Features

- **Ophthalmopathy (50%)**
  - Lid lag
  - Proptosis
  - Periorbital edema
  - Prominent stare
  - Spasm of upper eyelid

- **Etiology**
  - Orbital fibroblasts and muscles are thought to share a common antigen TSH-R. There is inflammation of the periorbital fibroblasts.
Clinical Features

- **Hyperthyroidism**
  - Tachycardia
  - Heat intolerance
  - Palpitations
  - Hyperhydrosis
  - Nervousness
  - Fatigue
  - Emotional lability
  - Tremors
  - Increased BMs
  - Diarrhea
  - Weight loss
  - Fatigue

**Others:** gynecomastia, onycholysis, atrial fibrillation
Diagnosis

- **Laboratory work up:**
  - Suppressed TSH
  - +/- elevated T4 and T3 levels

- **Iodine uptake scan:**
  - Elevated uptake
  - Diffusely enlarged gland
Management of Graves’ Disease

Medical Therapy
- Anti-thyroid drugs
- Beta-blockers
- Lugol’s Solution

Radioactive Iodine

Surgery
- Total thyroidectomy
- Subtotal thyroidectomy
Medical Management

- **Anti-Thyroid Medications**
  - High incidence of failure (40-80% develop recurrence in 1-2 years)
  - Usually administered in preparation for iodine ablation or surgery
  - Curative intent indicated in:
    - small non toxic goiters
    - mildly elevated hormone levels
    - patients who experience rapid remission with reduction of thyroid gland
**Antithyroid Medications (Continued)**

- Options: Propylthiouracil (PTU), Methimazole

- Action: both reduce thyroid hormone production by inhibiting organic binding of iodine and coupling of iodotyrosines

- PTU decreases the peripheral conversion of T4 to T3, used in pregnant women
- **Antithyroid Medications (Continued)**

  - Side Effects: rash, joint pain, liver inflammation, and agranulocytosis (0.1-0.3%)

  - Medications titrated to normalize serum levels of T4 and T3 and maintain TSH in normal range.

  - Symptoms improve by 2-3 weeks and patients are euthyroid by 6 weeks
Medical Management

- **Beta-Blockers**
  - Block adrenergic signaling which is potentiated in hyperthyroidism

  - Commonly used agents: Propranolol, atenolol, metoprolol

  - Propranolol additionally has the ability to inhibit peripheral conversion of T4-T3

  - Important for patients with significant sympathetic symptoms (tremor, tachycardia, sweating). Symptoms improve in 1-2 days.
Radioactive Iodine Therapy ($^{131}$I)
Advantages: avoidance of surgery, reduced treatment cost, ease of treatment

Indications:
- Older patients
- Small to moderate sized goiters
- Patients who relapsed after medical/surgical therapy

Contraindications
Absolute
- Women who are pregnant or breastfeeding

Relative
- Young patients
- Thyroid nodules
- Ophthalmopathy
Radioactive Iodine Therapy (¹³¹I)
- Antithyroid drugs are given until patient is euthyroid, then discontinued 3-7 days before therapy to maximize uptake.

- The dose of ¹³¹I is calculated based on the size of the gland and an uptake scan and then it is administered orally.

- After treatment, patients become euthyroid within 2 months (only 50% euthyroid after 6 months).

- Side effects: radiation thyroiditis and neck tenderness, possible worsening of opthalmopathy.
# Indications for Surgery

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
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<tbody>
<tr>
<td>Suspicious/Malignant nodules</td>
<td>Poor compliance with medications</td>
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<tr>
<td>Pregnant patients uncontrolled on medications</td>
<td>Rapid control of symptoms is needed</td>
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<td>Patients wishing to become pregnant</td>
<td>Severe Graves’ Ophthalmopathy (iodine ablation may aggravate)</td>
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<td>Compressive symptoms</td>
<td>Large thyroid glands+low iodine uptake</td>
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<td>Children</td>
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Advantages of Surgery

- Resolution of Graves hyperthyroidism is most rapid with surgery

- Most patients can be prepared for surgery in less than 6 weeks

- Surgery is curative and definitive in almost 100% of patients.
  (Recurrence rates are less than 1% with total thyroidectomy)

- Other reasons: Cosmesis, Salvage after failed therapy, less costly
Surgical Management

- **Disadvantages of Surgery**
  - Nerve injury (damage can result in vocal cord dysfunction in up to 5% of patients)
  - Parathyroid compromise (permanent hypoparathyroidism in up to 4% patients)
  - Bleeding or infection
  - Hypothyroidism
Preparation for surgery:
- Before surgery the patient must be rendered euthyroid by the use of PTU or Methimazole.
- Beta Blockers can be administered to control catecholamine response in patients with thyrotoxic symptoms.
- Lugol’s solution can be added 10 days to 2 weeks before the operation to decrease vascularity of thyroid gland.
Lugol’s Solution (Iodine + Potassium Iodide)

- Actions: acute inhibition of thyroid hormone synthesis and release, reduces vascularity of the thyroid gland

- Administered for rapid reduction in thyroid hormone levels in patients with severe cardiac disease, thyroid storm, or in preparation of surgery.

- Conflicting opinions regarding the use of Lugol’s solution - no agreement on its effectiveness
Effect of Lugol Solution on Thyroid Gland Blood Flow and Microvessel Density in the Patients with Graves’ Disease

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Review of the literature:

- **Objective:** Evaluate the effectiveness of Lugol’s solution ability to decrease thyroid gland vascularity and intraoperative blood loss in patients with Graves disease.

- **Methods:** 36 patients randomized to receive or not receive Lugol’s pre-operatively

- **Measures:** Blood flow through thyroid arteries was measured by doppler, microvessel density assessed by the level of expression of CD-34 in thyroid tissue
• Review of the literature (continued):

Results

- The mean *blood flow* and *blood loss* in the (+) Lugol’s solution group were significantly lower than the (-) Lugol’s group.

- The mean CD-34 expression (determined by western blot) was lower in the (+) Lugols group than the (−) Lugol’s group.

- Lugol solution treatment resulted in decreases in blood flow, blood loss, and microvascular density.
Definitions:

**Total Thyroidectomy** = division of all thyroid tissue between the entrance of the recurrent laryngeal nerve bilaterally at the ligament of Berry. Complete removal of all visible thyroid tissue.

**Near Total Thyroidectomy** = complete dissection on one side while leaving a remnant of thyroid tissue laterally on the other side, which incorporates the parathyroid.

**Subtotal Thyroidectomy** = leaves a rim of thyroid tissue bilaterally to ensure parathyroid viability and avoid the recurrent laryngeal nerve.
- **Total Thyroidectomy**

  Technique

- Branches of the inferior thyroid artery are divided at the surface of the thyroid gland

- Inferior thyroid veins then ligated and divided

- The Recurrent laryngeal nerve is vulnerable

- The ligament of Berry is then divided
Total Thyroidectomy is Recommended for:
- Patients with co-existent thyroid malignancy
- Severe ophthalmopathy
- Patients unwilling to accept a reoperation for recurrence
- Patients who refuse radioactive iodine
Surgical Management

Subtotal Thyroidectomy

- Technique:
  - parathyroids, inferior thyroid artery, and recurrent laryngeal nerve identified
  - The line of resection is selected to preserve the parathyroid glands
  - Recurrent laryngeal nerve protected

Thyroid tissue divided using harmonic scalpel
- **Subtotal Thyroidectomy**
  - Recommended for the majority of patients
  - Adults: 4-7 g remnant, Children: <3 g remnant
  - Remnants > 8 g decreases risk of post op hypothyroidism, but increase incidence of persistent or recurrent disease
  - Remnants <3 g have a 40% risk of hypothyroidism
Graves disease has thyroidal and extrathyroidal manifestations

Management options are: antithyroid medications, radioiodine ablation, surgery

Patient must be euthyroid preoperatively

Two primary surgical options are total vs. subtotal thyroidectomy


Question #1

Which of the following is not an acceptable indication for surgical treatment of hyperthyroidism?

A. A nodule confirmed or suspicious for malignancy
B. Non compliance with medical management
C. Multinodular goiter
D. Age younger than 15 years old
E. Severe Graves ophthalmopathy

Answer: C
Pre-operative preparation of patients with Graves’ disease should include all of the following except?

A. Thyroid Ultrasound
B. Pre-operative beta blockade
C. Achievement of euthyroid state through use of antithyroid drugs
D. Administration of supersaturated potassium iodide or lugol’s solution 10 days before surgery
E. Lithium

Answer: E