Hyperthyroidism

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concepts

- Thyroid overactivity
- F:M = 5:1
- 2.5% of all females at sometimes; get affected
- 20-40 years: peak
- 90% of cases are intrinsic thyroid disease, pituitary causes extremely rare

Etiology

Graves’ Disease (Basedow’s disease)

- Most commonest cause for ~, esp young pt
- Autoimmune disorder affecting thyroid gland—increase in synthesis & release of thyroid hormones
- F:M = 8:1
- Familial tendency: HLA-B8; DR3, DR2

Graves’ Disease

Accompanied by proptosis and pretibial myxedema: when present indicates graves disease (90%) but not the other cause of ~

Graves exophthalmos: leads to corneal ulcer/blindness
1. Proptosis: >22mm
2. Lid retraction: staring expression
3. Lid lag: downward gaze, upperlids
4. Diplopia: upward/ lateral gaze
5. Periorbital edema

Classic severe Graves’ ophthalmopathy demonstrating a widened palpebral fissure, peri orbital edema, proptosis, chemosis, and conjunctival injection.
Graves’ Disease

- May also associated with other autoimmune ds: pernicious anemia, DM, myasthenia gravis
- TSH-R AB +ve: 80% cases
-ANA may be +ve
-TG/TPO may be positive but weak, ~10%
-Enlarged thyroid firm, diffusely enlarged with bruits, non-tender

Toxic adenomas

Without infiltrative opthalmopathy: dermatopathy; TSH-R Ab, TG, TPO –ve
- Single (Plummer’s disease): single nodule, firm/hard, non-tender; 5% of case–; Antithyroid Rx—no remission
- Multiple (Toxic multi nodular goiter): usually euthyroid, common in older pt, may cause tracheal/esophageal compression/ laryngeal N palsy; multiple-large firm nodules and nontender

AC thyroiditis (de Querrains thyroiditis)

- Viral infection: after 1 wk-10 days
- c/o: fever, malaise, tachycardia, pain in the neck (thyroid tender)
- Moderately large, diffuse, firm, tendered thyroid
- initially ↑FT3, ↑FT4 ↓TSH with ↑ESR-- after few wks gradually hypothyroidism but transient
- Thyroid uptake scan is suppressed
- Rx: B-blockers and add Aspirin/ ?predisolone
- Silent thyroiditis: if non-tendered thyroid esp post-partum thyroiditis, self limiting

Hashimoto’s thyroiditis

- More common if female; late middle age
- May cause transient ~ during initial destruction phase—hypothyroidism
- Firm/soft/rubbery/hard; diffusely enlarged
- TG +ve; TPO +ve higher titre >1000 u/l

Pituitary tumors

- Rare case
- TSH hyper-secretion and features of hyperthyroidism
- Serum TSH may be normal coz of –ve feedback or ↑ with ↑T3/ ↑T4
- -ve antibodies
- CT/MRI of pituitary
- Rx: surgery/radiation therapy; B-lockers for symptomatic relief
• Iodine induced/drugs induced ~
  1. Occurs in pt with multinodular goiter after intake of large amount of iodine diet/contrast materials of radiographic/drugs like amiodarone
  2. Amiodarone may lead both hypo/hyper~

Clinical features: symptoms
• Irritability/restlessness/increased temper/anxiety
• Weight loss
• Increased appetite
• Malaise/weakness
• Heat intolerance ↑sweating
• Muscle cramps
• Altered bowel habits: diarrhea common
• Menstrual irregularities
• Hypokalemic periodic paralysis: 15% of Asian/native americans; often after IV dextrose/vigorous exercise, last 7-72 h
• Eye complaints: only for Graves dis
• Children present with excessive height or growth rate & hyperactivity

Clinical features: sign
• Fine resting tremor
• Irritability/psychosis
• Hyper-reflexia
• Tachycardia/AF
• Moist warm peripheries
• Fine hair
• HTN/ cardiac failure

Ocular signs in Graves’ disease
• Ophthalmic phenomena reflecting thyrotoxicosis per se and apparently resulting from sympathetic overactivity:
  - Lid reaction
  - Lid lag/stare look
  - Ophthalmoplegia
  - Bruits in thyroid area
  - Pre-tibial myxedema/glycosaminoglycan & lymphoid infiltration
  - Thyroid acropachy-clubbing and swelling of finger & periostal new bone formation

Investigation
• TFT: overt/subclinical ~
  ↑FT3/FT4, ↓↓ TSH
• Antibodies
  TPO/TG, TSH-R Ab
• Thyroid radioactive iodine uptake and scan: not useful in dx of ~
  1. Usually performed on pt with established ~
  2. ↑: Graves dis, toxic nodular goiter, dietary iodine deficiency, early hashimotos thyroiditis
  3. ↓: subacute thyroiditis, administration of iodine in any forms eg drugs, radiological contrast

• Imaging:
  Not helpful in Dx of ~
• FNAC
Helpful in the dx of thyroid disorder esp nodular lesions/masses.
Treatment

- 3 modes: RAI, anti-thyroid Rx and subtotal thyroidectomy
- During Treatment, pt are followed up by clinical evaluation and measurement of FT4
- TSH remain suppressed until after the pt is euthyroid so not used for monitoring the response esp initial
- Graves disease pt require for life long f/u regardless of mode of management

Symptomatic therapy with β–blocker

- Propranolol 40-80 mg q6-8h, atenolol 25-100mg/d
- Use for symptomatic relief of palpitation and tremors and anxiety
- Until hyperthyroidism is controlled by definitive method
- Also used for management of Hashimoto thyroiditis and subacute thyroiditis
- Verapamil 40-80mg TID if β-blocker contraindicated

DEFINITIVE THERAPY

Antithyroid drugs

- Antithyroid drugs are the the management of choice during pregnancy
- Carbimazole (methimazole, active metabolite) and propylthiouracil (PTU)
- Half life of T4 is 7 days, clinical benefit is not apparent for about 3 weeks, so use β-blockers for symptomatic relief
- Carbimazole: initially 20-40mg/day (OD/TID → max. 60mg/day). It has mild immunosuppressive activity
- PTU: initially 100-200mg 8 hourly → max. 300mg QID (blocks the conversion T4 to T3)
- Adverse effects: rash, nausea/vomiting, agranulocytosis, jaundice – in these later two cases stop the drug immediately

Antithyroid drugs

Dose titration

- Review after 4-6 weeks, adjust the dose depending on clinical status and fT4/fT3 levels
- When clinically and biochemically euthyroid, stop β-blockers
- Review after 2-3 months, if controlled, reduce the dose of antithyroid drugs
- Gradually reduce to 5mg OD of carbimazole or 50mg TID of PTU over 6-24 months if hyperthyroidism is controlled
- If patient is euthyroid in above dose, discontinue
- Majority of patients with Graves disease, hyperthyroidism recurs within 6 months after therapy is stopped

RAI therapy

- May be given to patients of all ages, except pregnancy and breastfeeding – before Rx pregnancy should be ruled out for fertile woman
- Single dose permanently control hyperthyroidism in ~90%
- RAI uptake is usually measured and calculate the dose of RAI (usually 200-500 MBq)
- Antithyroid drugs should be stopped 3 days before the RAI therapy

RAI therapy cont.

- If iodine therapy is given, should be stopped 2 weeks before RAI
- Usually takes several months (3-6 months) to restore euthyroid status
- Hypothyroidism and worsen of severe cardiac disease are the two main side effects
- After 4-6 weeks of RAI therapy, patient is evaluated
  1. thyroid function normal, monitor TSH
  2. hypothyroidism with symptoms: T4 therapy
  3. symptomatic hyperthyroidism persist after 6 months: repeat RAI
Subtotal thyroidectomy

Indications:
- Patient’s choice: eg. Goiter
- Persistent side effect of drugs
- Poor compliance with drugs therapy
- Compression of trachea/oesophagus
- Retrosternal thyroid
- Recurrent hyperthyroidism after drugs
- Toxic goiter and suspicious of carcinoma

Preparation for surgery

- Antithyroid drugs are given until patient is euthyroid and 10 days before surgery is stopped
- Potassium iodide 40-80mg BD/TID is given at least for 1-2 weeks before surgery (reduces vascularity)
- Atenolol 50-100mg OD is given 1-2 weeks before surgery (HR<90 bpm) and continue 1-2 weeks after surgery
- fT4 and TSH to be accessed after 4-6 months of surgery
- Complication: hypothyroidism, hypoparathyroidism and laryngeal nerve injury

Special considerations

Subclinical hyperthyroidism

→ Indications to treat:
1. Clinically symptomatic
2. Atrial fibrillation in the elderly
3. Osteoporosis in the postmenopausal women

Thyroid storm/crisis

- Rare condition, ~10% of mortality
- Rapid deterioration of hyperthyroidism with hyperpyrexia, severe tachycardia, extreme restlessness, delirium and precipitates heart failure/CAD
- Precipitated by stress, infection, surgery in unprepared patient or RAI therapy
- Treatment is urgent and intensively, and confirmatory (fT4, TSH) test should be obtained before the therapy is started

Thyroid storm - therapy

- PTU 300mg Q6h stat
- Potassium iodide 40-80mg BD after 2 hours od PTU (to inhibit thyroid hormone secretion rapidly)
- Propranolol 40mg Q6h oral or iv., esp. if patient have angina/tachycardia/MI
- fT4 is measured every 3-7 days and when serum T4 is in normal range, then PTU and iodide should be gradually decreased
- RAI therapy can be given 2 weeks after iodide is stopped

Hyperthyroidism in pregnancy

- TSH and fT3/fT4 monitored
- RAI therapy is contraindicated
- Rx with PTU only
- Adjust the dose of PTU in every months
- Target is fT4 is maintained near the upper limit of normal range
- Later stages of pregnancy dose requirement is often less
- Atenolol 25-50mg OD can be used to reduce the symptoms
Thyroid eye disease

- Thyrotoxic status should be treated but avoid hypothyroidism
- Stop smoking
- Methylcellulose eye drop – lubrication and comfort
- Eyelid should be tapped, upright sleeping
- Systemic steroids (prednisolone 30-120mg OD)
- Irradiation of the orbits
- Lid surgery to protect the corneal damage
- Surgical decompression of the orbits
- Correcting eye muscles – improves diplopia