TILL THE STORM PASSES BY

Dr. YK Chung

ICU TKOH
Ms. Yeung

- F/49 housewife
- NSND
- History of DM and thyrotoxicosis
- Previously FU in China and put on antithyroid drugs
- Defaulted FU for 5 years
History

- C/O right leg painful swelling for 4 days
- Started from right knee extending down to ankle
- No marine contact/ IVDU/ trauma/ laceration/ animal bite/ long-distance travel
- Not on OCP or HRT
- No recent surgery/ immobilization
Physical examination

- Temp 37 ºC
- GCS 15/15
- BP 150/70 mmHg
- Pulse 120-140 bpm, irregular
- SaO₂ 95% (RA)
Physical examination

• Chest - ↓ bilateral breath sound and stony dullness on percussion (right side more severe)

• CVS/CNS/abdomen - normal

• Urine PT negative
Physical examination of right leg

- Overlying skin erythematous
- Tender and swollen
- No blister/bulla/crepitus/discholoration/gangrene/anaesthesia
- Peripheral circulation normal, distal pulses palpable
- Bilateral ankle pitting edema
Investigations

- XR right lower limb: no fracture/ subcutaneous emphysema
- CXR cardiomegaly + bilateral pleural effusion (R>L)
- ECG AF 123 bpm
Investigations

- WCC 5.6 Hb 12 Plt 190
- Na 138 K 4 Urea 8 Cr 60
- Bili 51 ALP 167 ALT 18
- CK n
- pH 7.44 HCO3 27
- INR 1.3 APTT 28.5
- Amylase 15
- TNT not elevated
Management in medical ward

- IV ampicillin + cloxacillin
- Urgent doppler right leg → no DVT
- Amiodarone
Day 2

- Increased dyspnea
- Nausea, vomiting and abdominal pain
Day 2

• Afebrile

• SaO₂ 95% ↑ 4L O₂ NC

• BP 140/80 mmHg

• Fast AF 130-150 bpm

• RR 30 bpm

• Abdomen exam repeated - NAD
Day 2

- CXR - ↑ bilateral pleural effusion and pulmonary congestion

- AXR - NAD

- Serial examination of right leg - no deterioration or NF changes
Blood tests

- WCC 14 Hb 14 Plt 159
- RFT n Na 136 K 3.7
- Bili 76 ALP 180 ALT 54
- Amylase 90
- CK 140
- Spot glucose 2.1
- TNT not raised
- Paracetamol/salicylate/ethanol level not elevated
Blood gas

- ABG
  - pH 7.14
  - pCO₂ 3.2 kPa
  - pO₂ 12.9 kPa
  - HCO₃ 9.6
  - BE -18

- Chloride 99
  - AG = 29.4
  - ΔAG = 17.4
  - ΔHCO₃ = 14.4
  - Δratio = 1.2
Blood gas

- Exp $pCO_2 = 1.5 \times HCO_3 + 8 \pm 2$

- Exp $pCO_2 = 2.6 - 3.2 \text{ kPa (measured } pCO_2 3.2\text{kPa)}$

- Uncomplicated high anion gap metabolic acidosis
High AG acidosis?

- Denied toxic alcohol contact

- Serum osmo 288

- Calculated osmolarity
  \[ = 2*(Na+K) + \text{urea} + \text{glucose} \]
  \[ = 286 \]

- Osmolar gap = 2 (<10)
High AG acidosis?

- X Toxic alcohol - normal OG
- X Uraemia - normal urea
- X Ketosis - ketone negative
- X Paraldehyde & ammonium chloride
- ✔ Lactic acidosis - serum lactate 4 (0.5-2.2 mmol/L)
CT thorax + abdomen + right leg

- No PE
- No haemoperitoneum/pneumoperitoneum
- No IO/bowel ischemia
- No subcutaneous emphysema of right leg
- Bilateral pleural effusion
ECHO

- Globally impaired EF 30%
- No significant valvular lesion
- No RWMA
- No pericardial effusion
TRANSFERRED TO ICU...
Problems

- CHF with pulmonary congestion & pleural effusion
- Deteriorating LFT
- Persistent fast AF despite amiodarone
- DIC
- Lactic acidosis
- Right leg cellulitis
ONE MAN ONE DISEASE...HOW TO LINK THESE UP?
The patients know more about their diseases than me. I must get faster modem, higher speed internet access than them.
History

- F/49

- History of DM and thyrotoxicosis

- Previously FU in China and put on antithyroid drugs

- Defaulted FU for 5 years
Physical exam
Physical exam

- Mild bilateral proptosis
Further history....

- No palpitation/ weight loss/ Δ appetite/ irritability/ tremor/ heat intolerance

- Diarrhea for 1 month
DDX

• Thyroid storm

• Sepsis with septic cardiomyopathy → septic workup

• Myocarditis/cardiomyopathy → blood & stool viral culture

• Drug toxicity → toxicology screening
Thyroid storm

HYPERTHYROIDISM

- Intolerance to Heat
- Fine, Straight Hair
- Bulging Eyes
- Facial Flushing
- Enlarged Thyroid
- Tachycardia
- Systolic BP
- Breast Enlargement
- Weight Loss
- Muscle Wasting
- Diarrhea
- Finger Clubbing
- Menstrual Changes (Amenorrhea)
- Localized Edema
Iodine Uptake

• Iodide (I-) actively transported into the follicular cells by an Na+/I- symport in the basal membrane

• This pump concentrates iodine in the colloid at a level up to 250x > plasma level - iodide trapping

• The pump activated by thyroid stimulating hormone (TSH)
Transport

• T½ of T3 - 1 day

• T½ of T4 - 6 days

• 99% TH are protein bound, mainly by TBG

• Remainder by pre-albumin or albumin
Degradation

- Only free T3 and free T4 enter cells to exert actions

- T3 (50%) deiodinated from T4 in peripheral tissues, esp. liver and kidneys
Deiodination

- 3 types of deiodinase
- Type I - primary source of T3
- In liver, kidney and thyroid tissues
- Inhibited by PTU, beta-blockers, iodide and steroid
- Forms the basis for drug treatment of thyrotoxicosis
Hypothalamic - Pituitary - Thyroid Axis

TRH = Thyroid Releasing Hormone
TSH = Thyroid Stimulating Hormone
Thyroid storm

- Syndrome of decompensated hyperthyroidism

- ≠ compensated thyrotoxicosis of severe illness

- Though management are similar for these 2 entities

- Typically occurs in patients with undiagnosed or under-treated hyperthyroidism


Takashi Akamizu. Diagnostic Criteria, Clinical Features, and Incidence of Thyroid Storm Based on Nationwide Surveys. *THYROID* Volume 22, Number 7, 2012
Thyroid storm

- Always evoked by a precipitating event

- Mortality 10-30%

- Commonest cause of death - MOF, CHF
Pathogenesis

• Unknown mechanism

• ?Exaggerated response to TH in target cells

• ?Increase tissue T3 level

• ?Exaggerated response to sympathetic stimulation
Causes of hyperthyroidism

• Graves’ disease (GD)

• Toxic adenoma or multinodular goitre

• Thyroiditis
Causes of hyperthyroidism

- Exogenous iodine/thyroxine
  
  - Excessive thyroxine intake (weight reduction pills)
  
  - Iodine-containing drugs (amiodarone, radiocontrast)
  
- Post-RAI

Lethal thyroid storm after uncontrolled intake of liothyronine in order to lose weight

Benno Hartung · Matthias Schott · Thomas Daldrup · Stefanie Ritz-Timme

DOI 10.1007/s00414-010-0423-y
Causes of hyperthyroidism (rare)

- Hypersecretory thyroid carcinoma
- TSH-secreting pituitary adenoma
- HCG-secreting tumour
- Hydatidiform mole
- Interferon alpha/ IL-2
Precipitating event

- Infection
- Discontinuation of antithyroid drugs
- Iodine, exogenous thyroxine
- Surgery or trauma
- Medical illness, e.g. myocardial infarction, thromboembolism
- Pregnancy
- Salicylate - ↑ free TH
Clinical presentation

• Hyperthermia

• Sinus tachycardia or supraventricular arrhythmias

• CHF

• CNS (agitation, seizure, confusion or coma)

• GI (vomiting, diarrhea, ileus or impaired LFT)

• Typical GD s/s - goitre, ophthalmopathy, tremor, hyperreflexia
Beware of atypical features in elderly!

Coma and Thyroid Storm in Apathetic Thyrotoxicosis

MICHEL W. GHOBRIAL, MD, and EDWARD B. RUBY, MD, Philadelphia, Pa

ABSTRACT: We report the case of an 87-year-old woman with coma who was found to be in thyrotoxic crisis. The patient had a recent history of decreased mentation and apathy, and laboratory findings were found to be consistent with hyperthyroidism. After a stormy course, the clinical condition recovered to baseline, with return of laboratory values to normal following antithyroid therapy. We provide the details of this rarely documented presentation of apathetic hyperthyroidism with thyroid storm and coma and review the characteristics of similar cases in the literature.
Laboratory investigations

- Low levels of TSH and high levels of free T3 and free T4

- GD/toxic nodules have higher proportion T3 (T3/T4 ratio > 20)

- Thyroiditis/iodine exposure have higher proportion T4 (T3/T4 ratio < 15)
Laboratory investigations

• Diagnosis of TS is not judged by the extent of TFT elevation

• No cutoff value for TS

• Thyroid profile similar to overt uncomplicated thyrotoxicosis

• Sometimes even not elevated

• TFT results not always available in emergency condition
Imaging

• USG
  • Easily available & non-invasive
  • Size and vascularity of thyroid gland
  • GD: enlarged gland with enhanced Doppler flow
  • Thyroiditis or exogenous cause: small gland with diminished flow
  • Expertise required
Figure 1. Graves’ disease: the transverse sonogram of the left lobe shows diffusely enlarged, heterogeneous and hypoechoic parenchyma (like the near neck muscles); the power-Doppler study demonstrates a typical hypervascular pattern referred to as the “thyroid inferno”.
ANY DIAGNOSTIC CRITERIA FOR THYROID STORM?
**Burch & Wartofsky’s scoring system**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Scoring system</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thermoregulatory dysfunction</strong></td>
<td></td>
</tr>
<tr>
<td>Oral temperature (°F)</td>
<td></td>
</tr>
<tr>
<td>99.9-99.9</td>
<td>5</td>
</tr>
<tr>
<td>100-100.9</td>
<td>10</td>
</tr>
<tr>
<td>101-101.9</td>
<td>15</td>
</tr>
<tr>
<td>102-102.9</td>
<td>20</td>
</tr>
<tr>
<td>103-103.9</td>
<td>25</td>
</tr>
<tr>
<td>104</td>
<td>30</td>
</tr>
<tr>
<td><strong>Cardiovascular dysfunction</strong></td>
<td></td>
</tr>
<tr>
<td>Tachycardia</td>
<td></td>
</tr>
<tr>
<td>90-109</td>
<td>5</td>
</tr>
<tr>
<td>110-119</td>
<td>10</td>
</tr>
<tr>
<td>120-129</td>
<td>15</td>
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<tr>
<td>130-139</td>
<td>20</td>
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<tr>
<td>&gt;140</td>
<td>25</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild (pedal edema)</td>
<td>5</td>
</tr>
<tr>
<td>Moderate (bilateral edema)</td>
<td>10</td>
</tr>
<tr>
<td>Severe (pulmonary oedema)</td>
<td>15</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
</tr>
<tr>
<td>Central nervous system symptoms</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild agitation</td>
<td>10</td>
</tr>
<tr>
<td>Moderate (Delirium, psychosis, extreme lethargy)</td>
<td>20</td>
</tr>
<tr>
<td>Severe (Seizure, coma)</td>
<td>30</td>
</tr>
<tr>
<td>Gastrointestinal /hepatic dysfunction</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (Diarrhea, nausea, vomiting, abdominal pain)</td>
<td>10</td>
</tr>
<tr>
<td>Severe (Unexplained jaundice)</td>
<td>20</td>
</tr>
<tr>
<td>Precipitating event</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
</tr>
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</table>

≥45 suggestive of TS

25 - 44 suggestive of “impending” TS

< 25 unlikely TS
Critics on BWS

• Can’t distinguish TS from severe compensated thyrotoxicosis

• Non-specific

• Complicated

• Not evidence based

• Not formally validated

• New criteria proposed by Japan Thyroid Association in 2012

• Based on analysis of literatures, followed by survey of thyrotoxic cases in Japan

• Different from BWC in 2 ways:

  • Requirement of laboratory evidence of thyrotoxicosis as a prerequisite

  • Not a scoring system
Symptoms

1. CNS
2. Fever (≥38ºC)
3. Tachycardia (≥130bpm)
4. CHF
5. GI and hepatic
Diagnostic criteria for “Definite” TS

• Meet the prerequisite and either:
  
  • (i) At least one CNS symptom plus one other symptom
  
  • (ii) Three or more symptoms other than CNS
Diagnostic criteria for “Suspected” TS

• A prerequisite plus two manifestations other than CNS symptom

• If prerequisite cannot be met, but the patient has history of thyroid disease, presents with exophthalmos and goiter, and meets (i) or (ii) from the criteria for definite cases, still a suspected case
Limitations of the Japanese criteria

- Prerequisite needs lab. data which is not always available
- TH may be normal in some TS cases
- Study confined in Japan ?generalizability
**HYPERTHYROIDISM AND OTHER CAUSES OF THYROTOXICOSIS: MANAGEMENT GUIDELINES OF THE AMERICAN THYROID ASSOCIATION AND AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLIGISTS**

Rebecca S. Bahn (Chair), MD⁴; Henry B. Burch, MD²; David S. Cooper, MD³; Jeffrey R. Garber, MD, FACP, FACE¹; M. Carol Greenelee, MD; Irwin Klein, MD⁶; Peter Laurberg, MD⁷; I. Ross McDougall, MD⁸; Victor M. Montori, MD¹; Scott A. Rivkees, MD⁹; Douglas S. Ross, MD¹⁰; Julie Ann Sosa, MD¹¹; Marius N. Stan, MD¹

### Table 5. Point Scale for the Diagnosis of Thyroid Storm

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<td>20</td>
</tr>
<tr>
<td>103.0–103.9</td>
<td>25</td>
</tr>
<tr>
<td>≥104.0</td>
<td>30</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
</tr>
<tr>
<td>Tachycardia (beats per minute)</td>
<td></td>
</tr>
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<td>100–109</td>
<td>5</td>
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<td>110–119</td>
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<td>120–129</td>
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<tr>
<td>130–139</td>
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</tr>
<tr>
<td>≥140</td>
<td>25</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>5</td>
</tr>
<tr>
<td>Moderate</td>
<td>10</td>
</tr>
<tr>
<td>Severe</td>
<td>20</td>
</tr>
</tbody>
</table>

### Points for Gastrointestinal-Hepatic Dysfunction

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
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</thead>
<tbody>
<tr>
<td>Manifestation</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Moderate (diarrhea, abdominal pain, nausea/vomiting)</td>
<td>10</td>
</tr>
<tr>
<td>Severe (jaundice)</td>
<td>20</td>
</tr>
</tbody>
</table>

### Points for Central Nervous System Disturbance

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manifestation</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild (agitation)</td>
<td>10</td>
</tr>
<tr>
<td>Moderate (delirium, psychosis, extreme lethargy)</td>
<td>20</td>
</tr>
<tr>
<td>Severe (seizure, coma)</td>
<td>30</td>
</tr>
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### Precipitating History

<table>
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<th>Criteria</th>
<th>Points</th>
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<tbody>
<tr>
<td>Status</td>
<td></td>
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<tr>
<td>Positive</td>
<td>0</td>
</tr>
<tr>
<td>Negative</td>
<td>10</td>
</tr>
</tbody>
</table>

**Scores totaled**

- >45: Thyroid storm
- 25–44: Impending storm
- <25: Storm unlikely

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>0</td>
</tr>
<tr>
<td>Tachycardia ~ 130</td>
<td>15</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>15</td>
</tr>
<tr>
<td>AF</td>
<td>10</td>
</tr>
<tr>
<td>Precipitating event</td>
<td>10</td>
</tr>
<tr>
<td>Jaundice</td>
<td>20</td>
</tr>
<tr>
<td>CNS</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><strong>70</strong></td>
</tr>
</tbody>
</table>
• Prerequisite not confirmed….has **history of thyroid disease**, presents with **exophthalmos and goiter**, …..3 systems of involvement (**GI + tachycardia + CHF**)  

• A suspected TS case
IS DIAGNOSTIC CRITERIA REALLY IMPORTANT IN MANAGEMENT?
Principles of thyroid storm management

- Stop synthesis of new hormone
- Stop release of stored thyroid hormone
- Prevent conversion of T4 to T3
- Control adrenergic symptoms
- Supportive care
Beta-blockers

- Block T4 conversion to T3
- Block beta adrenergic response
- Pay extreme caution in heart failure cases
- Can induce hypotension or even cardiac arrest in severe heart failure cases
- Used under close hemodynamic monitoring
Propranolol

- Oral/NG

- 60-80 mg every 4 hours

- Onset 1 hour, half life 4-6 hours

- IV propranolol (0.5-1 mg over 10 minutes, then 1-2 mg over 10 minutes, repeated every few hours)

- Non-selective blocker → C/I in asthma
Esmolol

- Short acting

- Half life 9 minutes

- Loading iv 250-500 mcg/kg followed by infusion of 50-100 mcg/kg/min
## Thionamides

<table>
<thead>
<tr>
<th>Imidazole</th>
<th>Thiouracil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbimazole – a/v in UK &amp; Commonwealth</td>
<td>Propylthiouracil</td>
</tr>
<tr>
<td>Methimazole – a metabolite of CMZ</td>
<td></td>
</tr>
<tr>
<td>Inhibit new TH synthesis</td>
<td>Inhibit new TH synthesis + inhibit peripheral T4 to T3 conversion</td>
</tr>
<tr>
<td>Longer half life</td>
<td>Shorter half life</td>
</tr>
<tr>
<td>Once daily dose</td>
<td>3-4 times per day</td>
</tr>
<tr>
<td>20-25mg Q6h (more frequent dose in TS due to poor GI absorption)</td>
<td>200-300mg Q6h</td>
</tr>
<tr>
<td>Oral or rectal route</td>
<td>Oral or rectal route</td>
</tr>
<tr>
<td>No IV preparation</td>
<td>No IV preparation</td>
</tr>
</tbody>
</table>
Thionamides

• Block TH synthesis within 1-2 hours

• Cannot block release of pre-formed thyroid hormone

• PTU preferred in TS due to additional benefit in blocking peripheral conversion of T4 to T3

• CMZ less hepatotoxic than PTU

• Common mild S/E - bad taste, pruritus, urticaria, fever and joint pain
Thionamides

- IV thionamide use has been reported in small case series

- Dissolve oral tablets in normal saline

- Potential risk of contamination and embolism
Agranulocytosis

- 0.4%
- Slightly higher incidence in PTU
- G-CSF can be considered in drug induced agranulocytosis
Hepatotoxicity

- 0.2%
- PTU - allergic hepatitis with hepatocellular injury
- CMZ - cholestasis
Vasculitis

• More common with PTU

• ANCA related
  • ARF
  • Arthritis
  • Skin ulcer
  • Rash
  • Haemoptysis
Iodine

- Block new hormone synthesis

- Block the release of pre-stored hormone (where thionamides unable to do so)
WHY IODINE CAN INHIBIT THYROID HORMONE SYNTHESIS?
Wolff-Chaikoff effect

- A normal physiological phenomenon to protect human from wide variety of iodine intake and to maintain euthyroidism

- Sudden increase in serum iodine (>1 µmol/L) inhibits oxidation of iodide inside follicles

- Inhibit TH synthesis
Escape phenomenon

- Within 2-4 weeks of continued exposure to excess iodide, iodide organification and TH synthesis resume in a normal fashion

- Results from decreased trapping of iodide and restoration of intrathyroidal iodide pool to normal level

- Adaptation of the iodide transport system
Jod-Basedow effect

• “Jod” = iodine (German)

• Development of hyperthyroidism following administration of iodine independent of intrathyroidal iodine autoregulation

• Typically occurs in people, who live in iodine deficient areas (with underlying autonomous thyroid gland), when given small increase in iodine intake, resulting in increase TH synthesis independent of normal regulatory mechanism
Formulation

- Lugol’s solution & potassium iodide (SSKI)
  - 0.2–2 g daily
  - 4–8 drops Lugol’s (8 mg iodine/drop) every 6–8 hours

- Esophagitis & duodenitis
  - 5 drops of potassium iodide (38 mg iodine/drop) every 6 hours

- Rectal route possible

- IV in case reports

- Oral radiocontrast - ipodate and iopanoic acid not available in many countries? HK (0.5–1 g once daily)
When to start iodine?

• Start iodine 1 hour after antithyroid drugs

• Prevent stimulation of new thyroid hormone synthesis by iodine
Steroid

- Inhibits peripheral conversion of T4 to T3

- Treat relative adrenal insufficiency

- Direct effect on autoimmune process in GD

- Hydrocortisone 100 mg Q8h iv
Lithium

- Used when thionamide contraindicated

- Decrease TH synthesis and secretion

- 300 mg every 8 hours oral

- Maintain serum level of Li at 1.0 mEq/L
Potassium perchlorate

- Perchlorate anion (ClO₄⁻) is a competitive inhibitor of iodide transport

- Fell out of favor due to its side effects - aplastic anemia & nephrotic syndrome

- Resurgence of interest - effective treatment in type 1 amiodarone-induced thyrotoxicosis (AIT)

- < 1 g daily; limited treatment course to 4 weeks
Antiadrenergic agents

- Reserpine & guanethididine
- Depletes catecholamine stores in sympathetic nerve terminals
- Inhibits release of catecholamines
- Side effects - hypotension, diarrhea, CNS depression
- Consider when beta-blockade contraindicated
Cholestyramines

- Anion exchange resin
- Decrease reabsorption of thyroid hormone from enterohepatic circulation
- Especially useful in iatrogenic hyperthyroidism
Plasmapheresis

• Removal of protein bound hormone, catecholamines, cytokines and antibodies

• Rapid improvement in clinical condition

• Considered early in desperate cases (MOF) or when traditional treatment fails

• Combined use with antithyroid drugs
Plasmapheresis

• Grade 1c recommendation in American Society for Apheresis (ASFA)

• Indications
  • Cardiothyrotoxicosis – rapid improvement
  • Neurological – slow response due to blood brain barrier
  • Severe myopathy
  • Rapid clinical deterioration
  • Contraindications or failure to conventional treatment
  • As a preparation before emergency surgery

Plasmapheresis

- TH tends to rise again after TPE
- Mobilization effect from extravascular compartment
- **Daily** TPE until clinical improvement
- 40-50 ml/kg replacement per session
- Check fT3 and fT4 before and after each session

Supportive treatment

- ABC
- Antipyretics
  - X salicylates (displace TH from TBG)
- External cooling
- Fluid and electrolyte (avoid fluid overload in CHF)
- Diuretics for CHF
- Nutrition
- Treat underlying precipitating cause
BACK TO OUR PATIENT …
Day 2

- Consult endocrinologist
- Thyroid USG - diffusely enlarged thyroid glands with increased blood flow
- TFT pending
Treatment

- PTU 200mg Q6h oral
- Hydrocortisone 100mg Q8h iv
- Esmolol (start @ 50 mcg/kg/min infusion)
- Lugol’s solution 6 drops Q6h oral (1 hour after)
- Supportive treatment
Day 3

- $fT4$ 63.6 (12-22)
- $fT3$ 21.3 (3.9-6.7)
- TSH <0.01
- Anti-thyroglobulin antibody negative
- Anti-thyroid microsomal antibody positive (1:6400)
Day 3

- Right leg cellulitis resolved
- Septic workup negative
- Toxicology screen negative
- Stool culture negative
Day 3

- CHF improved

- Persistent fast AF 120-140 bpm (esmolol ↑ 90 mcg/kg/min)
Another problem arises....
Day 3

• Confused speech E4V4M6

• CT brain normal

• NH3 90 (11-51)
Day 3

- USG abdomen normal
- Viral hepatitis serology negative
- Anti-mitochondrial (AMA)/ anti-smooth muscle antibody (ASMA) negative
Impaired liver function in hyperthyroidism

- Common 45-90%
- Usually mild and asymptomatic
- ↑ ALP most common - bone resorption
- Followed by ↑ AST and bilirubin
Causes of liver injury in hyperthyroidism

• Thyrotoxic hepatitis
  • Thyrotoxicosis induce hypermetabolism
  • Inducing relative ischemia in liver (ischemic hepatitis)
  • Further exacerbated by right heart failure
  • Resolve when euthyroidism achieved
Causes of liver injury in hyperthyroidism

- Antithyroid drugs
  - Metabolized mainly in liver
  - CMZ $\rightarrow$ cholestasis
  - PTU $\rightarrow$ hepatocellular injury
Causes of liver injury in hyperthyroidism

- PTU
  - More hepatotoxic than CMZ
  - Hepatotoxicity occurs within first 3 months after use
  - Induce liver injury by immunological mechanism
  - Usually benign prognosis
  - Mild asymptomatic case → observe
  - Severe symptomatic → withdrawal
Causes of liver injury in hyperthyroidism

• Autoimmune hepatitis

  • Associated with GD

  • Sometimes triggered by PTU by unknown mechanism

  • Requires immunosuppressive therapy in severe case
Day 3

- Impaired LFT multifactorial
- Thyroid storm
- PTU related
- PTU is metabolized by liver in greater proportion than CMZ
- Switched to CMZ 20mg TDS oral
Amiodarone, PTU, Esmolol, Lugol's, and Steroid CMZ.

Esmolol to Propranolol, Tail down steroid, Off Lugol's, Return to sinus rhythm.
Progress

• Discharged to ward on day 7

• Home on day 10
On discharge

- LFT
  - Bilirubin 45
  - ALP 117
  - ALT 56

- fT4 14.7 (12-22)

- fT3 4 (3.9-6.7)
Beta-blocker use in this case

- Use of esmolol uncomplicated despite poor EF

- Effect in controlling tachycardia not obvious until T4/T3 under control

- Initial ineffectiveness in heart rate control might be due to ↑ no. of β receptors in heart

- Useful in stopping peripheral conversion

- Damped down peripheral adrenergic action

Other anti-arrhythmics in TS

- CCB should be avoided due to risk of severe hypotension unless beta-blocker contraindicated
- Digoxin usually ineffective in TS
Amiodarone and thyroid function

- Associated with thyroid dysfunction

- Also has a long half-life (100 days) and adheres to adipose tissue due to its lipophilic nature.

- Most patients remain euthyroid (>90%) when treated with amiodarone.

- Risk of developing amiodarone-induced hypo- or hyperthyroidism depends on underlying thyroid status and dietary iodine intake.
Amiodarone and thyroid function

- Direct effect
  - Inhibits 5’-monodeiodination of T4 and therefore ↓ T3 production
  - Blocks T3 binding to nuclear receptors
  - Destructive thyroiditis
Amiodarone and thyroid function

- Indirect effect (high iodine content)
  - Each amiodarone molecule has 2 iodine atoms
  - 100mg amiodarone releases 3mg iodine into circulation (average diet contains 0.3mg iodine per day!!!)
  - Provides abundant iodine substrate for TH synthesis
  - In normal people, iodine transport and TH synthesis inhibited when iodine concentration reaches high level (Wolff-Chaikoff effect)
Amiodarone and thyroid function

- Indirect effect

- In those who have autoimmune thyroid disease “fail to escape” from Wolff-Chaikoff effect → results into hypothyroidism in Hashimoto’s thyroiditis

- Patients with nodular goitre which fails to autoregulate, such a high iodine substrate results in excessive TH synthesis and thus thyrotoxicosis (Jod-Basedow)

- People from iodine deficient areas more prone to develop hyperthyroidism; while those from iodine sufficient areas more prone to have hypothyroidism
Type 1 amiodarone-induced thyrotoxicosis (AIT)

- Common in individuals with nodular goitre, latent autoimmunity or those coming from iodine deficient countries
- Pathogenesis - Jod-Basedow effect
- Treatment - potassium perchlorate & thionamides
Type 2 AIT

- Destructive thyroiditis $\rightarrow$ inflammation

- Occurs in those without underlying thyroid disease

- More common than type 1 AIT

- Treatment - steroid

- Mixed type AIT - both type 1 & 2 mechanisms
Differentiate type 1 and type 2 AIT

• Thyroid ultrasonography
  • Absent hypervascularity in type 2 AIT; type 1 AIT show increased vascularity

• Thyroidal 131I uptake
  • Very low (3%) in type 2 AIT; normal, or even increased in type 1 AIT

• MIBI (99mTc) scintigraphy
  • Hyperfunctioning tissue in type 1 AIT; no uptake in type 2 AIT

• IL-6 or C-reactive protein
  • Elevated in type 2 AIT, non-specific

• TSH receptor autoantibody
  • Type 1 AIT/ GD
Amiodarone in thyroid storm

- Immediate effect
  - Control heart rate
  - Inhibit TH synthesis at high dose (Wolff-Chaikoff effect)

- Later effect
  - Type 1 AIT (Jod-Basedow)
  - Type 2 AIT
  - Takes weeks or months to develop
IF PATIENT REQUESTS RAI DURING FU, WHAT SHOULD WE ADVISE HER?
RAI (I-131)

- Make sure no contraindications: pregnancy, lactation, severe ophthalmopathy or very large goitre

- Avoid pregnancy for at least 12 months after RAI

- Pregnancy test before RAI

- Avoid close contact with children or pregnant women for 2 to 4 weeks depending on the dose and type of RAI used
RAI (I-131)

- Delayed for several weeks or months following treatment of iodine

- Iodine can impair uptake and efficacy of RAI therapy
Hyperemesis gravidarum

- Serum TSH low and FT4 high
- Result of crossreactivity between hCG and TSH at the thyroid receptor
- Supportive therapy - antiemetics, hydration, electrolyte replacement and nutrition
- Spontaneous recovery occurs by 18 wga
- Anti-thyroid medications indicated only if persistence of thyrotoxicosis beyond 18 to 20 wga
Management of hyperthyroidism in pregnancy

- Thionamide is the mainstay treatment
- PTU is used more frequently than methimazole
- Methimazole may be teratogenic
- Reported anomalies - cutis aplasia, choanal atresia, gastrointestinal, and facial abnormalities
Anti-thyroid drugs in pregnancy

- All anti-thyroid drugs can cross placenta
- Cause fetal hypothyroidism
- Lowest possible dose should be used
- To achieve a maternal FT4 slightly more than normal level
Novel therapy

CLINICAL REPORT

Thyroid arterial embolization for the treatment of hyperthyroidism in a patient with thyrotoxic crisis

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Thyroid artery embolization

- Zhao et al reported treatment of 41 patients with hyperthyroidism using thyroid arterial embolization

- 38 patients who had been followed up for 1-3 years

- 27 became euthyroid (71.1%), 4 improved (10.5%) with reduced dosage of antithyroid drugs for maintenance and 7 recurred (18.4%)

THANK YOU & GOOD LUCK IN EXAM!