ENDORAMA: THE THYROID AND PERSISTENT ATRIAL FIBRILLATION

DISHA KUMAR NARANG, M.D.
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OUR PATIENT

- 51-year-old woman presents to the ER with a 3-day history of shortness of breath and chest tightening
HISTORY OF PRESENT ILLNESS

• The patient was diagnosed with Graves’ disease in 2010, and took methimazole 20mg TID and propranolol 40mg TID until 2012, when she self-discontinued it after experiencing mild hair loss.

• 3-4 days ago, she started experiencing SOB, chest tightness, agitation, palpitations, heat intolerance, and RUQ pain.
REVIEW OF SYSTEMS

- Constitutional: Negative fevers, chills, night sweats, weight loss, cold intolerance; **heat intolerance**
- HEENT: Negative for headaches, blurry vision, double vision, tinnitus, rhinorrhea, sore throat
- Respiratory: Negative for cough, wheezing
- Cardiovascular: **chest tightness, SOB, light headedness, palpitations**
- GI: **abdominal pain, nausea, vomiting**; negative for diarrhea, constipation
- GU: Negative for urinary frequency, hematuria
- Skin: Negative for diaphoresis, rash
- Neuro: Negative for weakness, numbness, tingling
- Psych: **Agitation**; negative for depression
PHYSICAL EXAM

• VS: T 36.9°C; HR 130; BP 104/71; RR 22; SaO2 100% RA; BMI 36.28

• General: Appears anxious; cooperative
• HEENT: PERRLA; no scleral icterus; clear oropharynx; moist MM; +thyroid bruit; diffuse thyromegaly with no palpable nodules; non-tender
• CV: irregularly irregular rhythm; tachycardic; no extra heart sounds
• Resp: Good respiratory effort; mild bibasilar crackles
• Abd: RUQ tenderness; soft; positive bowel sounds
• MSK: Moving all extremities; no LE edema
• Skin: warm, dry; slightly velvety-appearing skin
• Psych: Agitated
PATIENT HISTORY

- Past Medical History
  - Graves’ Disease
- Surgical History
  - Cholecystectomy
- Medications
  - Vicodin prn
  - Docusate prn
- Allergies
  - NKA

- Family History
  - Mother: Thyroidectomy (reason unknown)
  - Grandmother: Uterine cancer

- Social History
  - Works as a rehabilitation aid and CNA
  - Lives with daughter
  - Denies tobacco/EtOH/illicit
ER COURSE

- Atrial fibrillation with HR 180s
  - Treated with metoprolol 10mg IV, diltiazem 10mg IV
  - Mild improvement of HR to 140s
## Burch and Wartofsky Criteria

Table 2
Semiquantitative scale assessing the presence and severity of the most common signs and symptoms

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thermoregulatory Dysfunction</strong></td>
<td></td>
</tr>
<tr>
<td>Temperature 99°–99.9°F (37.2°–37.7°C)</td>
<td>5</td>
</tr>
<tr>
<td>Temperature 100°–100.9°F (37.8°–38.2°C)</td>
<td>10</td>
</tr>
<tr>
<td>Temperature 101°–101.9°F (38.3°–38.8°C)</td>
<td>15</td>
</tr>
<tr>
<td>Temperature 102°–102.9°F (38.9°–39.3°C)</td>
<td>20</td>
</tr>
<tr>
<td>Temperature 103°–103.9°F (39.4°–39.9°C)</td>
<td>25</td>
</tr>
<tr>
<td>Temperature &gt;104°F (40°C) or higher</td>
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<tr>
<td><strong>Central Nervous System Effects</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild agitation</td>
<td>10</td>
</tr>
<tr>
<td>Delirium, psychosis, lethargy</td>
<td>20</td>
</tr>
<tr>
<td>Seizure or coma</td>
<td>30</td>
</tr>
<tr>
<td><strong>Gastrointestinal Dysfunction</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea, nausea, vomiting, abdominal pain</td>
<td>10</td>
</tr>
<tr>
<td>Unexplained jaundice</td>
<td>20</td>
</tr>
<tr>
<td><strong>Cardiovascular Dysfunction (beats/min)</strong></td>
<td></td>
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<tr>
<td>90–109</td>
<td>5</td>
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<tr>
<td>110–119</td>
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<tr>
<td>120–129</td>
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</tr>
<tr>
<td>130–139</td>
<td>20</td>
</tr>
<tr>
<td>≥140</td>
<td>25</td>
</tr>
<tr>
<td><strong>Congestive Heart Failure</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Mild (edema)</td>
<td>5</td>
</tr>
<tr>
<td>Moderate (bibasilar rales)</td>
<td>10</td>
</tr>
<tr>
<td>Severe (pulmonary edema)</td>
<td>15</td>
</tr>
<tr>
<td><strong>Atrial Fibrillation</strong></td>
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</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
</tr>
<tr>
<td><strong>History of Precipitating Event</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>10</td>
</tr>
</tbody>
</table>
## Burch and Wartofsky Criteria

### Thermoregulatory Dysfunction
- Temperature 99°–99.9°F (37.2°–37.7°C): 5
- Temperature 100°–100.9°F (37.8°–38.2°C): 10
- Temperature 101°–101.9°F (38.3°–38.8°C): 15
- Temperature 102°–102.9°F (38.9°–39.3°C): 20
- Temperature 103°–103.9°F (39.4°–39.9°C): 25
- Temperature >104°F (40°C) or higher: 30

### Central Nervous System Effects
- Absent: 0
- Mild agitation: 10
- Delirium, psychosis, lethargy: 20
- Seizure or coma: 30

### Gastrointestinal Dysfunction
- Absent: 0
- Diarrhea, nausea, vomiting, abdominal pain: 10
- Unexplained jaundice: 20

### Cardiovascular Dysfunction (beats/min)
- 90–109: 5
- 110–119: 10
- 120–129: 15
- 130–139: 20
- >140: 25

### Congestive Heart Failure
- Absent: 0
- Mild (edema): 5
- Moderate (bibasilar rales): 10
- Severe (pulmonary edema): 15

### Atrial Fibrillation
- Absent: 0
- Present: 10

### History of Precipitating Event
- Absent: 0
- Present: 10

### Score
- Thermoregulatory Dysfunction: 0
- CNS Effects: 10
- GI/Hepatic Dysfunction: 10
- Cardiovascular dysfunction (tachycardia): 25
- Heart Failure: 10
- Precipitant History: 10

**Score: 65**
**LABORATORY RESULTS**

<p>| | | | |</p>
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<td><strong>106</strong></td>
<td><strong>10</strong></td>
<td><strong>9.3</strong></td>
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<tr>
<td><strong>3.9</strong></td>
<td><strong>21</strong></td>
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<td><strong>87</strong></td>
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<td><strong>6.7</strong></td>
<td><strong>3.7</strong></td>
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<tr>
<td><strong>0.6</strong></td>
<td><strong>0.2/0.4</strong></td>
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<tr>
<td><strong>107</strong></td>
<td><strong>117</strong></td>
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<tr>
<td><strong>190</strong></td>
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</tr>
</tbody>
</table>

- CK – 70
- CK-MB – 1.8
- Troponin-T – <0.03
- Pro-BNP – 718
- Cortisol – 16.9
- Urine pregnancy test – Negative
<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
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<tbody>
<tr>
<td>TSH</td>
<td>0.01</td>
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<tr>
<td>Free T4</td>
<td>4.88</td>
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<tr>
<td>T4</td>
<td>18.0</td>
</tr>
<tr>
<td>T3</td>
<td>310</td>
</tr>
<tr>
<td>Free T3</td>
<td>1145</td>
</tr>
<tr>
<td>Thyroglobulin Ab</td>
<td>&lt;0.4</td>
</tr>
<tr>
<td>TPO Ab</td>
<td>&gt;20</td>
</tr>
<tr>
<td>TSI</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Thyrotropin Receptor Ab</td>
<td>2.35</td>
</tr>
</tbody>
</table>
THYROID ULTRASOUND

- Right lobe: 5.5 x 2.3 x 2.2 cm
- Left lobe: 7.0 x 2.6 x 2.5 cm
- Isthmus: 1.0 cm
- Enlarged, heterogeneous gland with mildly increased vascularity and no discrete nodule
INITIAL MANAGEMENT

- Initiated on Propylthiouracil 600mg, and transitioned to PTU 200mg q4 hours
- Hydrocortisone 100mg IV q8 hours
- HR only mildly improved with propranolol, metoprolol, and diltiazem
  - Patient started on esmolol drip
  - Transitioned to diltiazem drip
**DAY OF ADMISSION 2**

- Patient appeared more lethargic
- SSKI 5 drops q 4 hours initiated

<table>
<thead>
<tr>
<th>Thyroid Labs</th>
<th>3/4/15</th>
<th>3/6/15</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Free T4</td>
<td>4.88</td>
<td>3.48</td>
</tr>
<tr>
<td>T3</td>
<td>310</td>
<td>125</td>
</tr>
</tbody>
</table>
TTE

- LV performance moderately-severely reduced
- LV normal in size, with no LV thrombus
- EF is 34.4%
- Flattened septum is consistent with RV pressure and volume overload
- RV is moderately dilated
- RV performance is moderately reduced
- Right atrium is severely dilated
- No valvular abnormalities or pericardial effusion
TTE (2010)

- LV size normal
- Normal LV systolic performance
- Normal ventricular wall thickness
- No LV wall motion abnormalities
- RV size normal
- Normal RV systolic performance
- Trace tricuspid regurgitation, but structurally normal tricuspid valve
- Moderate pulmonary hypertension
CARDIOLOGY CONSULT

- Severe biventricular dysfunction
- Concern for negative inotropy and deterioration into cardiogenic shock from current treatment of atrial fibrillation
  - CVPs ~19
  - SVO2 50s-60s
- Diuresis initiated for heart failure exacerbation
WHAT ABOUT HER ATRIAL FIBRILLATION?

- The patient continued to be in A.fib with RVR with HR 160s-180s
- No improvement with weaning down of propranolol, addition of Digoxin
CLINICAL QUESTIONS

• Why is the patient continuing to have atrial fibrillation with RVR, despite trending towards euthyroidism? Is this underlying cardiac dysfunction?

• What other options do we have to make the patient clinically less toxic?
# TFT TREND

<table>
<thead>
<tr>
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<tbody>
<tr>
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<td>&lt;0.01</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Free T4</strong></td>
<td>4.88</td>
<td>3.48</td>
<td>3.35</td>
<td>2.81</td>
<td>2.61</td>
<td>1.91</td>
</tr>
<tr>
<td><strong>T3</strong></td>
<td>310</td>
<td>125</td>
<td>149</td>
<td>126</td>
<td>114</td>
<td>83</td>
</tr>
</tbody>
</table>

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<thead>
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<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>HR</strong></td>
<td>136</td>
<td>132</td>
<td>163</td>
<td>165</td>
<td>181</td>
<td>76</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>105/89</td>
<td>125/85</td>
<td>140/108</td>
<td>143/93</td>
<td>125/94</td>
<td>150/74</td>
</tr>
</tbody>
</table>
ATRIAL FIBRILLATION IN THE POST-THYROTOXIC STATE

- Retrospective study of 163 patients with thyrotoxic atrial fibrillation
  - 101 patients had spontaneous reversion of atrial fibrillation to sinus rhythm
  - 62 patients had persistent atrial fibrillation
    - ¾ of those with spontaneous reversion had conversion to NSR within 3 weeks of becoming euthyroid
    - No spontaneous reversion occurred if atrial fibrillation was still present after the patient had been in a euthyroid state for 4 months

- Spontaneous reversion of atrial fibrillation to sinus rhythm is unlikely if duration of atrial fibrillation before the euthyroid state is achieved exceeds 13 months, or if it is still present after the patient has been in a euthyroid state for 4 months
THYROID STORM

- First described by Lahey in 1926 as “crisis of exophthalmic goiter”\(^2\)
- Even with early diagnosis, mortality 10-30%
  - Multiple organ failure is most common cause of death, followed by CHF, respiratory failure, arrhythmia, DIC, GI perforation, brain hypoxia, and sepsis
## TREATMENT

<table>
<thead>
<tr>
<th>Therapy against new thyroid hormone production</th>
<th>Oral Dose</th>
<th>Rectal Dose</th>
<th>Intravenous Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propylthiouracil</td>
<td>Loading dose of 500-1000 mg followed by 250 mg every 4 hours</td>
<td>400-600 mg every 6 hours</td>
<td></td>
</tr>
<tr>
<td>Methimazole</td>
<td>60-120 mg per day in 4-6 doses</td>
<td>20-40 mg every 8-6 hours</td>
<td>10-30 mg every 8-6 hours</td>
</tr>
<tr>
<td>Therapy against thyroid hormone release</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSKI</td>
<td>5 drops every 6 hours</td>
<td>250-500 mg every 6 hours</td>
<td></td>
</tr>
<tr>
<td>Lugol’s solution</td>
<td>8 drops every 6 hours</td>
<td>80 drops per day/5-10 drops every 8-6 hours</td>
<td></td>
</tr>
<tr>
<td>Sodium iodide</td>
<td></td>
<td></td>
<td>0.5 g every 12 hours</td>
</tr>
<tr>
<td>Lithium</td>
<td>300 mg every 8-6 hours</td>
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<tr>
<td>Blocking the peripheral effects of thyroid hormone</td>
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<tr>
<td>Propranolol</td>
<td>60-120 mg every 4-6 hours</td>
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<tr>
<td>Esmolol</td>
<td></td>
<td></td>
<td>50-100 mcg/kg/min</td>
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<tr>
<td>Hydrocortisone</td>
<td></td>
<td></td>
<td>300 mg loading dose IV then 100 mg every 8 hours</td>
</tr>
<tr>
<td>Enhancing thyroid hormone clearance</td>
<td></td>
<td></td>
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<tr>
<td>Cholestyramine</td>
<td>1-4 g twice a day</td>
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</tbody>
</table>

Abbreviations: IV intravenous; SSKI, saturated solution of potassium iodine.
OTHER THERAPIES

- Plasma exchange
  - Rapidly reduces thyroid hormone levels
- IV TBG
- Oral iodinated contrast agents (used mainly as oral cholecystographic agents): Iopanoic acid
  - Potent inhibitors of both deiodinases D1 and D2
  - Lead to significant decrease of T3 levels, decrease new thyroid hormone production, prevent the release of preformed hormone from the gland, and reduce thyroid hormone effect
PLASMA EXCHANGE

• TBG (and other binding proteins) removed (with bound thyroid hormone and TSI), and albumin provides low-affinity binding of thyroid hormone

• First report of plasmapheresis in thyroid storm: 1970, by Ashkar et al

• Varying techniques of exchange transfusion: plasma exchange, single-pass albumin dialysis, charcoal hemoperfusion

• Most studies: decrease in free T3 and free T4

• Complications: Hypotension, hemolysis, anaphylaxis, coagulopathy, vascular injury, and infection
PLASMA EXCHANGE

- **Ezer, et al (2009)**: Largest plasma exchange series, with 11 patients with thyrotoxicosis undergoing preoperative preparation with TPE prior to thyroid or non-thyroidal surgery.
- After TPE, decline in biochemical values were not statistically significant.
- Signs and symptoms of thyrotoxicosis improved in all patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Before TPE</th>
<th>FT3 (pmol/L)</th>
<th>FT4 (pmol/L)</th>
<th>After TPE</th>
<th>FT3 (pmol/L)</th>
<th>FT4 (pmol/L)</th>
<th>Number of sessions</th>
<th>Solution</th>
<th>Complication</th>
<th>Cause</th>
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<td>1</td>
<td>16.7</td>
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<td>7.5</td>
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<td>None</td>
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<td>2</td>
<td>20</td>
<td>35</td>
<td>10.3</td>
<td>22.9</td>
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<td>None</td>
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<td>3</td>
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<td>FF</td>
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<td>None</td>
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<td>5</td>
<td>42.9</td>
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<td>FF</td>
<td>Allergic reaction</td>
<td>G</td>
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<td>6</td>
<td>8.5</td>
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<td>None</td>
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<td>41.8</td>
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<td>FF</td>
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<td>None</td>
<td>TNG</td>
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</table>

TPE, therapeutic plasma exchange; FT4, free thyroxin; FT3, free triiodothyronin; Alb, albumin; FF, fresh-frozen plasma; JB, Jod Basedow; TNG, toxic nodular goiter; G, Graves.
**PLASMA EXCHANGE**

- **Muller et al (2011)**: Suggestion of early initiation of TPE with following indications:
  - Severe symptoms (cardio-thyrotoxicosis, neurologic manifestations, myopathy, etc), rapid clinical deterioration, contraindications to other therapies, and failure of conventional therapies
  - 2 of the 3 patient cases had amiodarone-induced hyperthyroidism
GUIDELINES

- American Society of Apheresis (2010) guidelines
- TPE is grade IIc, category III
- Perform TPE daily to every 2-3 days until clinical improvement is noted
- Sample Free T3 and T4 before and after TPE
- TPE should be continued if clinical stabilization is seen regardless of hormone levels
- TPE is considered as an adjunct to medical therapy to provide clinical stabilization while awaiting drug efficacy or prior to definitive management with thyroidectomy
SURGICAL MANAGEMENT

- Standard protocol: Achieve euthyroidism prior to surgery
- Patients who require immediate surgery:
  - Fail medical management or clinically deteriorate
  - Develop side effects from treatment
  - Require expedient resolution of their hyperthyroidism due to severe underlying cardiac or pulmonary comorbidities

- Surgical preparation:
  - Iopanoic acid
  - Plasmapheresis

- Sholz et al.⁹: Long-term overall mortality of patients treated with thyroidectomy was 10%
  - Early surgical management may reduce mortality in selected patients
BACK TO OUR PATIENT

- Given new biventricular dysfunction and low SVO2, endocrine surgery was consulted for thyroidectomy.
- While symptomatically improved with diuresis, patient persisted in A.fib with RVR (HR 150s-170s).
- Consider amiodarone for management of A.fib?
TEE

- Left atrial appendage thrombus is present
- No evidence for ASD
- No valvular abnormalities
- No atheromatous disease of ascending aorta or aortic arch
CLINICAL COURSE

- The patient was attempted on the following for treatment of A.fib with RVR with no response:
  - Esmolol gtt
  - Propranolol
  - Verapamil
  - Diltiazem
- Sinus rhythm finally achieved on metoprolol XL 50mg BID and Digoxin 0.35mg qday
- Continued heart failure optimization
- Continued PTU and steroid wean
- Plan for thyroidectomy postponed due to atrial appendage clot
- Patient transferred to UIC due to lack of insurance coverage of heparin bridge to Warfarin
CONCLUSIONS

• If thyroid storm is suspected, start treatment early
• Alternative therapies such as plasmapheresis have mixed opinions on effectiveness
• Therapies such as iopanoic acid and IV thyroxine binding globulin are not approved in the US
• Consider surgical consultation for thyroidectomy early in a patient’s course if response to anti-thyroid treatment is delayed or refractory
• Patients must be optimized for heart failure in the setting of thyroid storm, as improvement in cardiac status will likely lag behind
REFERENCES