WEAK IN THE KNEES
ACUTE FLACCID PARALYSIS IN A YOUNG MALE

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MCMASTER UNIVERSITY
TED GILES CLINICAL VIGNETTES
CSIM ANNUAL MEETING
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CASE

ID: 31 year old male in ER
RFR: Lower extremity weakness
A: Mentating well, able to provide a history – no airway concerns
B: SpO2 99% (room air)
C: HR 120 beats/min, BP 190/110 mmHg

TRIAGE NOTE

PT WOKE THIS AM AT 0730HRS FEELING WEAK. PT TRIED TO AMBULATE OUT OF BED BUT FELL TO THE FLOOR, DENIES HITTING HEAD. PT STATES HE HAD A HEADACHE LAST NIGHT. PT DOES FEEL SOME NAUSEA, NO VOMITING. PT HAS LEG WEAKNESS, ARM WEAKNESS, CANNOT MOVE EXTREMITIES FREELY. JOINTS ARE STIFF. PUPILS EQUAL AND REACTIVE TO LIGHT.
HISTORY

• Was eating and drinking with some friends the night before: ate a grilled cheese sandwich x 2, drank 2 – 4 bottles of beer
• Went to sleep afterward ~midnight
• Woke up ~6h later – attempted to walk to the washroom
• Was able to get out of bed, but then collapsed (“my legs gave out”) – called for brother, who brought him to the ED
EXAM

• **Vitals:**
  - **BP:** 190/110 mmHg, **HR:** 120 BPM, **SpO$_2$:** 99%, **T:** 36.9

• **CVS:** Tachycardic, regular – S1/S2, no additional heart sounds, no murmurs

• **Resp:** Normal breath sounds bilaterally. RR 18

• **Abdo:** SNT
EXAM

Neurologic/MSK exam

- **General:** GCS 15, A/O x 3
- **CNs:** II-XII normal. No oculomotor/bulbar dysfunction
- **Sensory:** fully intact – sharp + dull
- **Motor:** lower extremity muscle groups: 3/5
- **Reflexes:** 2+ at patella
- **Tone:** no spasticity, no rigidity
- **UMN:** downward going toes
- **Gait:** deferred
- **Cerebellar:** normal rapid-alt.motions, unable to perform heel – shin. No dysmetria
**Interpretation:** Sinus rhythm, diffuse ST depressions with possible U wave formation
INVESTIGATIONS

Chemistry

- Na⁺: 139
- K⁺: 1.9
- Cl⁻: 103
- Cr: 50
- Urea: 1.9
- CK: 3853

VBG

- pH 7.37/pCO₂ 39/HCO₃ 23

CBC

- unremarkable

Severe hypokalemia with elevation in creatinine kinase. No overt acid/base abnormalities
CASE CONTINUED

- Approach to hypokalemia
  - **Extrarenal**: intake normal, no GI losses
  - **Renal**: no drugs affecting renal $K^+$ handling, 24h $K^+$ collection normal
  - **Shift**: no alkalosis
- $K^+$ replenished through IV and PO
- Normalized on repeat that evening (3.6)
- Improved strength + patient seen ambulating independently that evening
- Remained hypertensive and tachycardic
HYPERTENSION/TACHYCARDIA IN A YOUNG MALE

- **Drugs**
  - Sympathomimetics - cocaine, methamphetamines, amphetamines, energy drinks

- **Endocrinopathy**
  - Hyperthyroidism
  - Hyperaldosteronism
  - Pheochromocytoma/paragangliomas
  - Hypercortisolism/Cushing’s

- **Structural**
  - Renal artery stenosis
  - Coarctation of the aorta
  - CKD

- **“Appropriate”**
  - Anxiety
  - Pain
THE ANSWER...

<table>
<thead>
<tr>
<th>Thyroid testing</th>
<th>Value</th>
<th>Normals</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.01 mIU/L ▣</td>
<td>0.5 – 5.0 mIU/L</td>
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<tr>
<td>Free T4</td>
<td>29 pmol/L ▲</td>
<td>10-20 pmol/L</td>
</tr>
<tr>
<td>Free T3</td>
<td>21.0 pmol/L ▲</td>
<td>3.5-6.5 pmol/L</td>
</tr>
<tr>
<td>TRAB</td>
<td>405 U/L ▲</td>
<td>negative</td>
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</table>

- **Further history:** 40 lb unintentional weight loss in the last ~2 months
- **Family history:** “something to do with the thyroid” on his maternal side.

- **Other testing:** plasma renin/aldosterone ratios normal, dexamethasone suppression testing initially ordered but then cancelled. CT head + MRI spine initially considered, but cancelled
THYROID EXAMINATION

Examination of thyroid: Diffuse enlargement, nontender. No skin changes, no palpable nodules, no lymphadenopathy. No signs of obstructive goiter (SVC obstruction, distention of veins on chest).

Side note: pistol shot sounds heard along femoral arteries (picked up by endocrinology fellow) – indicative of **high cardiac output state**
IMAGING

Thyroid scintigraphy with I-131 administered orally and subsequent administration of Tc-99 (pertechnate). Avid trapping of pertechnate demonstrated within an enlarged thyroid gland, with diffuse nonuniformity consistent with…

GRAVE’S DISEASE
THYROTOXIC PERIODIC PARALYSIS

- **Definition:** a transient state of painless, flaccid paresis/paralysis secondary to hypokalemia mediated by thyrotoxicosis

- **Epidemiology**
  - Well described among East Asian, Japanese populations (1.8-1.9% of thyrotoxic patients)
  - In North American populations: 0.1-0.2% (but increasing)
  - Predominantly seen among men (as opposed to hyperthyroidism, which has a greater female preponderance)
  - Minimal genetic or epidemiologic features in common with familial hypokalemic periodic paralysis
  - Majority of cases associated with Graves’ disease
<table>
<thead>
<tr>
<th>Feature</th>
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<tbody>
<tr>
<td>✔ Adult young men</td>
</tr>
<tr>
<td>✔ Sporadic</td>
</tr>
<tr>
<td>✔ Recurrent acute paralysis with complete recovery</td>
</tr>
<tr>
<td>✔ Limb &gt; trunk involvement</td>
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<tr>
<td>✔ Precipitated by heavy carbohydrate load, high-salt diet, alcohol,</td>
</tr>
<tr>
<td>exertion</td>
</tr>
<tr>
<td>✔ Family history of hyperthyroidism</td>
</tr>
<tr>
<td>✔ Clinical features of hyperthyroidism</td>
</tr>
<tr>
<td>✔ Hypokalemia</td>
</tr>
<tr>
<td>✔ Normal acid-base balance</td>
</tr>
<tr>
<td>✔ Low potassium excretion rate</td>
</tr>
<tr>
<td>✔ Low phosphate excretion</td>
</tr>
<tr>
<td>✔ EMG: low-amplitude compound muscle action potential with no</td>
</tr>
<tr>
<td>change after epinephrine</td>
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</tbody>
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Pathophysiology: hypermetabolic state leading to increased transcription and activity of the Na⁺/K⁺ ATPase pump

- Pump causes influx of 2 K⁺ ions and efflux of 3 Na⁺
- Leads to membrane hyperpolarization
- Failure of skeletal/striated muscle cells to depolarize and initiate action potentials
  - Action potentials in neurons seem to be unaffected
- Dysfunction in somatic control of large, proximal muscle groups
**TRIGGER?**

- Precipitants: trauma, cold exposure, alcohol, infections, carbohydrate-heavy meals
- Patient’s meal prior to admission:
Enrolled 20 Thai patients with a history of thyrotoxicosis and split them into two groups

- History of TPP
- No history of TPP

75g oral glucose tolerance test and euglycemic hyperinsulinemic clamp administered to both groups
Serum insulin levels of hyperthyroid patients during administration of 20% dextrose solution (euglycemic clamp).

- White: TPP
- Black: no TPP

...Role for compensatory hyperinsulinemia in TPP?
OUTCOME

- Patient was initiated on nadolol and methimazole while hospitalized – became clinically euthyroid and was discharged
- Followed up with endocrinology as an outpatient
- Chose radioiodine ablation of his thyroid 2-3 months after his initial admission for TPP
- Biochemically and clinically euthyroid at follow up 6 months after discharge
- No further attacks of periodic paralysis
TAKE HOME POINTS

• Thyrotoxic periodic paralysis (TPP) is an uncommon presentation of a common illness (hyperthyroidism)
• Predominantly seen in Asian populations, but prevalence in North American populations is increasing
• Metabolic causes of paralysis/paresis are not often high on the differential
• Thyrotoxicosis should be considered as a cause of acute flaccid paralysis, particularly in patients with a high pre-test probability
REFERENCES


7. Dias da Silva MR, Cerutti JM, Tengan CH et al. Mutations linked to familial hypokalaemic periodic paralysis in the calcium channel alpha1 subunit gene (Cav1.1) are not associated with thyrotoxic hypokalaemic periodic paralysis. Clin Endocrinol (Oxf) 2002;56:367-75

DISCLOSURES

No financial disclosures.
QUESTIONS?

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ACUTE APPENDICULAR PARALYSIS

- Infectious
  - Poliomyelitis
  - West Nile virus
  - Epidural abscess
  - Botulism
- Inflammatory
  - Multiple sclerosis
  - Guillain – Barre syndrome
  - Transverse myelitis
- Structural
  - Spinal cord infarct
  - Spinal cord injury
### TABLE 2. Distinguishing features between TPP and FHPP

<table>
<thead>
<tr>
<th></th>
<th>TPP</th>
<th>FHPP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>20–40</td>
<td>&lt;20</td>
</tr>
<tr>
<td>Sex distribution</td>
<td>Predominantly male</td>
<td>Equal</td>
</tr>
<tr>
<td>Heredity</td>
<td>Sporadic</td>
<td>Autosomal dominant</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Asian, American Indian/Hispanic, Caucasian</td>
<td>Caucasian, Asian</td>
</tr>
<tr>
<td>Family history</td>
<td>History of thyrotoxicosis</td>
<td>History with hypokalemic paralysis</td>
</tr>
<tr>
<td>Clinical features of hyperthyroidism</td>
<td>Associated with SNPs of Ca,1.1 (−476A→G, intron 2 nt 57G→A, intron 26 nt 67A→G)</td>
<td>No</td>
</tr>
<tr>
<td>Genetic predisposition</td>
<td>Yes</td>
<td>Mutations of Ca,1.1 (R5258H, R1239H, R1239G), Na,1.4 (R669H, R672G, R672H), K,3.4 (R83H)</td>
</tr>
</tbody>
</table>
Patients with TPP usually experience the attack a few hours after a heavy meal or in the early morning upon waking: more than two thirds of patients present to the emergency department between 2100 and 0900 h. Such timing of presentation led the condition to be initially described as nocturnal paralysis or night palsy (16). Patients may give a history of similar but milder attacks before presentation.

Electromyogram (EMG) performed during spontaneous weakness typically reveals myopathic changes with reduced amplitude of compound muscle action potentials (34). There is no notable change in the amplitude on epinephrine stimulation. Nerve conduction studies are normal with no peripheral nerve involvement. Similar to FHPP, exercise can
COMPARISON OF CELLULAR ACTION POTENTIALS

Action Potentials from 3 Vertebrate Cell Types

Note the different time scales
Hyperthyroidism and thyrotoxicosis workup. Medscape.