Exercise and a high carbohydrate diet can lead to paralysis
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INTRODUCTION

- Thyrotoxic periodic paralysis (TPP) is a rare but potentially life-threatening complication of hyperthyroidism which is usually seen among the Asian population.
- With recent globalization and immigration, the incidence of TPP has been reported more frequently among different ethnic groups.
- It is important for clinicians to understand this disease because it is easily reversible and recurrent events are preventable when recognized and appropriately treated.

CASE

- A 21 years old Hispanic male presented to the emergency room with acute onset of generalized weakness which was worse in the bilateral lower extremities. On the day of admission, he played five hours of basketball in the morning. He denied any trauma, tick bites, flu-like symptoms, prior history of weakness or family history of paralysis.
- Physical exam: BP 145/85, HR 104, O2sat 95%
- HEENT: Lid lag, exophthalmos, bilateral thyroid enlargement
- Heart/lung: Tachycardia, no M/G/R, CTA
- Neuro: 1/5 motor strength in the lower extremities and 2/5 motor strength in the upper extremities
- Deep tendon reflex of the biceps, triceps, patella and ankles was absent. Sensation was intact throughout.
- Skin: Warm and moist
- Studies/labs:
  - EEG: ST segment depression, decreased amplitude T wave and possible U waves
  - Hypokalemia of 1.3, hypophosphatemia of 1.5 and hypomagnesium of 1.7
  - Suppressed TSH < 0.03 mIU/mL, elevated free T4 5.98 ng/dL
  - ETOH negative and urine toxicity screen was negative
- Hospital course:
  - The patient was treated with intravenous potassium and phosphate, and his weakness improved.
  - Prior to starting his antithyroid medication, patient left against medical advice.
  - Patient was re-admitted one year later due to another paralysis attack.

Thyrotoxic Periodic Paralysis

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Thyrotoxic Periodic Paralysis</th>
<th>Hypokalemic Periodic Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–40</td>
<td>20–20</td>
<td>≥20</td>
</tr>
<tr>
<td>Sex distribution</td>
<td>Predominantly male (M:F 20:1)</td>
<td>Equal</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 thyroid disease</td>
<td>History of hypokalemic paralysis</td>
</tr>
<tr>
<td>Precipitating factors</td>
<td>Yes (carbohydrate load, exertion, ETOH)</td>
<td>Yes (carbohydrate load, exertion, ETOH)</td>
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<tr>
<td>Clinical feature</td>
<td>Proximal muscle weakness, Limb/trunk hyperreflexia, sensation intact</td>
<td>None</td>
</tr>
<tr>
<td>Labs</td>
<td>Hypokalemia, low urine potassium excretion</td>
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</tr>
<tr>
<td>Genomic predisposition</td>
<td>Associated with SNP’s of Cav1.1 (476AG, intron 2 nt 57GA, intron 2 nt 67AGA) and newly discovered Kir 2.6 (potassium channel mutation)</td>
<td>Mutations of Ca_{v} 1.1 (R5258H, R1239H, R1239G), Na_{v} 1.4 (R669H, R672G, R672H), Kir 3.4 (R538H)</td>
</tr>
</tbody>
</table>

Thyrotoxic Periodic Paralysis

Patient noted to have lid lag and exophthalmos on exam

PATHOPHYSIOLOGY

The exact mechanism of paralysis is not well characterized but is believed to be a result of acute intracellular shift in potassium into muscle cells rather than depletion of total body potassium.

Mechanism if associated with hyperthyroidism:
- Thyroid hormones can directly stimulate Na-K (ATPase).
- Patient with TPP has higher pump activity than a patient without TPP. Pump activity level returns to normal in an euthyroid state.
- Amplify the response to beta adrenergic stimulation. This may explain why nonselective beta blockers can abort attacks and stressful events can initiate one.
- Severity of hyperthyroidism does not correlate to cause or the severity of attacks.
- Thyroid hormones may regulate different ion channel genes.

Why does high carbohydrates lead to attacks?
- Insulin induces potassium shift into the cell.
- TPP patients have exaggerated insulin response to CHO.
- Insulin up-regulates transcription of ATPase gene.

Why exercise induces TPP
- Exercise releases potassium from skeletal muscle and rest leads to influx of potassium.

TREATMENT

Emergency therapy:
- Potassium replacement usually reverses paralysis.
- Avoid rebound hyperkalemia (40% of case series).
- Propranolol may reverse paralysis and can be used if potassium replacement fails. More studies are needed before using it as the sole form of therapy.
- Prevention:
  - Prevention of recurrent attacks requires restoration to a euthyroid state and avoiding precipitating events.
  - Propranolol, a nonselective beta blocker, may help prevent recurrent events when euthyroid state is not yet achieved.

References: References are provided in a separate sheet.