A Rare Cause of Sudden Progressive Weakness

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Case Presentation

- 60 YOWM with CAD, ankylosing spondylitis presents with severe weakness
History of Present Illness

• The patient is on vacation in Gulf Shores with his family when he develops:
  • Acute proximal muscle pain and weakness
  • Rapidly progressive:
    • Independent \(4\) days \(\rightarrow\) Unable to walk
  • Persistent nausea and emesis
  • Anorexia
Past Medical and Surgical History:

• CAD s/p PCI 4 months ago
• Atrial flutter s/p ablation
• HTN
• Hurthle Cell Carcinoma of the thyroid
  • s/p thyroidectomy
• Ankylosing spondylitis
• Lumbar spinal stenosis
• CKD stage IIIb
Medications

• Long term medications:
  • Adalimumab 40 mg every 2 weeks
  • Aspirin
  • Methylprednisolone 4 mg daily
  • Levothyroxine
  • Hydrocodone-apap

• New medications
  • Rosuvastatin
  • Prasugrel
  • Metoprolol
Physical Exam

- Afebrile, HR 85 bpm, RR 18 bpm, BP 130/85 mmHg

- General: No acute distress, thoracic kyphosis, forward stoop of the neck

- MSK: Proximal muscle atrophy.

Admission Evaluation

- CK 7421, UA sp g 1.008, 3+ blood, 0 RBCs
- MRI of lumbar spine: No evidence of cord compression, mass, hematoma.
Hospital Course

• Admitted to OSH, where statin was stopped and he was aggressively fluid resuscitated

• Kidney function continued to worsen, CK remained elevated, weakness progressed, and he developed respiratory distress

• Transferred to UAB
Hospital Course

• Hemodialysis was initiated shortly after arrival due to volume overload and uremia

• Rheumatology consulted for persistently elevated CK and worsening weakness

• EMG obtained which showed subacute irritable myopathy

• Muscle biopsy was obtained
Muscle Biopsy

H&E stain reveals atrophic and necrotic myofibers undergoing phagocytosis. No inflammation or evidence of vasonecrosis.
Older man presents with rapidly progressive weakness two months after initiation of statin therapy. Evaluation is notable for markedly elevated CK, AKI requiring HD.

- Weakness and elevated CK persist after statin is discontinued.
- EMG reveals subacute irritable myopathy
- Biopsy shows necrosis without inflammation

Diagnosis: Statin-induced Immune-Mediated Necrotizing Myopathy (IMNM)
Hospital Course

• Pt started on prednisone 60 mg daily. CK down trended to 400, but weakness continued to progress

• After 10 days of steroids without improvement, he was started on mycophenolate 500 mg BID

• Strength began improving almost immediately

• Mycophenolate was continued for 12 days
Case Resolution

• Patient was discharged to acute rehab facility with aggressive PT and slow steroid taper

• Continues to receive adalimumab every 2 weeks

• AKI improved and HD stopped 2 weeks after discharge from rehab

• Strength improved and now ambulating with a cane
## Types of Statin Muscle Interactions

<table>
<thead>
<tr>
<th>Class</th>
<th>Characteristics</th>
<th>Laboratory changes</th>
<th>Muscle symptoms</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRM 0</td>
<td>Asymptomatic</td>
<td>Increase in CK &lt;4x UML</td>
<td>None</td>
<td>1.5-26%</td>
</tr>
<tr>
<td></td>
<td>CK elevation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SRM 1</td>
<td>Tolerable Myalgia</td>
<td>No CK elevation</td>
<td>Mild</td>
<td>0.3-33%</td>
</tr>
<tr>
<td>SRM 2</td>
<td>Intolerable Myalgia</td>
<td>CK 4-10 x ULN</td>
<td>Significant</td>
<td>0.1-1/1000</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SRM 3</td>
<td>Myopathy</td>
<td>CK 10-50x ULN</td>
<td>Variable</td>
<td>5/100,000 patient years</td>
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Adapted from Babu, et al.
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<tr>
<td>SRM 4</td>
<td>Severe myopathy</td>
<td>Increase in CK &lt;4x UML</td>
<td>Significant</td>
<td>0.11%</td>
</tr>
<tr>
<td>SRM 5</td>
<td>Rhabdomyolysis</td>
<td>CK &gt; 10x ULN + renal impairment or CK &gt;50 x ULN</td>
<td>Significant</td>
<td>0.1-8.4 /100,000 patient years</td>
</tr>
<tr>
<td>SRM 6</td>
<td>IMNM</td>
<td>Variable</td>
<td>Incomplete resolution upon DC</td>
<td>~2/million per year</td>
</tr>
</tbody>
</table>

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When to Suspect IMNM

- Persistently elevated or rising CK, AST, ALT after statin is discontinued
- Muscle symptoms persisting at least 12 weeks after statin is discontinued
- EMG with muscle irritability in absence of other explanations
- MRI with diffuse muscle edema
- Muscle biopsy showing necrotizing myopathy with little to no inflammation
Diagnosis of IMNM

• Electromyography: Detects myopathy and shows chronicity, distribution, and degree of severity

• Muscle Biopsy: Exclude other diagnoses such as dystrophy or metabolic myopathy

• MRI: Optional, allows evaluation of extent of muscle involvement and helps optimize biopsy location

• Serology: HMG-CoA reductase Ab
Management of IMNM

• 1st: Steroids

• 2nd: Methotrexate, azathioprine, mycophenolate, rituximab

• Refractory myopathy: IVIG
Key Points

• Recognize immune mediated necrotizing myopathy as a rare but serious adverse effect of statin therapy

• Understand the diagnosis and management of this complication


Questions?

- Tinsley Harrison Internal Medicine Residency Program