Heparin-Induced Thrombocytopenia causing Adrenal Insufficiency

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Objective

- Describe mechanism of HIT
- Describe a rare presentation of adrenal insufficiency
Heparin-Induced Thrombocytopenia (HIT)

- An immune-mediated adverse reaction to heparin products
  - Resulting in paradoxical thrombus formation
  - Autoantibody IgG against PF4–heparin complex
- Occurs in up to 5.0% of patients receiving heparin products \(^1\)
- Thrombosis occurs in 35-50% of patients
  - As high as 50-89% in those left untreated \(^2\)
Presentation

- HIT typically presents within 5 to 10 days of first exposure
  - Typically presents in 1-5 days with re-exposure
- Common:
  - Deep vein thrombosis of the extremities
  - Pulmonary emboli
- Rare:
  - Arterial thrombosis
  - Stroke
  - Myocardial infarction
  - Cerebral vein thrombosis
  - Adrenal vein thrombosis
Use the 4T score when suspecting HIT:

- **Thrombocytopenia**: new-onset, % drop in platelet count, platelet nadir
- **Timing**: onset within 5-10 days with current heparin use
- **Thrombosis or other sequela** (skin necrosis, recurrent thrombosis)
- Another cause for **Thrombocytopenia**

Confirmed with anti-PF4-heparin antibody and serotonin-release assay
<table>
<thead>
<tr>
<th>Category</th>
<th>2 Points</th>
<th>1 Point</th>
<th>0 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>• Platelet count fall &gt; 50% AND</td>
<td>• Platelet count fall 30%-50% OR</td>
<td>• Platelet count fall &lt; 30% OR</td>
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<tr>
<td></td>
<td>• Platelet nadir ≥ 20,000</td>
<td>• Platelet nadir 10-19,000</td>
<td>• Platelet nadir &lt; 10,000</td>
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<tr>
<td>Timing of platelet count fall</td>
<td>• Clear onset between days 5 and 10 OR</td>
<td>• Consistent with days 5-10 fall, but not clear or onset after day 10 OR</td>
<td>• Platelet count fall &lt; 4 days without recent heparin exposure</td>
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<tr>
<td></td>
<td>• Platelet fall ≤ 1 day (prior heparin exposure w/in 30 days)</td>
<td>• Fall ≤ 1 day (prior heparin exposure 30-100 days ago)</td>
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<tr>
<td>Thrombosis or other sequelae</td>
<td>New thrombosis or skin necrosis at heparin injection sites or acute</td>
<td>Progressive or recurrent thrombosis or nonnecrotizing (erythematous)</td>
<td>None</td>
</tr>
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<td></td>
<td>systemic reaction after intravenous heparin bolus</td>
<td>(skin lesions or suspected thrombosis</td>
<td></td>
</tr>
<tr>
<td>Other causes for thrombocytopenia</td>
<td>None apparent</td>
<td>Possible</td>
<td>Definite</td>
</tr>
</tbody>
</table>

≤ 3 = Low probability for HIT  
4 - 5 = Intermediate probability of HIT  
≥ 6 = High probability of HIT

The Case

- 63-year-old female with a history of hypertension and hypothyroidism who presented 10 days after a routine total knee replacement with a 4-day history of worsening dyspnea, nausea, vomiting, abdominal pain, diaphoresis, and fatigue.
- Discharged home on LMWH for DVT prophylaxis
On initial presentation to the ED:

- Vitals: BP 110/71 HR 98 RR 18 O2 97% on RA
- Pertinent positives on exam:
  - Appeared pale, dry mucous membranes, moderate abdominal distension, well-healed incision of R knee
Clinical Workup

- High suspicion for HIT given a 60% platelet drop 10 days after starting heparin
  - 197,000 > 82,000
  - **4T score** was 8 – high pretest probability for HIT
- Heparin was discontinued and **Argatroban** was started
- **PF4 antibody** positive – high probability for HIT
- **SRA assay** 100% positive in the presence of low-dose heparin
CTA chest: no pulmonary emboli
CT abdomen/pelvis: enlargement of bilateral adrenal glands with fat stranding
  Suspicious for bilateral adrenal hemorrhages
Doppler ultrasound of the lower extremities were negative for DVT
A plasma cortisol level was < 1.0 ug/dL x2 one day apart
Highly concerning for adrenal insufficiency
Treatment

- Patient was treated with steroids
  - **Hydrocortisone** 50 mg every 8 hours
  - Tapered slowly during her hospital stay
- Symptoms improved shortly after starting this medication
- Treated with **Argatroban** and her platelet count returned to normal within several days
- Transitioned to **Warfarin** and discharged home
- Her platelet count was **280,000** on discharge
Follow-up

- Patient presented to outpatient Endocrinology clinic a few days after discharge
- Worsening nausea, fatigue and low SBP in the mid-90s
  - Positive orthostatic vitals
- Downtrending Na (129) and uptrending K (5.0)
- Started on Fludricortisone 100 mcg daily in addition to Hydrocortisone 20 mg qAM and 10 mg qHS
- Her symptoms subsequently resolved
This presentation of adrenal insufficiency is rare

- Our case is rare in particular – no adrenal crisis

A literature review in 2012: seventeen individual cases of bilateral adrenal hemorrhage secondary to HIT

- Overall mortality of 27.5%
- Mortality was 100% in the 3 cases where adrenal insufficiency went unrecognized

- Majority of patients were post-surgical, typically orthopedic procedures
- Majority were hypotensive or in shock on presentation
Mechanism

- Bilateral adrenal hemorrhage in the context of HIT
- Suspected to be secondary to an adrenal vein thrombosis
- Adrenal vascular anatomy is susceptible to hemorrhage – over 60 arterioles and one central outflow vein
- An autopsy of one case confirmed that the pathology of hemorrhage was due to a venous thrombus
- Can be visualized on CT scan with contrast
Another proposed mechanism:

High catecholamine surge during times of stress induces an adrenal vein spasm

Adrenal vein spasm leading to venous stasis and further risk of thrombus formation

Assumed to occur with patients in shock
Adrenal Recovery

- It is not well-documented if adrenal recovery is possible in bilateral adrenal hemorrhage secondary to HIT.
- One case in the literature demonstrated recovery after weaning steroids over 3 months.
- Our patient continues to require steroid replacement > 1 year since initial presentation.
Heparin-induced thrombocytopenia causing adrenal hemorrhage is a particularly difficult situation for providers as it forces counterintuitive decision making, to anticoagulate a patient with an active hemorrhage. Additionally, it is an interesting and fairly unrecognized presentation of adrenal insufficiency with a high associated mortality rate.
References


Thank you!