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

- Occurs in up to 5.0% of patients receiving heparin
- Thrombosis occurs in 25-50% of patients with HIT
- 10 times higher incidence among patients receiving UFH versus LMWH
HIT typically presents within 5 to 10 days of first exposure
  - Typically presents in 1-5 days with re-exposure

Common:
  - Thrombocytopenia
  - Deep vein thrombosis of the extremities
  - Pulmonary emboli

Rare:
  - Arterial thrombosis
  - Stroke
  - Myocardial infarction
  - Cerebral vein thrombosis
  - Adrenal vein thrombosis
Diagnosis

- 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**

![Score Table]

- \( \leq 3 \) = Low probability for HIT
- \( 4 - 5 \) = Intermediate probability of HIT
- \( \geq 6 \) = High probability of HIT
Diagnosis

- **Heparin-PF4 antibody**
  - Immunoassay detects a PF4-heparin antibody
  - High false-positive rate

- **Serotonin release assay**
  - Gold standard for diagnostic test
  - Sensitivity > 95%, Specificity > 95%
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 low-molecular weight heparin 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
Clinical Workup

- **SRA assay** 100% positive in the presence of low-dose heparin
- **Anti heparin-PF4 antibody** positive
- Confirming a heparin-induced thrombocytopenia in the setting of LMWH use
Clinical Workup

- Doppler ultrasound of the lower extremities were negative for DVT
- CTA chest: no pulmonary emboli
- CT abdomen/pelvis: incidental finding
  - Enlargement of bilateral adrenal glands with fat stranding
  - Suspicious for bilateral adrenal hemorrhages
Clinical Workup

- Given the CT findings:
- High concern for adrenal insufficiency

- A plasma cortisol level was < 1.0 ug/dL
  - Repeated the following day and was < 1.0 ug/dL again
Bilateral adrenal hemorrhage

Heparin-induced thrombocytopenia

To anticoagulate or not?
Literature Review

- 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 were hypotensive or in shock on presentation
  - Majority were post-surgical, typically orthopedic procedures
- Rare presentation of adrenal insufficiency
  - Our case is rare in particular – no adrenal crisis
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
  - “Vascular dam”
- An autopsy of one case confirmed that the pathology of hemorrhage was due to a venous thrombus
Another proposed mechanism:

- High catecholamine surge during times of stress inducing an adrenal vein spasm
- Adrenal vein spasm leading to venous stasis and further risk of thrombus formation
- Assumed to occur with patients in shock
Given the possibility of adrenal vein thrombosis
- 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

Patient was treated with steroids
- Hydrocortisone 50 mg every 8 hours
- Tapered slowly during her hospital stay
- Symptoms improved shortly after starting this medication
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
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.


Thank you!