

Heparin-Induced Thrombocytopenia causing Adrenal Insufficiency

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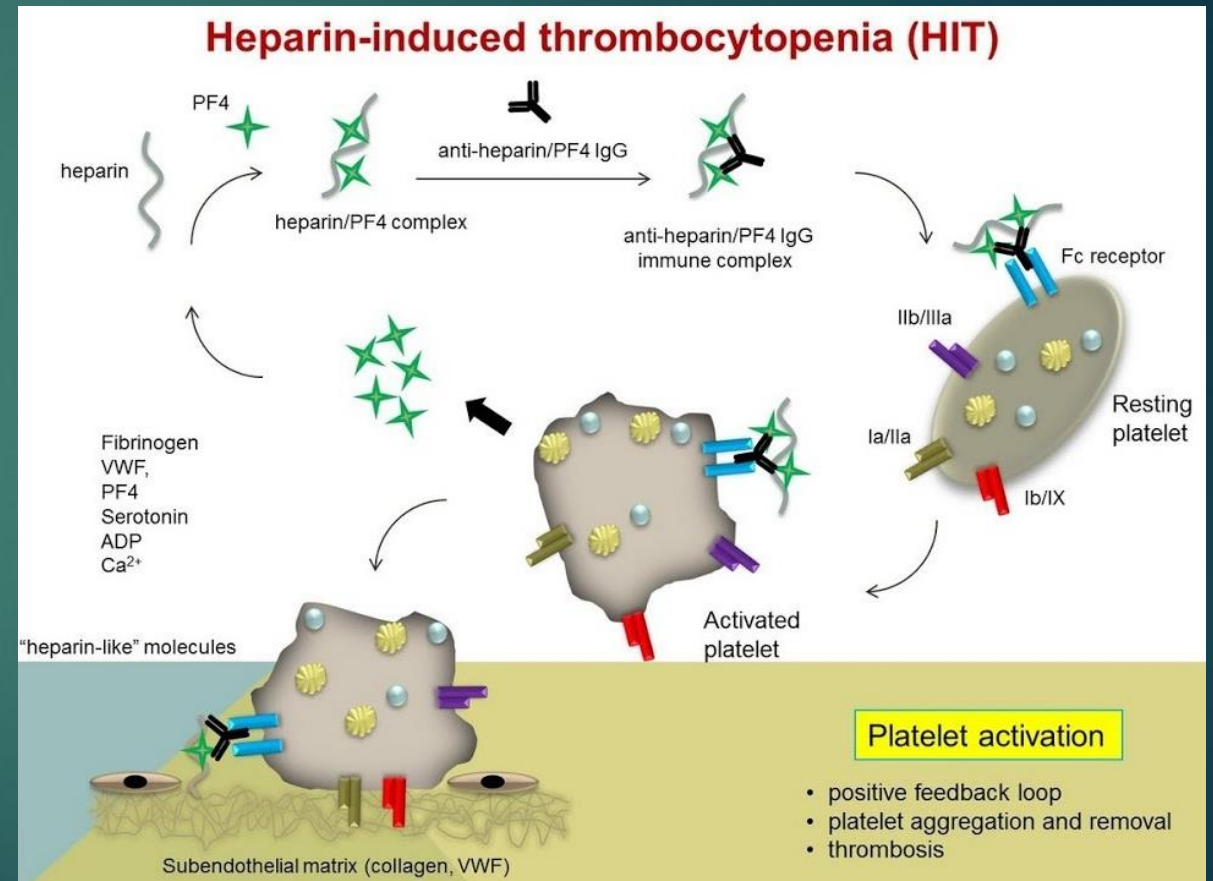
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Objective

- ▶ 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 ³
- ▶ Rare:
 - ▶ Arterial thrombosis
 - ▶ Stroke
 - ▶ Myocardial infarction
 - ▶ Cerebral vein thrombosis
 - ▶ Adrenal vein thrombosis

Diagnosis

- ▶ Use the 4T score when suspecting HIT:
 - ▶ **T**hrombocytopenia: new-onset, % drop in platelet count, platelet nadir
 - ▶ **T**iming: onset within 5-10 days with current heparin use
 - ▶ **T**hrombosis or other sequela (skin necrosis, recurrent thrombosis)
 - ▶ **T**hrombocytopenia not due to another cause
- ▶ Confirmed with anti-PF4-heparin antibody and serotonin-release assay

Pre-test Probability Scoring for Heparin-Induced Thrombocytopenia (The 4T Score)

Category	2 Points	1 Point	0 Points
Thrombocytopenia	<ul style="list-style-type: none"> • Platelet count fall > 50% AND • Platelet nadir \geq 20,000 	<ul style="list-style-type: none"> • Platelet count fall 30%-50% OR • Platelet nadir 10-19,000 	<ul style="list-style-type: none"> • Platelet count fall < 30% OR • Platelet nadir < 10,000
Timing of platelet count fall	<ul style="list-style-type: none"> • Clear onset between days 5 and 10 OR • Platelet fall \leq 1 day (prior heparin exposure w/in 30 days) 	<ul style="list-style-type: none"> • Consistent with days 5-10 fall, but not clear or onset after day 10 OR • Fall \leq 1 day (prior heparin exposure 30-100 days ago) 	<ul style="list-style-type: none"> • Platelet count fall < 4 days without recent heparin exposure
Thrombosis or other sequelae	New thrombosis or skin necrosis at heparin injection sites or acute systemic reaction after intravenous heparin bolus	Progressive or recurrent thrombosis or nonnecrotizing (erythematous) skin lesions or suspected thrombosis	None
Other causes for thrombocytopenia	None apparent	Possible	Definite

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

Adapted from: Lo GK, Juhi D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *J Thromb Haemost* 2006; 4: 759-65.

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

Initial Presentation

- ▶ 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

Clinical Workup cont.

- ▶ 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

Literature Review

- ▶ 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 ²
 - ▶ 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 ²
- ▶ Can be visualized on CT scan with contrast

Mechanism cont.

- ▶ 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 ⁴
- ▶ Our patient continues to require steroid replacement > 1 year since initial presentation

Conclusion

- ▶ 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

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Thank you!

