Coagulopathy Case - 6

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Clinical history: 53 y/o male with history of HTN, hyperlipidemia, no prior history of ischemic attacks

Patient had a near syncopy event while driving on I-10 in 5/02. Evaluation by cardiology: pos stress test, cardiac cath showed 3-vessel disease

Patient was admitted on 5/29/02, underwent 3-vessel CABG
## Laboratory tests

<table>
<thead>
<tr>
<th>Post-op day #</th>
<th>Platelet count</th>
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</thead>
<tbody>
<tr>
<td>4</td>
<td>183</td>
</tr>
<tr>
<td>5</td>
<td>143</td>
</tr>
<tr>
<td>6</td>
<td>90</td>
</tr>
</tbody>
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Differential Diagnosis

- DIC
- Heparin induced thrombocytopenia
DIC: normal parameters
Heparin-induced platelet aggregation (POD#6): Strong-positive

- NS 12%
- Hep (1 U/ml) 30%
- Hep (5 U/ml) 60%
- Hep (10 U/ml) 95%
# Platelet count follow-up

<table>
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<td>4</td>
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<tr>
<td>5</td>
<td>143</td>
</tr>
<tr>
<td>6</td>
<td>90 (Pos HIT, Heparin stopped)</td>
</tr>
<tr>
<td>7</td>
<td>73</td>
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<tr>
<td>8</td>
<td>82</td>
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<td>9</td>
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<tr>
<td>10</td>
<td>146</td>
</tr>
<tr>
<td>11</td>
<td>155</td>
</tr>
</tbody>
</table>
Diagnosis

- Heparin-induced thrombocytopenia (HIT)
Heparin Antibody: mechanism

- Anti-PF4/heparin, platelet-activating IgG
  - IgG Fc receptors
  - Platelet activation
  - Endothelial activation
  - Monocyte activation
  - Platelet-derived microparticles (procoagulant)
  - PF4 (neutralizes heparin)
  - Thrombin generation
  - Hypercoagulability state

- Platelet (and microparticle)-leukocyte — endothelial aggregates
- HIT-specific thrombosis ("white clot")

1) Venous and/or arterial thrombosis
2) Risk for warfarin-associated microvascular thrombosis, e.g., venous limb gangrene

Warkentin. Semin Thromb Hemost 2004
HIT

- Risk of HIT is higher with UFH than with LMWH
- Typical onset: 5 days after cardiac surgery
Typical-Onset

Platelet Count (x10^9/L)

- Cardiac Surgery
- Thrombosis

UFH, 5000 U q12h s.c.
Complications of HIT

- Venous thrombosis (50%)
- Arterial thrombosis (10-15%)
- Microvascular (5%), often warfarin-associated
Ischemic Limb Syndromes in HIT

White clot syndrome

Limb artery thrombosis

Acral necrosis

Warkentin J Crit Illn 2002
Heparin-induced Skin Lesions

Necrotizing lesions

Erythematous plaques

Warkentin Br J Haematol 1996
Microvascular thrombosis
(thrombosed venule)

Warfarin-induced Venous Limb Gangrene
(HIT $\rightarrow$ thrombin; warfarin $\rightarrow$ $\downarrow\downarrow$ Protein C)

palpable pulses

Testing for Heparin Antibody

- Heparin-induced platelet aggregation: sensitivity 70%, specificity 85%
- Serotonin release assay: sensitivity 80%, specificity 85%, limited use due to radioisotope ($^{14}$C)
- Heparin-PF4 antibody (ELISA): sensitivity 82%, specificity 70%
- Flow cytometry (investigative): HIT serum generates micro-particles from normal platelets
ELISA

Solid-phase Anti-PF4/heparin-ELISA
“Immunoassay”

Patient serum or plasma is added to microtiter plates coated with PF4 and heparin

Add alkaline phosphatase-conjugated goat antihuman IgG

Add substrate

COLOR

heparin
PF4
PF4/heparin complex
HIT-IgG (from serum or plasma)
Alkaline phosphatase-conjugated goat antihuman IgG

Heparin Antibody Testing by Heparin-induced platelet aggregation

- Positive for HIT
- Negative for HIT
Serotonin release assay

Heparin/PF4 complex

HIT IgG

Radiolabeled serotonin released from platelets
HIT Treatment Principles: Do

- Stop Heparin
- Switch to alternate anticoagulant
  Danaparoid, Lepirudin, Argatroban
HIT Treatment Principles: Don’t

- No warfarin (Vit K if warfarin given)
- No prophylactic platelets