Heparin Induced Skin Necrosis

Manuel A. Molina, M.D.
Kings County Hospital Center
VS T:98.7, BP:137/80, HR:84, RR:18

General: Alert and oriented X3, well developed, moderately obese (BMI 34), no apparent distress.

HEENT: Normocephalic, PERLA, midline trachea, no lymph nodes, no JVD.

Chest: RRR S1/S2, CTA B

Abdomen: Obese, NABS, lower abdominal midline scar with 6 cm fascial defect and reducible ventral hernia. Soft, non tender.

Neuro: Grossly intact.

Extremities: no edema, FROM
Heparin Induced Skin Necrosis

- Described for the first time in 1973 by O’Toole in the Annals of Internal Medicine.
- Affects middle age women with history of thrombotic disease
- Characterized by the formation of one or more painful red plaques or necrotic skin lesions.
- Occurs at sites of heparin injection or IV insertion. Can affect distal areas as well.
- 5 days or more after starting heparin treatment. Earlier in those treated previously with heparin.
- Some patients develop thrombocytopenia when lesion first appears, often with paradoxical thrombosis.
In post op, thrombocytopenia with thrombosis and positive heparin induced antibodies, may occur in 3% of patients.

HIT type II in 22% of patients with Heparin induced skin necrosis.

Immune mediated HIT in 1-3% of patients treated with fractionated heparin.

50% of HIT patients develop thrombotic complication over the week following the diagnosis.

80% of patients with skin necrosis one or more dermatological test (delayed hypersensitivity) or lab test are positive. (Harenberg et al, 1999).
Heparin Induced Thrombocytopenia

- HIT is defined as a decrease in platelet count below 150,000/ul or 50% from baseline occurring at least 5 days after beginning heparin therapy. (Can also occur with LMW Heparin).

- Heparin dependent anti-platelet antibodies detected by $^{14}$C- serotonin release assay.

- HIT Type 1: Benign form. Due to direct interaction between heparin and circulating platelets; generally resolves with continued heparin administration.

- HIT Type 2: Severe form. Immune-mediated reaction caused by IgG antibody that binds to platelets in the presence of heparin leading to platelet activation. Associated with thrombotic complications.
Pathophysiology

- Associated with formation of heparin-dependent, platelet activating IgG (Warkețin and Kelton, 1994)
- Target antigen is a multimolecular complex of heparin and platelet factor 4.
- The neoantigen induces the production of IgG, IgM, IgA.
- Is a manifestation of HIT (type II), associated with platelet activation and increased thrombin production
- Thrombosis of the perforating vessels produces ischemia and infarction progressing to inflammation and necrosis.
immune complex
PF4
heparin

Fc receptor
platelet

Platelet removal by splenic macrophages
Platelet activation
Platelet release
Platelet aggregation

Thrombocytopenia
Release of procoagulant microparticles
Thrombosis
Formation of PF4-heparin complexes

Formation of immune complexes (PF4-heparin-IgG)

PF4 release

Platelet activation

Heparin

IgG antibody

PF4

Blood vessel

EC injury

Heparin-like molecules

EC in vessel wall

Platelet

Fc receptor

Source: Prog Cardiovasc Nurs © 2002 Le Jacq Communications, Inc.
Diagnosis

- Heparin induced platelet activation assay (HIPA).
- Heparin induced IgG.
- Platelet based serotonin release assay.
- ELISA
Complications

- Myocardial infarction
- Cerebral infarction.
- Lower limb ischemia.
Treatment

- Immediate discontinuation of heparin.
- Danaparoid (heparan sulfate and dermatan sulfate) 90% of patients will improve, cross reactivity with heparin in <5% of cases.
- Hirudin. From leech salivary gland *Hirudo medicinalis*. Is a tight-binding thrombin inhibitor.
- Argatroban, thrombin inhibitor. Not FDA approved.
- Surgical debridment of necrotic tissue.
Conclusions

- Heparin induced skin necrosis is a rare complication of heparin used characterized by immune complex formation and thrombosis.
- Is not always associated with thrombocytopenia.
- Common in patients with HIT type 2.
- Should be suspected if the patient develop skin necrosis in areas of SQ injection or IV site.
- Cornerstone of therapy is cessation of Heparin therapy.
- Should be treated with heparinoids or thrombin inhibitors.