

Low molecular weight heparin induced bullous hemorrhagic dermatosis

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ABSTRACT

Heparin-induced bullous hemorrhagic dermatosis is a rare, recently described side-effect of subcutaneous heparin injection. We present a case of a male patient with a bullous hemorrhagic eruption following the administration of subcutaneous LMWH. A diagnosis of Heparin-induced bullous hemorrhagic dermatosis was made by HPE (Histopathological examination) of tissue biopsy from the bullous lesion and the exclusion of other laboratory finding.

Key word: Heparin, electrocardiograph, bullous, hemorrhagic dermatosis

Introduction

Heparin-induced bullous hemorrhagic dermatosis is a rare, recently described side-effect of subcutaneous heparin injection. ^[1] Low-molecular-weight heparin (LMWH) have been used for prevention and treatment of thrombo-occlusive and embolic disease due to their anticoagulant properties. ^[2] It produces anticoagulant effects by activating antithrombin III. ^[3] Many LMWH preparations are available such as Enoxaparin, Dalteparin, Tinzaparin, Ardeparin, Nadroparin, and Reviparin,

which differ considerably in their composition. The most common adverse skin effects with these anticoagulants are ecchymoses, skin necrosis, urticaria, angioedema and eczema. ^[4]

Case Report

A 70 year old man from Thongiao, Manipur was referred to RIMS casualty from Kakching CHC with complaint of difficulty in breathing and angina chest pain usually upper part with radiation to back. On subsequent investigation ECG showed ST

segment elevation and diagnosed as acute myocardial infarction. On examination patient was conscious, co-operative and well oriented with time, place and person. Temperature afebrile, no pallor, no icterus, no edema, no cyanosis, no raised Jugular venous pressure. Pulse Rate: 90/min(R) with good volume, BP: 130/90mmHg, RR:16/min, Spo 2:99% in room air. Chest was bilateral clear, no added sound, Cardiovascular system S1 and S2 heart sound heard, no added sound, no murmur, Abdomen soft, bowel Sound present, no tenderness, no guarding, no rigidity, no organomegaly, no thrill, no shifting dullness. Urgent ECG showed ST segment elevation in lead V1 to V6 and ST segment depression in lead II, III and avl, Serum Troponin and CK MB came positive with value 25 and 166u/l. (Fig.1) Intravenous thrombolysis done with streptokinase after taking valid and written consent. After thrombolysis blood pressure was monitored hourly. Patient started with low molecular weight heparin 1mg/kg. BW, Tab. Clopidogrel 75mg, Tab. Isosorbide dinitrate 5mg, Tab Trimetazidine CR 35mg, Tab Etizolam, Injection Levocarnitin, Tab Atorvastatin 10 mg and other symptomatic treatment also given. Other investigation were normal like Liver function Test, Kidney Function Test (urea/creatinine:66/1.4), serum electrolyte (Na⁺, K⁺, Cl: 138/3.0/89), RBS: 109mg/dl, Complete Blood Count, Hep B, C and Retro Ab: Non-Reactive. On the next 48 hours, patient developed haemorrhagic vesicles mainly over the upper extremities sparing other parts of the body. (Fig.2) So LMWH, Clopitab stopped and Dermatologist consultation was taken. Prothrombin Time / INR, APTT, Platelet count and LFT showed PT/INR:12.1/0.94, APPT:35 sec., PLT: 2 lakh and LFT:TP:7,

ALB:3, AST/ALT:248/102. Patient started Tab. Clopidogrel again and tissue biopsy taken from the lesion and sent for HPE which showed intraepidermal subcorneal bulla containing numerous RBC's. The underlying dermis consists of minimal pericapillary lymphocytic infiltration. No evidence of acantholysis or vasculitis. The picture was suggestive of Bullous Haemorrhagic Dermatitis. (Fig. 3, 4) Standard laboratory investigations and coagulation studies were unremarkable. Skin lesions disappeared 10 days after discontinuation of LMWH. The patient was diagnosed with a heparin-induced bullous Haemorrhagic Dermatitis. Discontinuation of heparin was recommended and the patient's eruption resolved without any complication and subsequently the patient was discharged with continuation of Tab. Clopidogrel 75mg and advised to follow up after 15 days.

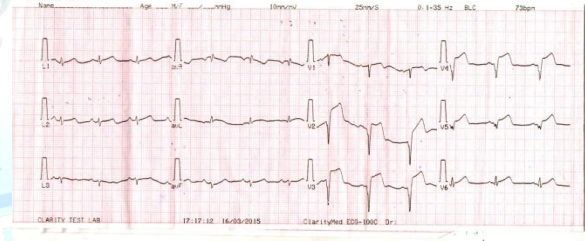


Fig.1 shows ST segment elevation in V1-V6

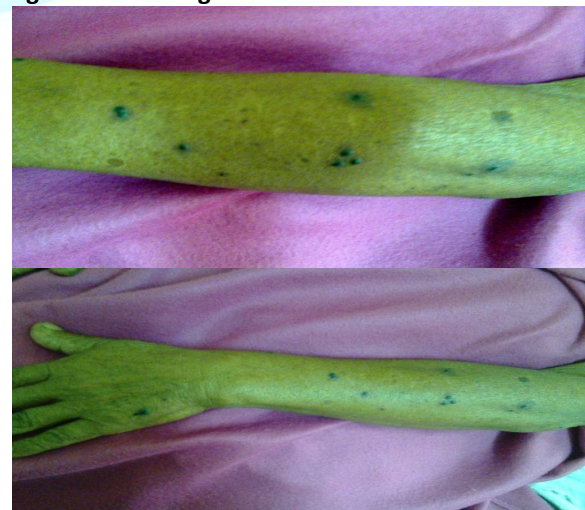


Fig.2 Haemorrhagic bulla upper left and right forearm

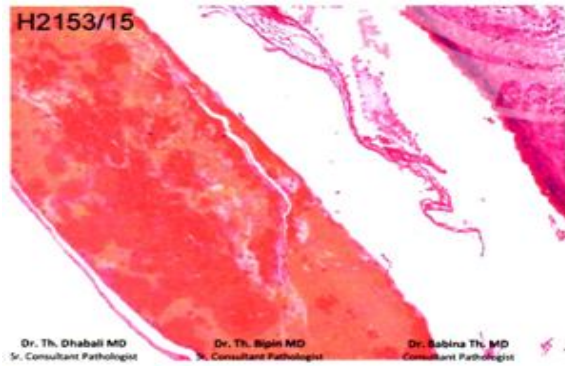


Fig.3 Intraepidermal bulla containing numerous RBC'S

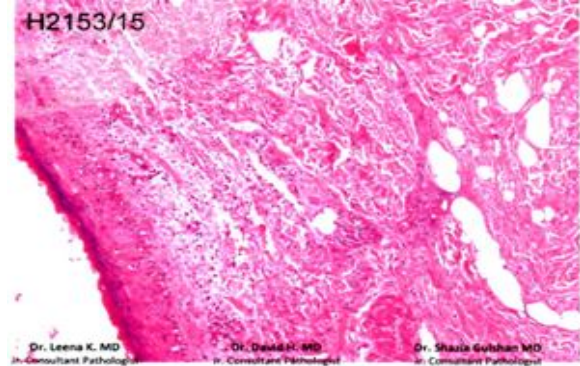


Fig.4 Pericapillary lymphocytic infiltration

Discussion

Low molecular weight heparin is isolated from standard heparin by gel filtration chromatography, precipitation with ethanol, or partial depolymerization with nitrous acid and other chemical or enzymatic reagents. The heparin-antithrombin complex inactivates several coagulation enzymes including prothrombin (factor IIa) and factors IXa, Xa, XIa, and XIIIa. Heparin also binds to platelet factor 4 and the vascular endothelium.^[5]

Bullous hemorrhagic eruption is a rare cutaneous side effect. No large studies of heparin-induced hemorrhagic bullous dermatosis have been performed to date and only a limited number of cases have been reported since 1998.^[6] Other cutaneous reactions include skin necrosis, immunologically mediated eruptions and bullae formation. The heparin-induced skin lesions might be caused by at least 5 mechanisms: delayed (type IV) hypersensitivity reactions, immune-mediated thrombocytopenia, type I allergic reactions, skin necrosis, and pustulosis.^[7] Other known side effects include heparin-induced thrombocytopenia (HIT) complicated by bilateral adrenal hemorrhage, hypertransaminasemia, abnormal liver function, alopecia, and

osteoporosis. The two most commonly reported causes of heparin-induced skin lesions are immune-mediated HIT due to antiplatelet factor 4 antibodies and delayed hypersensitivity reactions.^[8] Eosinophilic panniculitis is also rare cutaneous manifestation after subcutaneous injection of low molecular weight heparin.

Conclusion

Heparin-induced hemorrhagic bullous dermatosis is an uncommon reaction to heparin or low molecular weight heparin. Bullae usually appear 5 to 21 days after initiation of heparin therapy. Lesions arise on otherwise normal skin, distant from injection sites and are most commonly located on the extremities. Severe coagulopathy, progression to skin necrosis and associated systemic symptoms have not been observed. Histological examination reveals collections of epidermal red blood cells without associated vasculitis or thrombosis. The mechanism of heparin-induced hemorrhagic bullous dermatosis is not yet understood. Resolution occurs after cessation of heparin therapy in most cases but has also been reported to resolve with continued heparin treatment.

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