Nadroparin-induced skin necrosis: clinical manifestation of HIT-2 even in the absence of thrombocytopaenia

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Accepted 10 April 2016

DESCRIPTION

A 33-year-old man with chronic heart failure secondary to dilated cardiomyopathy who developed pneumonia during his stay in the intensive care unit (ICU), was started on subcutaneous nadroparin (2850 UI subcutaneously, once a day) as prophylaxis against venous thromboembolism. By day 7, he had developed a heart-shaped blistering skin lesion with central necrosis and surrounding erythaema at the nadroparin injection site (figure 1). Throughout his stay, laboratory tests revealed neither thrombocytopaenia nor evidence of systemic thrombosis; but despite this unusual presentation, we clinically suspected a high probability of type II heparin-induced thrombocytopaenia (HIT) and a score of 6 points according to the 4T's HIT score system was established. Nadroparin was replaced by dabigatran 150 mg two times a day.

Skin necrosis at the site of heparin injections is a well-described complication of treatment with unfractionated or low-molecular weight (LMW) heparin, and should immediately suggest the presence of HIT. The most common and often first manifestation of HIT is thrombocytopaenia, occurring in up to 90% of those affected. Thrombosis occurs in up to 50% of patients, more frequently due to venous than to arterial thrombi (4:1 ratio); thrombosis is the initial finding in up to 25% of patients. Thrombosis can lead to skin necrosis, limb gangrene and organ infarction.

Heparin-induced skin lesions are strongly associated with the formation of HIT-IgG antibodies and should be considered as a manifestation of the HIT syndrome, even in the absence of thrombocytopaenia as conventionally defined.[1] Skin lesions occur in 10–20% of patients with HIT. These lesions are due to intradermal microvascular thromboses; however, as in delayed-type hypersensitivity reactions, they begin as erythaematous lesions that subsequently lead to cutaneous necrosis, usually with a central black eschar surrounded by indurated erythaema. These painful lesions can also develop at a distance from the heparin injection sites, even in the absence of thrombocytopaenia.[1 2]

The paradoxical absence of thrombocytopaenia in patients with HIT is especially observed in the ICU setting. Several acute conditions can be associated with thrombocytosis (sepsis, inflammation, trauma, drug side effects, etc), and can mask thrombocytopaenia.[3]

The most relevant differential diagnoses include calciphylaxis, coumadin-induced necrosis and the antiphospholipid syndrome. The decisive diagnostic procedure in heparin-induced necrosis is HIT antibody testing, histological examination and the chronological connection between the initiation of heparin therapy and the first appearance of skin necrosis; this usually occurs 5–10 days later, either at the site of injection or far from the area of puncture.

Learning points

- Skin necrosis at either the heparin injection site or at a distance, should immediately suggest the presence of heparin-induced thrombocytopaenia (HIT), with a score of 2 points in the 4T's scoring system.
- Heparin-induced skin lesions are strongly associated with the formation of HIT-IgG antibodies and should be considered a manifestation of the HIT syndrome, even in the absence of thrombocytopaenia.
- In patients with a presumptive diagnosis of HIT, all sources of heparin should be discontinued, and a non-heparin anticoagulant should be administered to decrease the risk of life-threatening thrombosis.

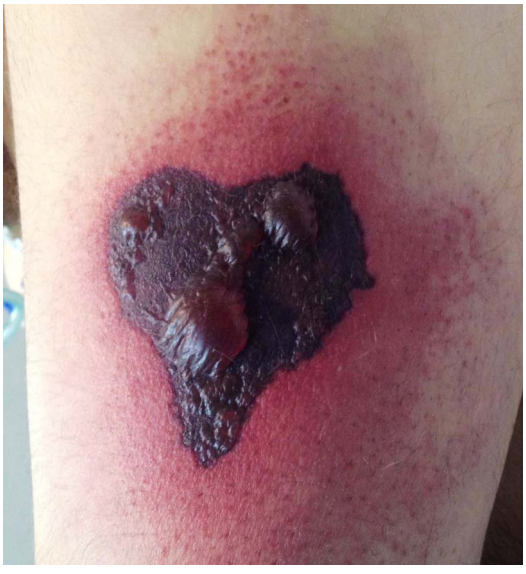

Figure 1 Heart-shaped skin necrosis and blistering.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite: Carrillo Pérez DL, Peña-Romero AG ,Díaz-González JM, *et al*. *BMJ Case Rep* Published online: [*please include* Day Month Year] doi:10.1136/bcr-2016-215288

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