SKIN NECROSIS AS A COMPLICATION OF IMPROPERLY ADMINISTERED SUBCUTANEOUS HEPARIN

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SYNOPSIS

Skin necrosis is a rare complication of subcutaneous heparin injections. It is regarded as a hypersensitivity reaction mediated via intravascular thrombosis due to heparin induced platelet aggregation or an Arthus-type reaction due to deposition of immune complexes within vessel walls. A case is presented below to illustrate the clinical features and the literature is briefly reviewed. It is also postulated that a third mechanism, which is non-immunological, may be responsible for the lesions seen in our patient. Recognition of this rare complication and its management is discussed.

INTRODUCTION

Skin necrosis as a rare complication of subcutaneous heparin injections was first reported by O'Toole in 1973. (1) It is thought to be immunologically mediated either via intravascular thrombosis resulting from heparin induced immune aggregation of platelets, (2) or an Arthus-type reaction due to formation of antigen-antibody complexes in cutaneous blood vessels. (3) We recently observed a patient with heparin skin necrosis in whom neither mechanisms seemed to have been involved. This case and the management of this unusual complication is discussed below.

CASE REPORT

A 27-year old Chinese woman (Gravida-3, Para-1) had received intravenous heparin followed by warfarin tablets for iliofemoral deep vein thrombosis 2-years previously. During her present pregnancy, she was instructed to inject heparin (Commonwealth Serum Laboratories) 10,000 units B.D. subcutaneously. About 2 months following injections she developed ulceration of the abdominal skin at the sites of injection. She was referred to us during the 5th month of her pregnancy. Examination disclosed multiple ulcers measuring 1-2 cm in diameter on the flanks of her abdomen. Some ulcers were indurated and covered by eschars and a few haemorrhagic bullae were also present (Fig. 1). Further enquiry revealed that she had injected heparin more and more superficially as her pregnancy progressed for fear of injuring the foetus.

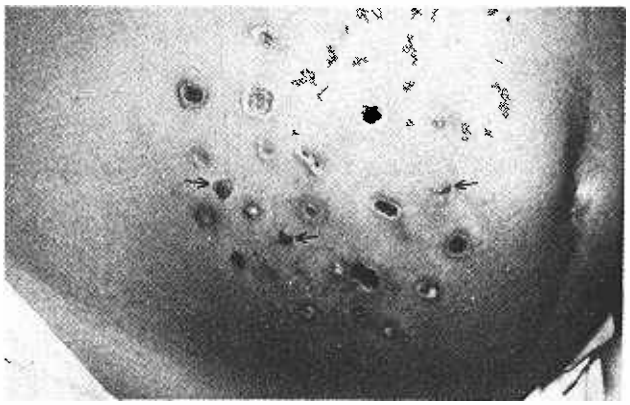

Figure 1. Multiple ulcers, some covered by eschars, and flaccid, haemorrhagic bullae (arrowed) on the abdomen.

It was felt, after she demonstrated her technique of injection, that she was injecting herself almost intradermally rather than subcutaneously. She was corrected on this and was then able to continue subcutaneous heparin till 2-months post-delivery without further complications. We were unsuccessful in obtaining her permission for a skin biopsy.

COMMENT

Heparin skin necrosis is believed to be a hypersensitivity reaction. White et al (2) reported 6 cases and suggested that ischaemic necrosis resulted from heparin induced immune aggregation of platelets. This was followed by intravascular thrombosis caused by the release of clotting factors from the damaged platelets. Support for the central role of platelets in the pathogenesis of heparin skin necrosis is derived from the observation of heparin induced throbocytopaenia associated with recurrent thromboembolism, (4, 5) and in-vitro demonstration of heparin induced aggregation of platelets in specific patients. (6, 7, 8) Although White et al (2) found no evidence of vasculitis and immune deposition in the cutaneous lesions, Jackson and Pollock (3) reported a case which showed leucocytoclastic vasculitis on histology. In addition, they were able to demonstrate fibrinogen, IgG and C3 in the walls of the inflammed vessels. These findings suggest that an Arthus-type reaction with the formation of antigen-antibody complexes was another possible mechanism.

Our patient, on the other hand, suggests that yet another mechanism, which is non-immunological, can also be involved. She had received intravenous heparin 2-years previously and the onset of lesions 2 months after starting subcutaneous heparin is unusual for a hypersensitivity reaction since she would have been sensitised previously. The absence of any local or systemic reactions after correctly giving subcutaneous heparin afterwards, also argue against a hypersensitivity reaction. It may be possible that in our patient, heparin given intradermally had caused local haemorrhage in a fairly tense dermis and pressure on small blood vessels, resulting in ischaemic necrosis of the overlying skin. In this case haemorrhage could have resulted from the anticoagulant effects of heparin in the vicinity of dermal blood vessels rather than a immunologically mediated reaction. It is possible that this complication may be averted by giving heparin properly into the lax subcutaneous tissue and does not preclude further use of heparin. We would caution, however, that appropriate investigations should first be carried out to exclude hypersensitivity to heparin. These investigations should include a platelet count, intradermal skin tests to 0.02ml of undiluted heparin (9) and platelet aggregometry tests (7) if available. No further heparin should be used if thrombocytopaenia is present or if intradermal skin tests or platelet aggregometry tests are positive. In their absence, the possibility of incorrect administration should be ruled out by history and injection under in-patient supervision, with regular monitoring of the platelet count. If no complications develop following proper injection, then subcutaneous heparin may be continued.

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REFERENCES

1. O'Toole R D: Heparin: Adverse reaction. Ann Intern Med 1973; 73: 759.
2. White P W, Sadd J R, Nensel R E: Thrombotic complications of heparin therapy including six cases of heparin-induced skin necrosis. Ann Surg 1979; 190: 595-608.
3. Jackson A M, Pollock A V: Skin necrosis after heparin injection. Br Med J 1981; 283: 1087-8.
4. Cines D B, Kaywin P, Mabin Bina A T, Schreiber A D: Heparin associated thrombocytopenia. N Engl J Med 1980; 8: 788-95.
5. Ansell J, Deykin D: Heparin-induced thrombocytopenia and recurrent thromboembolism. Am J Hematol 1980; 8: 325-32.
6. Towne J B, Bernhard V B, Hussey C, Garancis J C: White clot syndrome: Peripheral vascular complications of heparin therapy. Arch Surg 1979; 114: 327-77.
7. Hussey C V, Bernhard V M, McLean M R, Fobian J E: Heparin induced platelet aggregation: In vitro confirmation of thrombotic complications associated with heparin therapy. Ann Clin Lab Sci 1979; 9: 487-93.
8. Kapsch D N, Adelstein E H, Rhodes G R, Silver D: Heparin-induced thrombocytopenia, thrombosis, and haemorrhage. Surgery 1979; 86: 148-55.
9. Shelley W B, Sayen J J: Heparin necrosis: An anticoagulant-induced cutaneous infarct. J Amer Acad Dermatol 1982; 7: 674-7.