Heparin-associated priapism

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Summary

A patient who developed priapism 7 hr after stopping an intravenous heparin infusion is described. Abnormal spontaneous platelet aggregation was demonstrated whilst on heparin treatment and is thought to play a role in the aetiology of heparin induced priapism.

KEY WORDS: heparin, priapism platelet function.

Case report

A 37-year-old lorry driver was admitted complaining of 5 days pain and swelling of his left calf. Two and a half years earlier, he had suffered a thrombosis of his right femoral vein proven by venography. On the previous admission, he was treated initially with heparin, and subsequently with warfarin, for 6 months uneventfully.

Examination on this admission showed the classical signs of a deep venous thrombosis of his left calf. He was treated with an intravenous infusion of 40000 units of heparin (porcine mucosal origin, Paynes & Byrne Ltd.) per 24 hr and also started on warfarin 8 mg/day. Two days later, his calf pain was much improved and after 5 days of treatment when his British comparative ratio reached 2.5, the heparin was discontinued. Seven hours later, he developed priapism. Urgent treatment was attempted that day by embolisation of his right internal pudendal artery and repeated the next day in the left internal pudendal artery, anticoagulation was stopped. Detumescence did not occur and on the next 2 days drainage and washout procedures of the corpora cavernosa were performed after which his penis shrank towards normal size.

Eight days after discontinuing anticoagulants, signs of deep venous thrombosis returned to his left calf and an intravenous heparin infusion (40000 units/24 hr) was restarted. Four days after restarting

heparin treatment, platelet function and clotting studies were performed (Table 1, test 1). Platelet aggregation studies were performed according to the method of Born (1962) using a Labor dual channel aggregometer in plastic cuvettes with siliconized stirring bars, stirring velocity 1000 rpm, at 37°C. The platelet-rich plasma was defined as 0% aggregation and the platelet poor plasma as 100% aggregation. The percentage fall in optical density of the platelet-rich plasma, was recorded 3 min after the addition of the agonist. Spontaneous aggregation was determined by measuring a significant change in optical density, as compared to the control 10 min after a sample of platelet-rich plasma was placed in the aggregometer in the absence of any aggregating reagent. These showed abnormal spontaneous platelet aggregation and excessive platelet aggregation with low concentrations of ADP and adrenaline, whilst on heparin treatment, that produced adequate anticoagulation. These tests gave similar results 8 days after the first test (test 2). After 15 days of heparin treatment, warfarin was started and the heparin discontinued when he was adequately anticoagulated. Platelet function was restudied (test 3) one week later on warfarin alone and showed no spontaneous aggregation. To date he has remained well, but impotent, and has returned to work.

Discussion

An association between priapism and heparin treatment has been recognised since Duggan and Morgan (1970) reported 4 such cases. Subsequent reports (Klein, Hall and Smith 1972; Sale and Cameron 1974) of similar cases in at least 19 patients receiving heparin treatment, have strengthened this suspected association between the two. The precise relationship between heparin treatment and priapism remains obscure. Duggan and Morgan (1970) debated whether heparin contributed passively to priapism by allowing thrombosis to occur, or played

TABLE 1. Coagulation and platelet studies on heparin (Tests 1 and 2) and on warfarin alone (Test 3)

	Average control values	Test 1	Test 2	Test 3
Prothrombin time (s) (Normal range 12–15)	13	17	—	33
Activated partial thromboplastin time (s) (Normal range 30–40)	36	58	—	36
Thrombin clotting time (s) (Normal range 12–15)	13	56	—	14
Platelet count ($\times 10^9/l$) (Normal range 150–400)	—	317	—	295
Aggregation (%) in response to a final concentration of:				
2.0 μmol ADP	85	75	73	85
1.0 μmol ADP	35	70	70	30
0.5 μmol ADP	15	70	68	—
2.0 μmol Adrenaline	80	100	100	66
1.0 μmol Adrenaline	70	100	100	66
0.5 μmol Adrenaline	38	100	80	—
Test for spontaneous aggregation	Negative	Positive	Positive	Negative

an active role either by causing vasodilatation which can lead to priapism, or by stimulating rebound thrombosis which Mustard *et al.* (1963) showed could occur when heparin in adequate dosage for anticoagulation was stopped. These data were supported by Port *et al.* (1974) who reported 2 cases where priapism occurred within 90 min and 7 hr of discontinuing heparin infusions in patients undergoing haemodialysis, whilst Sale and Cameron (1974) reported that priapism is relatively common in patients receiving intravenous heparin for haemodialysis. Thomson, Forbes and Prentice (1973) showed that heparin can increase platelet aggregation by ADP and adrenaline *in vivo* and *in vitro*, and this mechanism might be involved in the causation of heparin associated priapism.

Our patient developed priapism within 7 hr of the cessation of intravenous heparin at a time when the plasma heparin concentration would have fallen to a low level, yet he was anticoagulated with warfarin. When tested, his platelets were shown to spontaneously aggregate whilst on heparin, but not 7 days

after heparin had been discontinued. It seems possible that his abnormal spontaneous platelet aggregation was caused by heparin and played a part in the development of priapism. This is the first time abnormal platelet function has been demonstrated in heparin associated priapism.

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