Skin Necrosis after Warfarin Therapy


SUMMARY

A rare but potentially lethal complication of coumarin and its congeners is skin necrosis. A case of skin necrosis due to warfarin is reported and the literature is reviewed. It is suggested that if necrosis develops, the coumarin therapy should be terminated, and the patient should immediately be heparinized. Heparin, which never causes necrosis, can be used freely if further anticoagulation therapy is required, and may well prevent necrosis due to the thrombotic process.


A complication of the administration of oral anticoagulants is bleeding, owing to depression of vitamin K-dependent clotting factors. Non-haemorrhagic complications include gastro-intestinal dysfunction, urticaria, dermatitis, fever and alopecia.

There remains one further complication, which is serious and may be life-threatening: that of necrosis of skin and subcutaneous tissue owing to coumarin congeners. Its occurrence is unpredictable and unrelated to dosage, and its course is influenced neither by stopping nor by continuing the administration of the drug.2 Therapeutic attempts have included the use of steroids, vasodilators, hypothermia and sympathetic nerve blockade, but all have proved ineffective. Two reports3,4 suggest that heparin will prevent the later stages of this complication. Few cases of this condition have been recorded; we wish to present one case in which it occurred after the administration of warfarin sodium.

CASE REPORT

An 18-year-old woman, in the 36th week of her pregnancy, presented with a 12-day history of a left iliofemoral vein thrombosis. A bilateral venogram was performed which confirmed the diagnosis. The patient was heparinized (10 000 units intravenously every 6 hours), and the clotting times were carefully controlled. After delivery, 12 days later, the patient was given warfarin sodium therapy.

Six days later, she complained of the sudden onset of a severe and diffuse swelling of the left leg, with extreme pain, and a diagnosis of phlegmasia caerulea dolens with peripheral venous gangrene was made. At this time the prothrombin index was 46%. The patient was treated with streptokinase (Kabikinase), with an excellent result. After this treatment, the patient was again heparinized for 14 days. Treatment with warfarin sodium was then instituted, and 9 days later the prothrombin index was 41%.

At this time the patient complained of pain in both the lateral aspect of the left buttock and the dorsum of the left hand. Examination of the buttock revealed a purple-black discoloration of the skin, measuring 10 x 10 cm, with surrounding erythema. There was an identical but smaller lesion (3 x 3 cm) on the left hand. Laboratory investigations at this time showed the platelet count, serum fibrinogen and fibrin degradation product levels to be within normal limits.

The warfarin sodium treatment was immediately terminated and heparin therapy was re instituted. The next day haemorrhagic bullae were seen in the centre of the buttock lesion (Fig. 1). Over the next few weeks there was progressive resolution of both lesions. The lesion on the hand showed evidence of partial thickness necrosis; however, the buttock lesion showed evidence of both partial and full thickness necrosis (Fig. 2). Neither lesion required skin grafting.

Fig. 1. Lateral aspect of buttock showing haemorrhagic bullae with surrounding skin necrosis.

DISCUSSION

Few cases of coumarin necrosis have been reported in the literature. In 1943 Flood et al.4 described a case of breast gangrene in a patient receivingbishydroxycoumarin (Dicumarol); however, he described this as a manifestation of thrombophlebitis migrans disseminata from which the
necrosis is caused by a toxic action resulting from the coumarin therapy. The initial site appears to be in the dermovascular loop at the junction of the capillary and precapillary arteriole. They believe that the initial erythema is caused by capillary dilatation in the dermovascular loop, and that the ecchymosis and then gangrene are caused by haemorrhage from the ruptured distal precapillary arterioles, followed by thrombosis in the venules, due to stasis, immediately distal to the dermovascular loop.

In several instances\textsuperscript{10,11} sophisticated coagulation studies have been carried out, and it is uniformly agreed that altered coagulation mechanisms play no part in this disorder. Stefanelli \textit{et al.}\textsuperscript{12} excluded an allergic basis by scarification and intracutaneous skin challenge, using phenprocoumon. No immediate or delayed hypersensitivity reaction occurred, and this would seem to preclude a hypersensitivity reaction.

Nalbandian \textit{et al.}\textsuperscript{9} have described 7 patients who were effectively treated with heparin. They believe that heparin acts by preventing thrombosis of the venules, and hence the development of infarction and necrosis. Beller suggests giving the patient vitamin K 20 mg intravenously and immediate heparinization until the lesion subsides. In our patient, the warfarin was stopped when the lesion developed, and the patient was immediately heparinized. It is possible that extensive necrosis was prevented.

Thus it seems that although lesions will heal during coumarin therapy, it would appear wise to stop giving the drug immediately. Heparin, which never causes necrosis, can be used freely if further anticoagulation is required, and may well prevent necrosis due to the thrombotic process.

The patient reported took part in a randomized study.

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REFERENCES