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CLINICAL REPORTS

Warfarin-induced vasculitis: A dose-related phenomenon in susceptible individuals?

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Summary

A case of warfarin-induced skin vasculitis in a 52-year-old female is reported. Bilateral breast involvement occurred but without progression to necrosis as in previously described cases. The pathogenesis is discussed and prescribing recommendations made in an attempt to avoid the complication in susceptible individuals.

Introduction

Haemorrhage is a common complication of anticoagulant therapy and is related to poor anticoagulant control. Haemorrhagic cellulitis, often proceeding to necrosis, is a rare, distinct complication, unrelated to poor control (Nalbandian *et al.*, 1965). It typically affects skin rich in fatty tissue such as thighs, buttocks and breasts, occurs mainly in women (Nalbandian *et al.* 1965; Nudelman and Kempson, 1966), and is usually a complication of oral anticoagulant drugs, less frequently of heparin (Stavorovsky, Lichtenstein and Nissim, 1979). Previous reports suggest that if the breast is involved necrosis invariably ensues often requiring mastectomy (Nudelman and Kempson, 1966; Davis, Wiley and Faulconer, 1972; Fourrier *et al.*, 1979). The authors report a case induced by warfarin in which bilateral breast involvement resolved spontaneously and in which warfarin, without an initial high dose, was later successfully given.

Case report

A 52-year-old woman was admitted with rheumatic mitral stenosis, atrial fibrillation, pulmonary oedema, right external jugular vein thrombosis and dilated veins over the right upper anterior chest. She was given digoxin, frusemide and warfarin, the latter in a dose of 9 mg on the first day, 6 mg on the second day and 6 mg on the third day. On the fourth day the right breast became acutely tender, tense and swollen. The overlying skin was initially erythematous, later ecchymotic. The prothrombin time was 45 sec (control 13 sec). Next day, similar changes occurred in the left breast (Fig. 1) and smaller lesions appeared on the left flank and over the right elbow. Warfarin was stopped and vitamin K_1 given. Ten days after the last dose of warfarin a final small lesion appeared on the left elbow. All the lesions resolved, the smaller ones in days, the breast and flank lesions in weeks. Cardiac failure came under control and echocardiography confirmed severe calcific mitral stenosis. Extensive investigations, including CAT scans of thorax and abdomen, failed to reveal any malignancy underlying her thrombotic tendency. No coagulation defect was found.

Five days after cessation of warfarin she developed thrombosis of the left external jugular vein and dilated veins over the left anterior chest. Venography confirmed bilateral subclavian vein thromboses. Heparin was given intravenously for 4 weeks with improvement. Long-term prophylactic anticoagulant therapy was considered essential. Twice daily self-administered subcutaneous heparin was tried but she found this burdensome and she also developed a pulmonary embolism within a few days of starting this treatment. At that time intravenous heparin was given again and, after one week, warfarin was reintroduced in a daily dose of 3 mg, producing successful anticoagulation after a further week. Heparin was then stopped. At the time of writing she has been on warfarin for 5 months without recurrence of soft tissue lesions.

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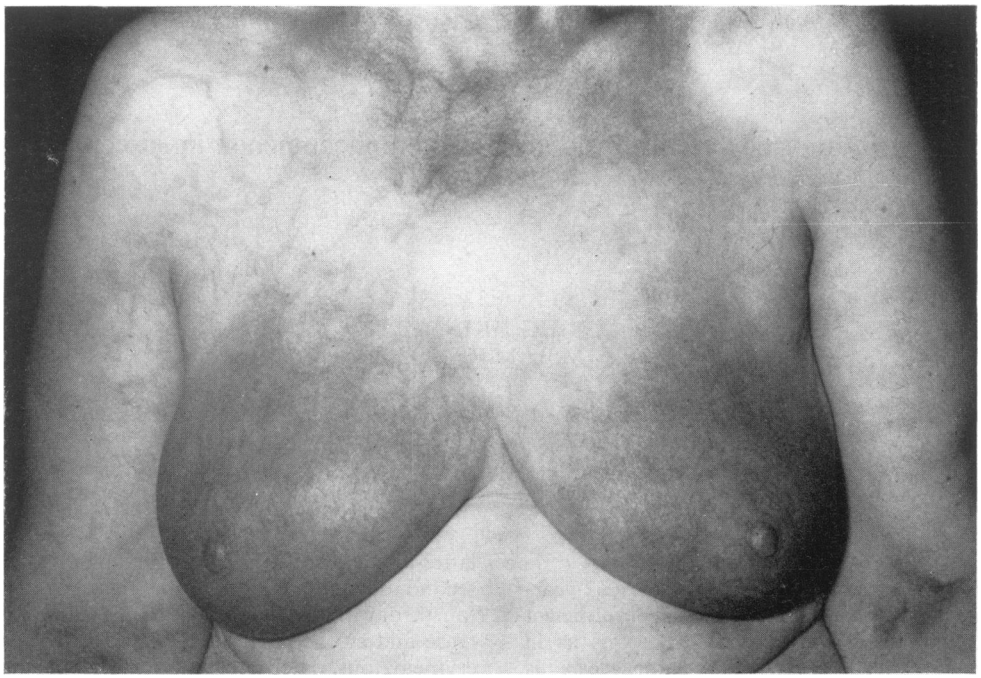

FIG. 1. Breast changes induced by warfarin.

Discussion

As in the present case the skin lesions in this rare reaction to anticoagulant drugs become dramatically evident between the third and tenth day of therapy (Nalbandian *et al.*, 1965; Nudelman and Kempson, 1966). The pathology appears to be a vasculitis with venous thrombosis (Stavorovsky *et al.*, 1979). The pathogenesis is uncertain but may be a direct toxic reaction to the initial high dose of the drug damaging the capillaries of the dermo-vascular loop (Stavorovsky *et al.*, 1979). Perhaps this effect is more evident in areas of skin which are already congested as a result of underlying thrombosis. The sequential involvement of the right then left breast and left elbow in the present case is in keeping with this view. The offending drug or a congener may be continued or given later without ill effect (Nalbandian *et al.*, 1965; Nudelman and Kempson, 1966), but it is not always clear whether a modified dosage schedule was used for retreatment in these cases. In this case the authors avoided any initial loading dose when warfarin was successfully reintroduced. Perhaps this more gradual approach to oral anticoagulation, if used in those patients particularly at risk (obese females with venous thrombosis) might reduce the incidence of this condition which, although uncommon, may require mastectomy.

Acknowledgment

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