Spontaneous bruising during treatment with isotretinoin

Sir, I read with interest the case report by Dootson et al. of a patient suffering from haemophilia A who developed an exacerbation of his bleeding tendency during treatment with isotretinoin (Roaccutane®).1 I report the case of a patient who developed spontaneous bruising during treatment with isotretinoin for hidradenitis suppurativa.

An otherwise fit 37-year-old woman suffering from hidradenitis suppurativa affecting the axillae, resistant to therapy with oral erythromycin, started treatment with isotretinoin 30 mg daily (0.5 mg/kg) in November 1991. She was not taking any other systemic medication. On review in December 1991 she was asymptomatic, but in February 1992, 9 weeks after starting isotretinoin, she complained of painless bruising on her thighs. A full blood count and clotting studies were normal.

She remained on isotretinoin for a further 10 weeks, and continued to develop painless bruises on both thighs every few days, the individual lesions fading within a few days. Repeat full blood count and clotting studies in May 1992 were normal.

She completed her course of isotretinoin in early July 1992 and 2 weeks later the bruising had ceased.

Haematological abnormalities are rare in patients taking isotretinoin. Two patients with reversible thrombocytopenia have been reported.2,3 Nineteen other cases are known to the manufacturer (personal communication), one of whom, a 29-year-old woman, developed bruising within 2 weeks of starting isotretinoin 60 mg daily. Following dosage reduction, the bruising resolved.

Neither our patient nor the patient reported by Dootson et al.,1 had thrombocytopenia. Dootson and her colleagues suggest that isotretinoin may stimulate plasminogen activator activity and hence fibrinolysis.4

Patients undergoing isotretinoin therapy are carefully monitored for abnormalities of blood lipids and liver function. They should also be observed for any tendency to spontaneous bruising, although in our patient this did not necessitate withdrawal of her isotretinoin therapy.

Department of Dermatology, Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland, U.K.

References

Klippel-Trenaunay syndrome: is it a paradominant trait?

Sir, A recent article by Aelvoet et al.5 provided evidence that the Klippel-Trenaunay syndrome (KTS) does not always occur sporadically, but exceptionally may show a familial aggre-gation. In addition, the authors found isolated vascular naevi to be overrepresented in family members of KTS patients. These findings appear to be important for the elucidation of the enigmatic genetic basis of KTS. Aelvoet et al. suggested multifactorial inheritance. In view of the fact, however, that the lesions of KTS are always arranged in a mosaic pattern, I should like to propose the concept of paradominant transmission.6

According to this concept, KTS would be caused by a single gene defect. Heterozygous individuals would be, as a rule, phenotypically normal, and therefore the allele would be transmitted imperceptibly through many generations. The trait would only be expressed when a somatic mutation occurs at an early stage of embryogenesis, giving rise to a clonal population of cells that display loss of heterozygosity, and therefore have become either homozygous or hemizygous for the KTS mutation. One example of the various genetic mechanisms that may cause homozygosity of a cell population arranged in a mosaic pattern is somatic recombination.7

Paradominant inheritance would explain why KTS virtually always occurs sporadically, why the familial occurrence of KTS reported by Aelvoet et al.5 does not show any Mendelian pattern, why naevi flammei show an increased incidence in relatives of KTS patients, and why the signs of KTS are always arranged in a mosaic distribution. Apparently, a diffuse involvement of the entire body is not possible, and this would be best explained by non-viability of embryos developing from a homozygous zygote.8,9

In conclusion, whereas a polygenic basis of KTS, as proposed by Aelvoet et al., cannot be rejected out of hand, the concept of paradominant inheritance appears to be a worthwhile alternative to explain the occasional familial occurrence of this phenotype.

Department of Dermatology, University of Marburg, Deutschhausstraße 9, W-3550 Marburg, Germany

R. HAPPLE

References

Reply

Sir, We read with interest the comments of Professor Happle on our article. At the time when we submitted this, we were not aware of any scientific publication on 'paradominant transmission'. Recently, Professor Happle used this term as a hypotheti-