Case reports

Progesterone-induced erythema multiforme[1]

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Autoimmune progesterone dermatitis (Hart 1977) is a well recognized though rare condition characterized by the recurrence of an eruption in the luteal phase of each menstrual cycle. The eruption may comprise erythema multiforme, pompholyx eczema or urticaria (Hart 1977, Georgouras 1981).

The patient reported here had cyclical erythema multiforme and is the first case in which the initiation of the eruption has been demonstrated to correspond to the postovulation rise in serum progesterone. Treatment with the antioestrogenic agent tamoxifen suppressed both ovulation and the eruption.

Case report

Mrs J M (aged 33) took an oral contraceptive pill for three months in 1972 without any adverse effects. From 1977 to 1983 she suffered from recurrent erythema multiforme, which was clinically typical. It comprised pruritic annular and target lesions on the hands, feet (Figure 1) and trunk, and oral ulceration. Trauma and insect bites could induce a lesion. The diagnosis was confirmed histologically. The eruption commenced in the second half of the menstrual cycle, worsened through the luteal phase and was at its most florid during menstruation (days (D) 2–4 of the menstrual cycle). She was almost never free of lesions. In 1982 she became pregnant and experienced erythema multiforme from the fifth week of her pregnancy until shortly before a spontaneous abortion at 10 weeks. There was no history of menstrual-associated herpex simplex or use of analgesics at the time of menstruation.

Investigation of her hormonal status and its relationship to her erythema multiforme was performed. Serial serum progesterone levels showed that the postovulatory progesterone peak corresponded to the initiation of her eruption (Figure 2) and that she experienced pruritus during the small preovulatory progesterone peak. There was

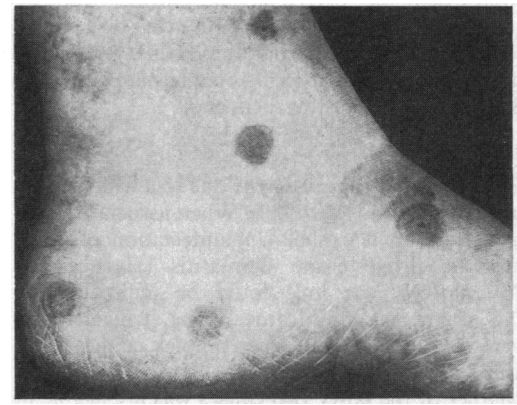

Figure 1. Typical lesions of erythema multiforme on the foot

no relationship to oestrogen levels. Intradermal testing with oestrogen and progesterone did not induce a lesion. Progesterone (10 mg) or the synthetic progesterone medroxyprogesterone (10 mg) intramuscularly induced erythema multiforme within 48 hours.

Immune complexes were not detected mid-cycle but were detectable for 48 hours after the administration of medroxyprogesterone. The patient's serum did not contain antibodies cross-reacting with ovarian tissue.

Herpex simplex was sought by oral, aural and cervical swabs and could not be demonstrated. Serum herpes simplex antibody titres varied from 1 in 16 to 1 in 32.

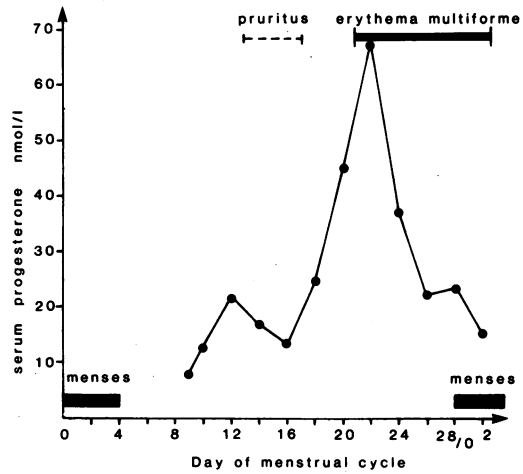

Figure 2. Relationship of eruption to serum progesterone levels

[1]Case presented to the Section of Dermatology, 15 March 1984. Accepted 7 December 1984

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Treatment with ethinyloestradiol (30 μg D 5–25) had no effect. Ethinyloestradiol (50 μg D 5–25), prednisone and fresh frozen plasma infusions produced only temporary remissions. The anti-oestrogen tamoxifen, 30 mg daily, completely suppressed the erythema multiforme, and its reduction to 10 mg daily was followed by a severe recurrence. She is now maintained on a regimen of tamoxifen 20 mg and 10 mg on alternate days. She is amenorrhoeic on this regimen.

Discussion

Erythema multiforme can be due to a wide variety of causes (Huff *et al.* 1983). When associated with menstruation it can be a manifestation of auto-immune progesterone dermatitis (Hart 1977). Alternatively the link could be indirect, with the erythema multiforme being triggered by menstrual-associated herpes simplex or the use of analgesics or other drugs at the time of the menses. Neither of the latter two causes was applicable in this patient.

Autoimmune progesterone dermatitis is frequently associated with prior exposure to synthetic progestogens, and this had occurred in our patient who had taken an oral contraceptive 5 years before the onset of the eruption. It has been suggested by Hart (1977) that the synthetic progestogen may act as a stimulus for antibodies which cross-react with natural progesterone. The cyclical erythema multiforme in this patient was provoked by both endogenous and exogenous progesterone and a synthetic progesterone. The onset of the eruption coincided with peak serum progesterone levels and, furthermore, it was induced within 48 hours by intramuscular injection of 10 mg progesterone or 10 mg medroxyprogesterone. The latter also evoked a rise in circulating immune complexes for 48 hours. The time interval is shorter than the 1–3 weeks usually described in erythema multiforme, but intervals as short as a few hours may occur in recurrent drug-induced erythema multiforme (Huff *et al.* 1983).

The antioestrogen tamoxifen was used successfully in this case. It has a peripheral antioestrogen action and by interfering with pituitary and hypothalamic feedback mechanisms suppresses ovulation and hence the postovulation rise in progesterone. Our patient has been amenorrhoeic on this drug and has been completely free of lesions. This treatment provides a valuable alternative to oophorectomy in the control of this prolonged and recalcitrant condition.

References

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Carcinoma of the adrenal cortex[1]

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A non-functioning adrenal carcinoma is reported in a patient who 10 years previously had had a large non-functioning adenoma excised from the same adrenal gland. Histology at that time showed some abnormal mitotic figures but no evidence of malignancy, and the possibility is raised that adrenocortical carcinoma may arise from malignant change within an adenoma, an association not hitherto described.

[1]Case presented to Clinical Section, 8 June 1984. Accepted 12 November 1984

Case report

A 56-year-old man was admitted for investigation of a mass in the left hypochondrium. Over the previous 18 months he had experienced backache and general malaise, but the symptoms had progressed rapidly a month prior to admission with a severe left hypochondrial ache. Ten years previously he had undergone laparotomy for excision of a mass in the left hypochondrium which was shown on histological examination to be an adrenocortical adenoma.

On this admission examination revealed a firm, tender, nodular mass deep in the left hypochondrium. There were no clinical signs of endocrine derangement. Investigations revealed a haemoglobin of 12.7 g/dl and ESR 64 mm in the first hour. Electrolytes, liver function tests and serum cortisol were within normal limits. Abdominal

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