Correspondence


A recurrent rash treated by oophorectomy

Sir,

A 45-year-old woman first presented in 1976 with a 5-year history of a pruritic rash on the elbows and dorsae and palms of both hands since menarche. This was accompanied by oral and sometimes genital ulceration, which required treatment with prednisolone 30 mg/day when severe. The oral ulceration was often of sufficient severity to prevent her from eating, and at age 25, she was investigated for weight loss; these investigations were normal. At age 20, she had started the combined oral contraceptive pill and remained on this for 10 years, but continued to require short courses of steroids every month.

The rash comprised erythematous papules and target-like lesions, distributed symmetrically on the hands and elbows, with haemorrhagic crusting and fissuring of her lip following blistering. Each episode began one week before menstruation and remitted afterwards.

Histology of a typical lesion showed a dermal inflammatory infiltrate with necrosis of keratinocytes in the epidermis, consistent with erythema multiforme (EM).

Many cases of EM, including cyclical EM, are secondary to *Herpes simplex* infection, \(^1\) which may be subclinical. There was no history or clinical evidence of *H. simplex* infection in our patient and long-term acyclovir as empirical treatment reduced her prednisolone requirement slightly but without significant symptomatic benefit. Azathioprine, dapsone and thalidomide were all tried in succession with little or no benefit.

Due to the cyclical nature of her EM, the disability caused by her mouth ulcers and the failure of standard treatments, medical ‘oophorectomy’ was induced with the gonadotrophin-releasing hormone agonist, Buserelin, via nasal spray, 300 mcg bd. This resulted in complete remission and obviated her requirement for steroids. After 6 months of treatment and extensive counselling, she underwent oophorectomy and remained symptom-free.

However, with the development of menopausal symptoms the patient commenced Saw Palmetto, an over-the-counter herbal anti-androgen preparation. Both this and subsequent treatment with Prempak C, a combined hormone replacement therapy, provoked recurrence of oral and genital ulceration.

Skin challenge tests with a 25 mcg oestrogen patch and an intradermal progestogen prick test (medroxyprogesterone acetate) showed no immediate reaction, but erythema and swelling was seen at the progestogen site 24 h later.

Because of menopausal symptoms and risk of osteoporosis, exacerbated by recurrent prednisolone treatment, she is now taking unopposed oestrogen HRT with transvaginal ultrasound monitoring and biopsy of her endometrium.

The spectrum of EM ranges from mild rash to life-threatening blistering and ulceration (Stevens-Johnson syndrome). The rash typically develops over a few days and may or may not show target features of different zones of erythema. The diagnosis is made clinically and by characteristic histology. EM generally resolves within a few days, but recurrent attacks are well recognized. Some 70% of cases are associated with *H. simplex*, which may be facial, genital or sub-clinical; viral antigens have been demonstrated in skin biopsies of some patients. \(^2\)

CD4+ and CD8+ lymphocytes can also be seen on histology and the condition is thought to be immune mediated, probably a delayed-type hypersensitivity, though immune complexes have been shown in some patients. There are many other rare causes of EM (Table 1), implying a range of triggering antigens.

Auto-immune progesterone dermatitis (AIPD) is a group of disorders first described in 1964. \(^3\) It is defined as a skin condition regularly appearing pre-menstrually and settling with the onset of menses, in other words associated with the post-ovulatory rise in serum progesterone. Recognized dermatoses which can behave in this way include eczema, pompholyx, urticaria and EM. Hypersensitivity to progesterone can be shown by the presence of auto-antibodies \(^4\) or, as demonstrated in this case, through a challenge test. The timing of onset of the rash in this case, together with its exacerbation following pharmacological progestins and suppression following ablation of ovulation and

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\(^1\) Experimental evidence has been presented of some cases showing immune complexes. Hypersensitivity reactions may be seen with a wide variety of agents, including drugs, and a wide variety of lipids, carbohydrates and proteins, some of which may be genetic.

\(^2\) Other rare causes of EM include neoplasms, drug reactions, vitamin B12 deficiency and viral infections.

\(^3\) A diagnosis of AIPD can only be made when all other causes have been excluded.

\(^4\) These are not all consistently seen.
Table 1 Causes of erythema multiforme

<table>
<thead>
<tr>
<th>Infections</th>
<th>Drugs</th>
<th>Other</th>
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<tr>
<td>Herpes simplex</td>
<td>Sulphonamides</td>
<td>Lupus erythematosus</td>
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<tr>
<td>Mycoplasma</td>
<td>Antibiotics</td>
<td>Polyarteritis nodosa</td>
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<td>AIDS</td>
<td>NSAIDs</td>
<td>Wegener’s granulomatosis</td>
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<td>Hepatitis B</td>
<td>Anticonvulsants</td>
<td>Lymphoproliferative disorders</td>
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<td>Orf</td>
<td>Allopurinol</td>
<td>Sarcoidosis</td>
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<td>Rickettsiae</td>
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<td>Pregnancy, pre-menstrual</td>
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<td>Infectious</td>
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<td>mononucleosis</td>
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subsequent oophorectomy strongly suggests an aetiological role for progesterone.

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References


**Diagnosing deep-vein thrombosis**

Sir,

There is much interest in ward-based screening tests that might avoid the need for imaging in patients presenting with suspected deep venous thrombosis, most of whom prove eventually not to have DVT. To be of use, such a test must have a high negative predictive value. We were interested to read of the experience in Bournemouth with computed strain-gauge plethysmography (CSGP). It is now in use in 100 UK hospitals. In Bradford, we had similar results when audited formally against ultrasound, with a negative predictive value of 97%. However other centres have reported better and worse experiences with the same equipment, reflecting the importance of assessing the equipment in the environment in which it is to be used.

An additional screening test is only of value if the attending clinician has enough confidence in the reliability and validity of a negative result to allow discharge of the patient. Most screening investigations have a small false negative rate, and clinicians will be naturally cautious about new diagnostic tests. We therefore looked at the impact of CSGP once introduced to the medical admissions ward as a stand-alone screening tool. The intention was to examine the level of confidence of clinicians in CSGP and to determine what they do in practice with patients with a negative CSGP result.

All patients presenting with suspected DVT in our medical admissions unit underwent investigation with CSGP performed by trained nursing and auxiliary staff. Imaging was used to investigate those patients with a positive or equivocal CSGP result. Patients with a negative CSGP result were discharged according to a written protocol and given advice. Returning patients were to be medically assessed and ultrasound performed. No formal pre-test clinical scoring for DVT was used at the initial presentation.

Patients who subsequently underwent further investigation with ultrasound or contrast venography, conventional or CT-pulmonary angiography and lung scintigraphy within 4 months of negative CSGP were identified and reviewed.

There were 354 CSGP examinations in an 8-month period: 209 (59%) were negative, 124 (35%) were positive and 21 (6%) were invalid or equivocal. In the negative CSGP group, 22 (10.5%) patients had ultrasound performed on the same day. Only one patient (0.5%) proved to have DVT identified.

There were a further 39 re-attendances for suspected thrombo-embolic disease within 4 months, of whom 28 had ultrasound performed. Four patients had DVT (1.9% of the negative CSGP group). These patients may either have had the diagnosis missed by the screening equipment or have had propagation of pre-existing calf vein clot above the trifurcation. A further 11 patients had ventilation/perfusion scans performed. Three patients (1.4% of the study group) had evidence of pulmonary emboli despite negative CSGP readings. No patient had clinical evidence of DVT on examination. Despite this, CSGP was performed outside of protocol. It is possible that the emboli originated from elsewhere, possibly the deep pelvic veins, or that no residual above-knee clot was present at the time of the CSGP study, or that these were false-negative CSGP studies. Management