CORRESPONDENCE

Successful treatment of erosive vulvovaginal lichen planus with topical tacrolimus

SIR, We report two women with erosive vulvovaginal lichen planus (LP) who responded within 4 weeks to topical tacrolimus. Both women were 54 years old when seen at our Institution. They had been suffering from erosive LP for 6 and 3 years, respectively; both had oral, vulval (Fig. 1a) and vaginal involvement. Vulval histology showed hypergranulosis, irregular acanthosis, vacuolar changes of the basal cells, cytoid bodies and a band-like lymphocytic infiltrate at the dermoepidermal junction, supporting the diagnosis of LP in both cases.

Both patients had received various treatments (very potent topical corticosteroids, systemic corticosteroids, dapsone, griseofulvin, acitretin and hydroxychloroquine) for their erosive LP prior to treatment with topical tacrolimus, without major improvement.

We started treatment with 0·1% topical tacrolimus (Prograf capsules, Fujisawa) in oculentum simplex FNA (paraffin ointment: cetostearyl alcohol 2·5 g, adeps lanae 6 g, paraffinum liquidum 40 g, vaselinum album ad 100 g) three times weekly in the evening: one fingertip of ointment (0·5 g) was applied to the vulva and 2 g was applied to the vagina using a vaginal applicator. The patients were reviewed monthly and treatment response was assessed by the patient and by the investigator who had seen the patient at the initial visit. All other treatments for the genital LP were stopped when topical tacrolimus was initiated. We noticed an improvement of the vulval symptoms after 4 weeks of topical tacrolimus application. The vulval mucosa was less erosive and less painful; the vagina was still erosive but less contact bleeding was noticed by the patient. Tacrolimus was continued and the symptoms improved after another 4 weeks of treatment. In one patient the vulval mucosa healed completely (Figs 1b.c) and there was no further contact bleeding. We reduced the frequency of application of tacrolimus to once weekly in the first patient; the LP has not relapsed after 16 weeks. In the other patient the disease was controlled after 12 weeks, as judged by the patient and the investigator; she continues to use tacrolimus ointment three times weekly, which has controlled her LP during a follow-up of 20 weeks. While applying the tacrolimus the patients experienced a slight burning sensation. No other side-effects were noticed. The tacrolimus concentration was measured 2 months after initiation of the treatment and was lower than 1·5 μg L^{-1} in one patient and 4 μg L^{-1} in the other (trough concentration after three consecutive applications). At 11 h after dosing, the therapeutic trough range for oral tacrolimus in organ transplant recipients has been defined at 5–20 μg L^{-1}. We are therefore below the systemic therapeutic level in our patients and do not expect serious adverse effects.

The conventional treatment for erosive LP of the mucosae is potent to very potent topical corticosteriods.[1–3] However, this did not lead to a major improvement in our patients, and many patients suffer from disabling symptoms such as fused labia minora with a narrowed introitus vaginae and a bleeding and fused vagina. Earlier studies with topical cyclosporin in erosive LP gave conflicting results.[4–6] Both cyclosporin and tacrolimus inhibit T-lymphocyte activation
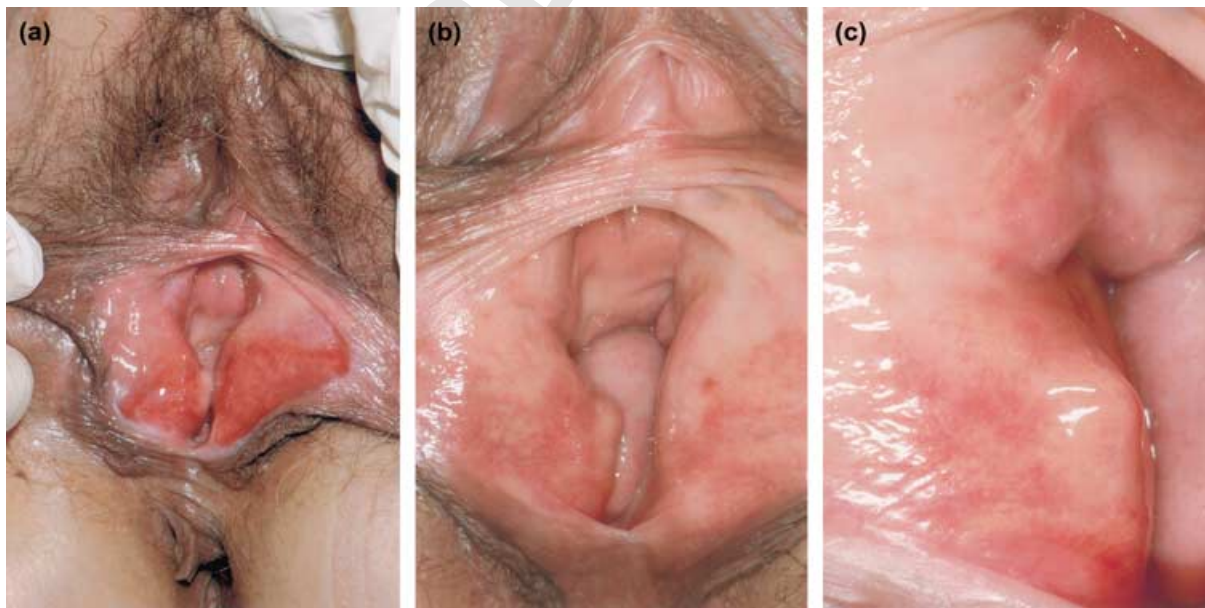

Figure 1. (a) Erosive vulval lichen planus before treatment; (b,c) condition of the vulva after 8 weeks of treatment with topical 0·1% tacrolimus.

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in preventing interleukin-2 production. However, topical cyclosporin may have failed to provide acceptable clinical efficacy when used topically because of its poor skin penetration.[7] Vente *et al.*[8] and Lener *et al.*[9] reported topical tacrolimus to be effective in mucosal LP (vulval and oral). We applied topical tacrolimus successfully in vaginal and vulval LP without serious side-effects. The long-term effect needs to be evaluated; it may be necessary to apply low-dose topical tacrolimus long-term in order to suppress the LP. However, this is the first time that a topical treatment has been shown to be effective in erosive LP. This therefore may prevent the disabling course of the disease in many women.

Topical tacrolimus ointment is available in the U.S.A and Japan; it is available via the International Pharmacy in Europe, but is expensive: 50 g of the ointment (Protopic ointment, Fujisawa, U.S.A) costs about 400 guilders (about £150). We decided to use a preparation suitable for the mucosa that was prepared by local pharmacists after discussing drug compatibility. However, we would prefer to use a manufactured preparation for reasons of drug compatibility and to ensure a constant concentration of tacrolimus. We are also unable to judge the shelf life of the 'home-made' ointment. If we are to recommend this very promising treatment for erosive LP of the mucosae it must be tested in larger groups, if possible in a randomized fashion.

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