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LETTERS TO THE EDITOR

Invasive Squamous Cell Carcinoma Treated with Imiquimod 5% Cream

Ángeles Flórez, Carlos Feal, Carlos de la Torre and Manuel Cruces
Department of Dermatology, Hospital Provincial, CHOP, C/Loureiro Crespo, n° 2, Pontevedra, ES-36001, Spain. E-mail: angeflor@hotmail.com
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Sir,

Imiquimod is an immune response modifier currently approved for the treatment of external genital and perianal warts in adults (1). It has been shown to have antiviral and antitumour effects in animal models by stimulating both the innate immune response and the cellular pathway of acquired immunity (1, 2). However, it does not exhibit direct antiviral or antiproliferative activity in cell cultures (3). Case reports and preliminary studies suggest the effectiveness of imiquimod 5% cream in the treatment of non-genital human papillomavirus infections, molluscum contagiosum and the following oncological lesions: basal cell carcinoma, actinic keratoses, Bowen's disease, vulvar intraepithelial neoplasia, cutaneous T-lymphoma, cutaneous extramammary Paget's disease and malignant melanoma (1–4). To our knowledge, the efficacy of imiquimod 5% cream in the treatment of invasive squamous cell carcinoma (SCC) has not been reported before.

CASE REPORT

An 87-year-old male presented with an 8-month-old lesion on his left leg. Previous medical history revealed a long-standing history of psoriasis, bilateral cataracts and depression. Psoriasis, which had been treated with phototherapy (topical PUVA), topical corticosteroids and topical calcipotriol, was not active on admission, and the patient was under no dermatological treatment. The patient was immunocompetent.

Physical examination revealed a sharply demarcated, 4 × 5 cm scaly erythematous plaque located on the anterior aspect of the left leg (Fig. 1). A 1 × 2 cm biopsy, including the edge of the tumour, showed irregular masses of atypical squamous epidermal cells invading the dermis (Fig. 2). The diagnosis of infiltrative squamous cell carcinoma was performed. Physical examinations and imaging studies disclosed tumour dissemination.

The patient declined to undergo surgery but accepted starting on topical therapy with imiquimod 5% cream under occlusion 8 h a day every other day for 8 weeks. The patient experienced local skin reactions such as moderate erythema, superficial erosive changes and discomfort, but he did not require rest periods because of them. No systemic side effects were observed during therapy. Two months after the end of treatment only a 1 × 1.5 cm papule, with the clinical appearance of scar tissue, could be seen at the treatment site. This residual lesion was removed and evaluated for the presence of remaining SCC. Serial sections showed a regenerative epidermis alternating areas of hyperplasia and atrophic areas. Important chronic mononuclear inflammation with focal granuloma formation, as well as proliferative fibrosis and hemosiderin deposits, were present in dermis. Remaining SCC was not found. The patient has attended follow-up visits every 3 months and has remained free from tumour recurrence for 12 months since therapy was discontinued.

DISCUSSION

Imiquimod 5% cream has been reported to be effective and safe for treating actinic keratoses and Bowen's disease (5–8), two conditions which have well recognized potential to transform into invasive SCC (7, 8). Indeed, several papers have documented the efficacy of treating actinic keratoses with imiquimod 5% cream.

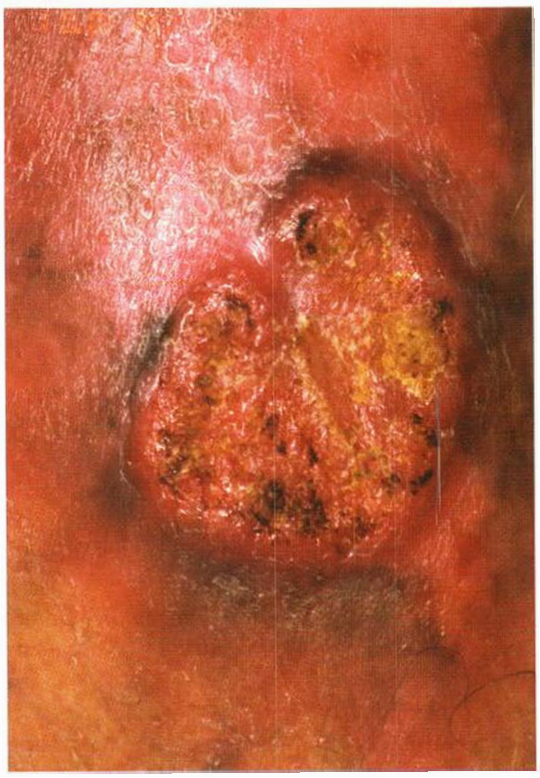

Fig. 1. Sharply demarcated, 4 × 5 cm squamous cell carcinoma located on the anterior aspect of the left leg.

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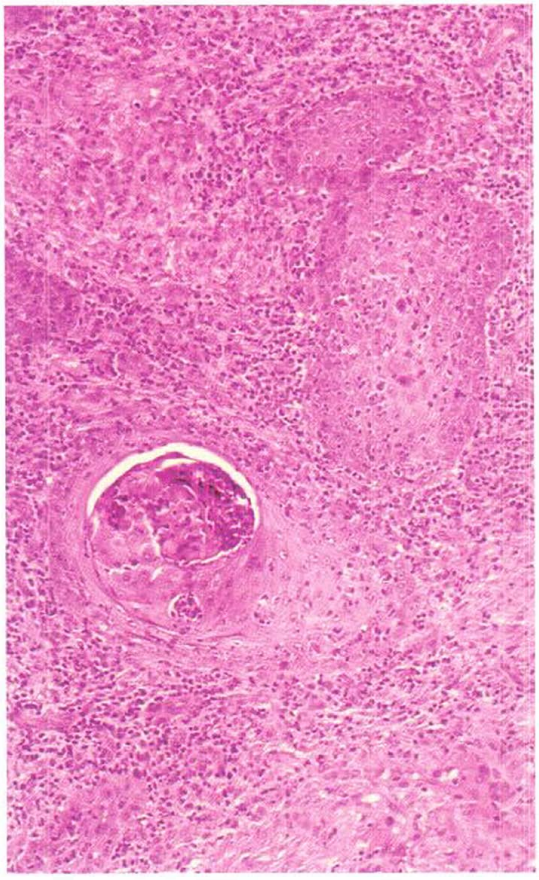

Fig. 2. Irregular masses of atypical squamous epidermal cells invading the dermis (haematoxylin-eosin stain; original magnification ×200).

These include case reports (5), small trials (9, 10) and randomized, double-blind, vehicle-controlled studies (11). In relation to Bowen's disease, Mackenzie-Wood et al. (8) examined the efficacy of once-daily imiquimod 5% cream to biopsy proven lesions of Bowen's disease in 16 patients. Fourteen of the 15 patients who completed the study had no residual tumour present in the 6-week post-treatment biopsy. In addition, several case reports have documented the efficacy of imiquimod 5% cream in treating anogenital Bowen's disease (12–15). In all cases, treatment was well tolerated, although patients experienced local adverse effects such as erythema, oedema, erosion, itching and scabbing (5–15).

The exact mode of action of imiquimod 5% cream when treating actinic keratoses and Bowen's disease remains to be determined, although all evidence points to an immunologic mechanism (6–8). The question has been raised as to whether imiquimod's mode of action is related to an immune mechanism against malignant cells or against human papillomavirus associated with cancerous lesions (7). Certainly, there is a strong correlation between anogenital Bowen's disease and infection with some human papillomavirus subtypes. In other areas of the body surface this association is currently under debate (7).

Of course, the current treatment of choice for invasive SCC is excision. Nevertheless, imiquimod 5% cream may be considered as a therapeutical option, particularly when treating large-diameter lesions and SCC at certain anatomic locations such as the scalp, face and shin, where surgery and other destructive techniques may carry the risk of scarring, deformity and impaired function. It could also be considered as an alternative therapy for patients in which surgery is contraindicated. Certainly, the efficacy and safety of treating invasive SCC with imiquimod 5% cream is still to be determined and further studies are needed.

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