Fig 1. Depigmented patches on genitalia occurring after treatment of verruca with imiquimod.

reports of pigmentary changes. Of these reports, 51/68 (75%) reported occurrences of depigmentation (43), vitiligo (7), or hypopigmentation (1), with the remaining cases reporting hyperpigmentation (17). Imiquimod was the only product used in 27.4% (14/51) of the pigmentary events and only 3 of the reported cases were using other topical agents.

Imiquimod's anti–human papillomavirus activity is mediated via the enhancement of host immune responses. The drug stimulates CD8 cells to become cytotoxic and lyse virus-infected cells, and induces maturation of Langerhans cells leading to enhancement of antigen presentation.[1,2] Similarly, vitiligo may be mediated through antigen presentation by activated Langerhans cells with resultant destruction of melanocytes by cytotoxic T lymphocytes directed to melanocyte surface antigens.[3] Expanded use of imiquimod may lead to increased occurrences of localized depigmentation as observed in our patient. Clinicians should be aware of potential pigmentary changes, particularly when using imiquimod on areas of skin that are readily visible.

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Infiltrative squamous cell carcinoma on the scalp after treatment with 5% imiquimod cream

To the Editor: We recently read results from the first clinical studies focusing on establishing the safety and efficacy of 5% imiquimod cream in the treatment of actinic keratosis.[1,2] We have started applying this treatment with the same indications, and we had the opportunity to observe the development of a squamous cell carcinoma at the site of an actinic keratosis previously treated with 5% imiquimod cream. The patient was an 81-year-old man with various lesions on the scalp; they were hyperkeratotic, not painful, slow growing, and of different sizes (Fig 1). A 3-mm punch biopsy was performed, which led to a diagnosis of actinic keratosis. We began treatment with 5% imiquimod cream once a day for 12 weeks. The typical local reactions—erythema, edema, desquamation, itch, and variable sore sensation—were observed after 4 weeks of treatment (Fig 2). These were more intense during the following weeks, but they did not lead to cessation of treatment. No important adverse systemic effects were observed. The patient was examined 2 weeks after cessation of treatment and complete disappearance of the actinic keratosis was noted. However, 1 month later he developed an asymptomatic tumor on one of the treated lesions, which grew quickly and had the appearance of a keratoacanthoma (Fig 3). Histologic study confirmed the diagnosis of a squamous cell carcinoma. The lesion was removed with solid cryosurgery (closed probe, local anesthesia, and double fast freezing–slow thaw cycle). After a year of follow-up, no recurrence has been observed on this location or on the rest of the area treated with 5% imiquimod cream.

Imiquimod cream is a modifying agent for the immunologic response that was first approved for the treatment of genital warts and condyloma. However, this drug has also an anti-tumor activity, because of the activation of natural killer cells provoked by an increase of the levels of cytokines such as interferon alpha (IFN-α), interleukin-6 (IL-6), and interleukin-8 (IL-8).[3] These modifications could be

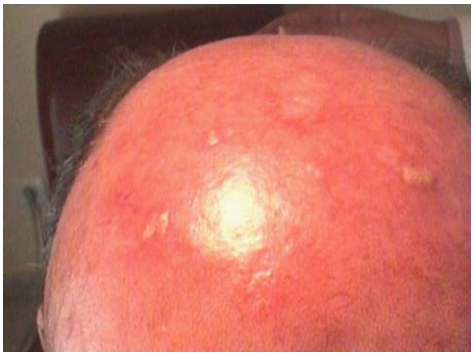

Fig 1. Aspect of the patient before the treatment with 5% imiquimod.

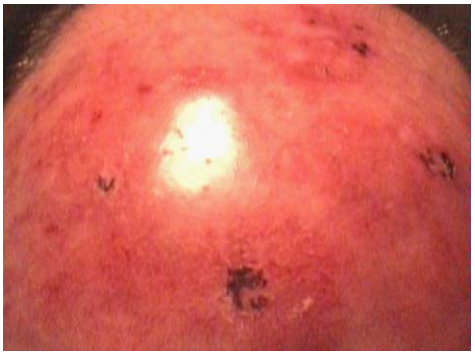

Fig 2. Erythema, edema, and desquamation caused by imiquimod.

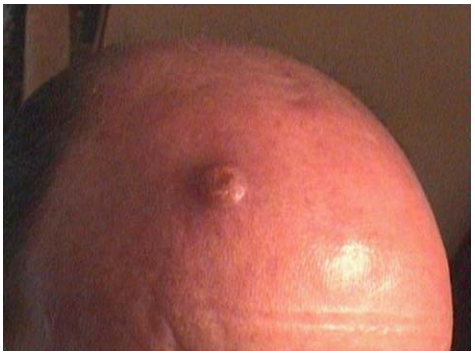

Fig 3. New, fast-growing tumor 1 month after the end of imiquimod treatment.

related to the interaction between the drug and the receptor toll-like receptor-7 (TLR-7).[4]

Several reports on the use of imiquimod cream to treat actinic keratoses have been published. Patients with multiple actinic keratosis treated with 5% imiquimod cream usually have good results and no recurrences during the follow-up period,[1,2,5,6] but the drug is now being used more widely, and the opportunity to observe more patients over longer follow-up times may be informative.

In conclusion, 5% imiquimod cream seems to be an effective treatment for actinic keratosis, although its cure ratio is variable. Local adverse effects are frequent, with a light or moderate intensity; these provoke halt periods in a high percentage of patients. In our case, we observed the development of an infiltrating squamous cell carcinoma on the exact location of a previous actinic keratosis, which had apparently disappeared after earlier treatment with 5% imiquimod cream. Although the drug seems to be effective, we think that the follow-up of these patients must be strict and long, because we are talking about tumor lesions and there is a risk of malignant neoplasia even on locations previously treated.

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A case of mucocutaneous Behçet's disease responding to etanercept

To the Editor: Behçet's disease is a systemic necrotizing vasculitis with potential involvement of arteries and veins of all sizes, but with a predilection for small venules. In mild cases, recalcitrant