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CASE REPORT

Spontaneous regression of keratoacanthoma can be promoted by topical treatment with imiquimod cream

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ABSTRACT

Imiquimod, the first member of a new class of immune response modifiers, is approved for the treatment of external genital and perianal warts. Recently, many clinical trials highlighted the potential of imiquimod as a treatment for other viral infections and cutaneous neoplasms. We report two cases of facial keratoacanthomas (KA) treated with topical 5% imiquimod cream. Patients were successfully cleared of KAs after treatment for 8 weeks. No recurrence occurred after a 1-year follow-up. Despite the fact that KAs are characterized by the potential for spontaneous regression, it is possible that a faster activation of CD4+ lymphocytes, via interferon release and cytokine secretion takes place after imiquimod application leading to KA regression.

Key words: imiquimod, interferon, keratoacanthoma, tumour

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Keratoacanthoma (KA) represents an epithelial tumour that is characterized by a keratin-filled crater, rapid growth in the proliferation stage, and the potential for spontaneous regression, which is likely to be mediated by activated CD4+ lymphocytes via cytokine secretion.[1] Clinically it appears as a rapidly enlarging, sharply demarcated, keratotic nodule. Histologically, KA displays distinct features that must be differentiated from squamous cell carcinomas (SCC) in the proliferation stage.

Imiquimod is an immune response modifier used primarily to treat anogenital warts. It induces cytokines and enhances cell-mediated cytolytic activity *in vivo* exhibiting antiviral and antitumour effects. By inducing cytokines, such as interferon α, imiquimod stimulates both the innate immune response and the cellular arm of acquired immunity. Given the convincing therapeutic results of imiquimod when used for treating selected types of epithelial skin cancer, we became interested in studying imiquimod as an adjuvant for treating KAs.

Case reports

Case 1

A 54-year-old otherwise healthy female presented with a 20-day history of a rapidly enlarging keratotic nodule on the left infrapalpebral region clinically consisting of a KA. Clinical examination revealed a dome-shaped tumour of about 10 mm in diameter with a central keratotic plug (fig. 1). Histological examination of a 3-mm punch biopsy specimen confirmed the diagnosis of KA, although an highly differentiated SCC could not be excluded. The lesion was treated with 3 weekly applications of imiquimod 5% cream. The treatment was completed 1 week after clinically successful clearance. The patient received a total of 24 treatments over a period of 8 weeks. She had a 1-week rest period due to erythema, erosion and crusting at the treatment site (fig. 2). The patient reported no systemic side-effects nor irritation at the treatment site during the last 2 weeks of treatment. There was a persisting, depigmented small atrophic area (3 mm in diameter) in the treatment area when the use of imiquimod cream was stopped (fig. 3). No new lesions were seen at 1-year follow-up.

Case 2

A 63-year-old otherwise healthy Caucasian female presented with a rapidly enlarging keratotic nodule on her face clinically consisting of KA. Clinical examination showed a dome-shaped tumour of about 9 mm in diameter with a central keratotic plug. Histological examination confirmed the diagnosis of KA,

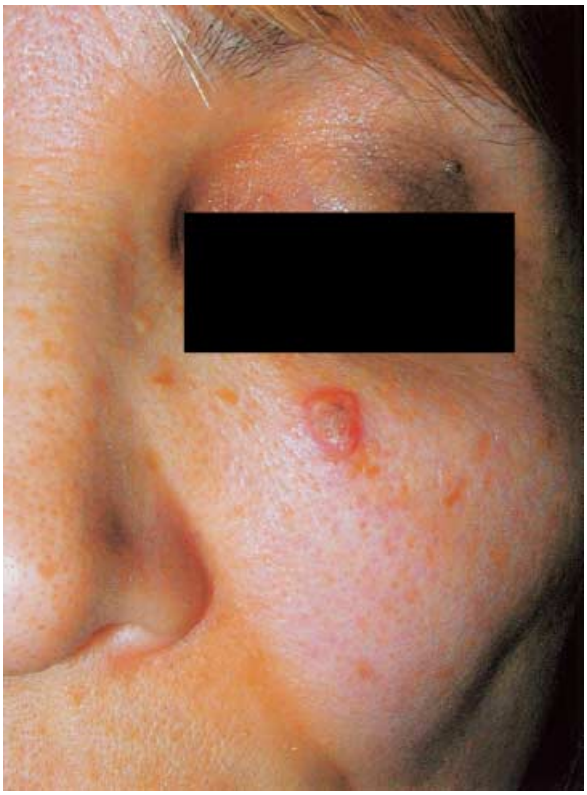

fig. 1 Patient 1: keratoacanthoma on the infrapalpebral left area.

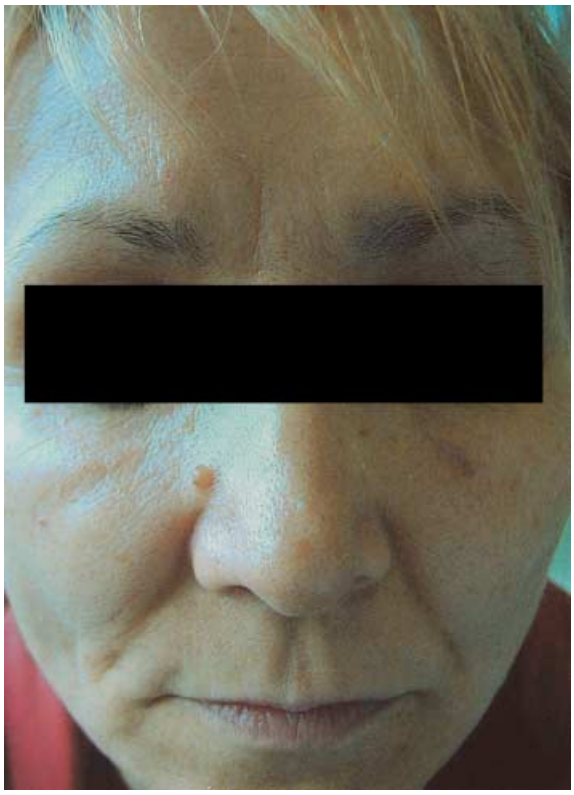

fig. 3 Patient 1: regression of keratoacanthoma.

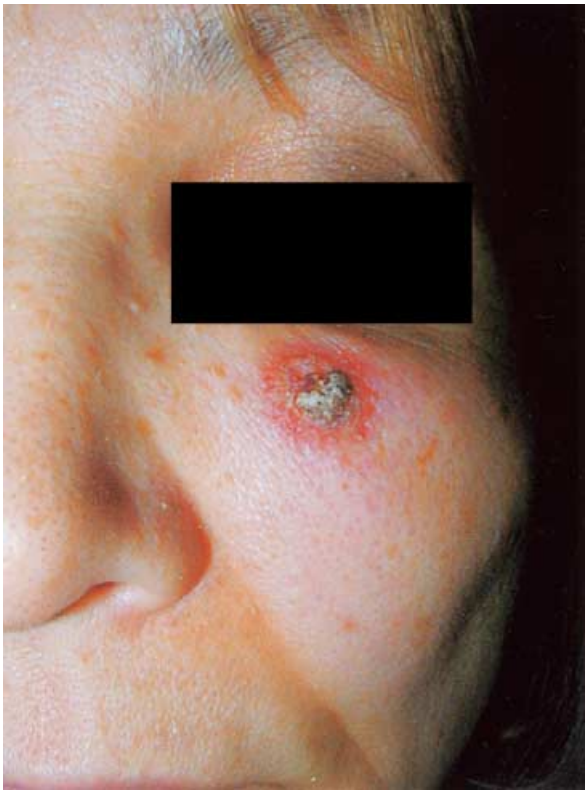

fig. 2 Patient 1: partial regression of keratoacanthoma with crusting.

although SCC could not be excluded. The lesion was treated with 5 weekly applications of imiquimod 5% cream. The treatment was completed 1 week after clinically successful clearance. The patient received a total of 40 treatments over a period of 8 weeks. She had a 1-week rest period due to erythema, erosion and crusting at the treatment site (fig. 4). No systemic side-effects or irritation at the treatment site were reported during the last 2 weeks of treatment. There was a persisting, depigmented small atrophic area (2 mm in diameter) in the treatment area when the use of imiquimod cream was stopped (fig. 5). No new lesions were seen at 1-year follow-up.

Discussion

KA is regarded as an immunologically well-controlled low-grade SCC;[2] however, others consider it a totally benign entity.

Although it can regress spontaneously, at least a quarter of them undergo malignant transformation, which occurs more frequently in older patients and exposed areas. This transformation is a focal event, which may happen at any stage of its development. Therefore, some authors suggest acting surgically on all KAs and to study them in serial paraffin blocks so as to disclose any focus of malignancy.[3] In addition, because of its rapid growth, unpredictable final size and possibility of local tissue destruction, it is routinely treated by surgical excision.

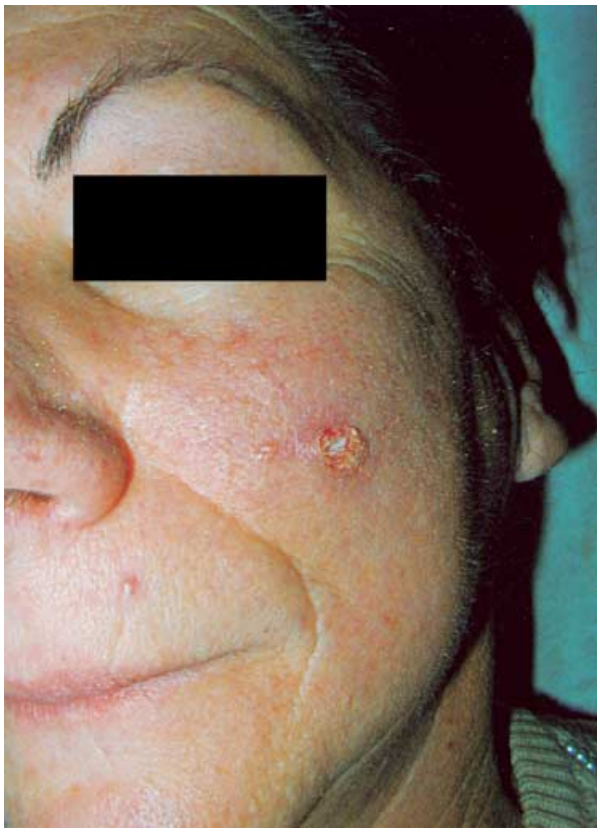

fig. 4 Patient 2: partial regression of facial keratoacanthoma with crusting after 3 weeks.

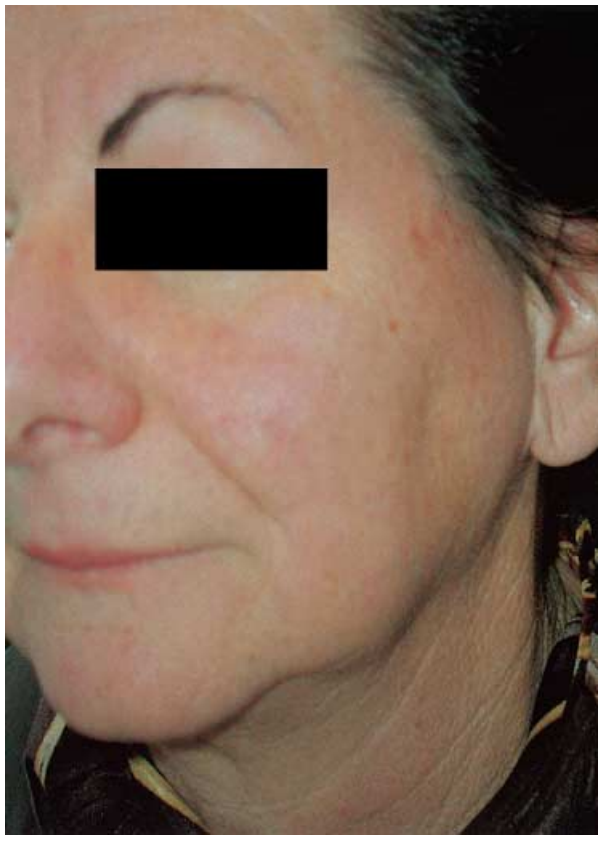

fig. 5 Patient 2: regression of keratoacanthoma.

Recently, treatment with intralesional interferon α proved beneficial in the treatment of KA.[4]

Beyond its established use in genital warts, there are many case reports and preliminary studies suggesting the effectiveness of the novel immune response modifier, imiquimod 5% cream in the treatment of actinic keratosis, basal cell carcinoma, SCC and Bowen's disease.[5–7] As imiquimod is a strong inducer of the production of interferon α, a favourable effect on the regression of KA is predictable as well. More recently four patients with facial KAs were successfully treated with imiquimod 5% cream applied every second day for 4–12 weeks.[8]

We present two cases of KAs of the face that were effectively treated with imiquimod 5% cream. The regression of the neoplasm appeared faster in patient 2, who was treated with 5 weekly applications of imiquimod. Clinical cure was confirmed after 8 weeks of monotherapy. The treatment was generally well tolerated and adverse effects consisted of localized tenderness, erythema and crusting. In both cases we observed a slight atrophic scarring, without loss of sensitivity. No tumour recurrence was noted after withdrawal of the drug and a 1-year follow-up.

Although KA can regress without treatment, in our patient we noted the rapid development of inflammation and tumour necrosis soon after starting topical applications of imiquimod. Rapid tumour regression on application of imiquimod 5% cream was also observed in four cases of KAs reported by Dendorfer *et al.*[8] It is likely that a faster activation of CD4+ lymphocytes, via interferon release and cytokine secretion, takes place after imiquimod application. In conclusion, imiquimod 5% cream may represent an alternative treatment option for KA offering a minimally invasive and promising therapeutic option. Therapy with topical immune response modifiers may prove beneficial in cases of KA. Also it may, if future studies confirm our findings, play a part in dealing with areas such as the face, in which more destructive techniques may result in cosmetic defects or functional impairment.

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