

Successful Treatment of Extensive Condyloma Acuminata of the Inguinal Area and Thigh with Topical Imiquimod Cream

Sir,

Imiquimod, a non-nucleoside heterocyclic amine, is a member of a new class of immune response-modifying agents (1). Topical use of imiquimod as an immune system modifier for the treatment of genital and perianal warts has recently been described (2, 3). However, the utility of this agent for the treatment of warts located on other areas of the skin is unknown. We describe here a patient with extensive condyloma acuminata involving the groin and thigh area who had a dramatic response to topical imiquimod cream.

CASE REPORT

A 51-year-old white man with no significant previous medical history presented with a 1-year history of multiple verrucous lesions of condyloma acuminata in his right genital area and thigh. He had previously been treated unsuccessfully for condyloma with cryotherapy, podophyllin, topical podofilox and laser therapy.

On physical examination, there was extensive involvement of the right inguinal area and thigh with verrucous papules. The total wart area was calculated as 1,770 mm². The patient was started on topical imiquimod 5% cream 3 times per week. He applied the medication at night and washed it off in the morning on the days of application.

At 1-month follow-up the patient noted improvement, with no erythema or irritation. The total wart area had decreased to 1,375 mm². The patient was told to increase the frequency of application of the imiquimod cream by applying it daily. When the patient returned 4 weeks later the original wart area had decreased greatly to 275 mm². He reported no adverse effects.

The patient continued to apply imiquimod cream 3 times weekly with monthly follow-up. At 3-month follow-up the total wart area was 20 mm², with only 3 discrete lesions remaining. At 4-month follow-up all of the original lesions had resolved. There were only 3 small new lesions on the right thigh, located medially to the original treatment area.

DISCUSSION

Imiquimod is an imidazoquinolinamine which has been used with success for treating both genital herpetic infections and certain tumors in murine models, as well as for treating external anogenital warts in human studies (1–3). Its mechanism, however, has not been completely defined. It has no direct antiviral properties, but has been shown to increase levels of interferon- α and other cytokines including tumor necrosis factor, thus upregulating natural immune defenses (1). These properties make imiquimod an interesting agent for the treatment of verrucae in immunosuppressed patients, such as those with HIV, as it is known that this subset of patients tend to have verrucae which are more extensive and more resistant to current therapies, most probably as a result of deficiencies in their immune system.

The treatment of warts in general involves physically destructive methods, and this often becomes a problem in the treatment of facial warts as patients are concerned about the cosmetic effects of the therapy used. This is even more of a concern in darkly pigmented individuals, as post-inflammatory hyper- and hypopigmentation can be a problem. A non-cytotoxic agent like imiquimod may therefore

have a role in the treatment of facial warts; however, its efficacy is unknown as studies in humans to date have only involved treatment of anogenital warts (2–4). There is no reason to assume, however, that treatment should only be limited to the genital area as the mechanism of human papillomavirus (HPV) infection does not vary with body site (although HPV type may) and neither should the immune response. The use of imiquimod has also been expanded to other viral infections of the skin. Syed et al. (5) recently reported on the treatment of molluscum contagiosum in males with an analog of imiquimod 1% cream. After 4 weeks of treatment imiquimod cream cured 82% of the patients and 86.3% of the molluscum lesions. The only side effects were mild, local reactions. The successful treatment of facial flat warts has also been reported (6), as has treatment of facial verrucae in a patient with HIV (7). Imiquimod cream has also been used successfully in the treatment of basal cell carcinomas of the skin (8).

In our patient, dosing both 3 times a week and daily was well tolerated, without any significant side effects, and therapy resulted in clinical regression of the condyloma lesions in the right groin and thigh area. The regression during the first 2 months was remarkable given the original extent and hyperkeratotic nature of the lesions. Imiquimod is less likely to work successfully in highly keratinized, non-mucosal surfaces, where its penetration is limited. This case is therefore highly interesting and of significant importance for elucidating the clinical efficacy of topical imiquimod against problem condylomas. The patient tolerated daily application of imiquimod for 1 month of treatment without any significant side effects. After dramatic improvement in the condition, application was reduced to 3 times per week, in consideration of the reduced area of involvement and in order to avoid irritation. The patient developed new lesions at the periphery of the original treatment area after that area had cleared. It is possible that there was spread of HPV from the original area, and that the local immunity was upregulated only within the treatment area.

The clearance of condyloma in the non-genital areas in our patient is encouraging. This finding suggests that imiquimod may be useful as a primary or adjunct therapy in the treatment of non-genital lesions caused by HPV. Further observations and studies will help to elucidate the efficacy of imiquimod in these settings.

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Unusually Large Cutaneous Metastases of Renal Cell Carcinoma

Sir,

Renal cell carcinoma (RCC) accounts for 2–3% of visceral malignant tumors and occurs with a male:female ratio of 3:1. Most cases of sporadic RCC develop in the 5th–7th decades of life, although younger patients may be affected by inherited forms. Metastases of RCC are present at the time of diagnosis in 10–45% of cases and preferentially involve the lung, bones and contralateral kidney (1). Cutaneous metastatic lesions have been reported in 2.8–6.8% of cases, with the most common sites being the head/neck region and the trunk (2). In the majority of patients, skin metastases of RCC develop in the late stage of the disease and are associated with visceral involvement. We describe here a young man with a history of RCC who presented with cutaneous metastases of unusually large size with a rapid and fatal clinical course.

CASE REPORT

A 35-year-old man was examined for the presence of multiple, rapidly growing cutaneous and subcutaneous masses in the head and neck



Fig. 1. Cutaneous metastases of renal cell carcinoma presenting as large nodules in the head and neck region.

region. One year earlier the patient had undergone right radical nephrectomy for a sporadic clear-cell adenocarcinoma (T_{3b}N₀M_X). At that time the patient refused any chemotherapy and radiation therapy, preferring to undergo an “alternative” treatment, which was not described in detail. Physical examination revealed three red–purplish masses, 3–7 cm high with a 5–7 cm base. One was coniform and located on the forehead, the second was lobulated and present on the left oral commissure and the third was roundish and located in the left parietal region (Fig. 1). In addition, a subcutaneous mass was evident on the left temporal area and multiple solitary papules and nodules were scattered over the face and neck. Histopathologic examination of a skin biopsy specimen showed a monomorphic infiltrate, located in the entire dermis and subcutaneous tissue, composed of irregular aggregates of large-sized neoplastic cells. Cytomorphologically, tumor cells were polyhedral with a central pale nucleus and abundant clear cytoplasm. Periodic acid–Schiff-positive granules were detected within the cytoplasm of the clear cells before, but not after, digestion with diastase. Immunohistochemical staining with anti-pan-cytokeratin, epithelial membrane antigen and vimentin antibodies was positive. These findings were consistent with the diagnosis of cutaneous metastases of renal cell adenocarcinoma. Routine laboratory investigations revealed hypochromic anemia and high levels of serum creatinine (4.2 mg/dl; normal range: 0.60–1.20 mg/dl), urea nitrogen (190 mg/dl; normal range: 10–50 mg/dl) and uric acid (15.5 mg/dl; normal range: 4–7 mg/dl). A chest X-ray showed multifocal lung metastases. The patient was treated with palliative therapy (blood transfusions and narcotic analgesics) and died of widespread disease 2 weeks later.

DISCUSSION

Cutaneous metastases of RCC most frequently occur as asymptomatic, pink to red to purplish, rapidly growing, cutaneous and/or subcutaneous nodules (3). They are often pulsatile but rarely ulcerated. An unusual presentation as a hyperkeratotic lesion mimicking a cutaneous horn has been described (4). The size of individual cutaneous metastatic lesions, as reported in the literature, varies greatly from 0.5 to 5.6 cm in diameter although most of the lesions measured <3 cm. In our patient, unusually large, exophytic cutaneous lesions, 3–7 cm high with a 5–7 cm base, were observed.

Clinical differential diagnosis of skin metastases of RCC may include pyogenic granuloma, angioma, Kaposi's sarcoma and cutaneous lymphoma. Histopathologically, differentiation between sebaceous tumors, ballniform cell melanoma and vascular tumors may be difficult. However, a cytomorphologic feature highly suggestive of metastatic RCC is the presence of