Sir,

Among the many methods used in the treatment of condylomata acuminata, imiquimod 5% cream is the sole medication that is approved by the United States Food and Drug Administration.\[1,2\] Since 2005, ten patients with condyloma acuminata have been reported to develop vitiligo or vitiligo-like depigmentation following the use of imiquimod.\[3-11\] Vitiligo is an acquired skin disorder characterized by the appearance of depigmented macules due to a reduction in the number and function of melanocytes. Although several hypotheses have been proposed, the mechanism of depigmentation remains uncertain and is thought to be due to an immune-mediated attack by auto-reactive cytotoxic T-cells on melanocytes. Like other autoimmune disorders, cytokines play a role in the recruitment of auto-reactive T cells to the skin, which in turn may be influenced by imiquimod.\[12\] An additional case of vitiligo-like lesions induced by imiquimod in a 26-year-old man is presented here with a short review of literature.

A 26-year-old Lebanese man presented with hypopigmented lesions on the penis. He had applied imiquimod 5% cream on three condyloma acuminata lesions on his penis, three months prior to presentation. He used to apply the cream at night and wash it off in the morning, once a week for 3 weeks. Although he noticed some irritation and excoriation in the treated areas, he continued the application. After stopping the application of imiquimod, he observed some hypopigmented lesions in the treated areas which did not expand in size; however, they did not repigment in the following 2 months. He and his family members had no history of skin disorders such as vitiligo, other depigmented dermatoses or autoimmune diseases. He denied use of any other topical treatment.

Clinical examination revealed the hypopigmented macules on the penile region [Figure 1] that were accentuated on Wood’s light examination. Laboratory tests (blood counts, liver and kidney function tests, thyroid function tests, human immunodeficiency virus (HIV) and syphilis serologies, hepatitis B and C serologies) were completely normal and a skin biopsy was recommended but refused by the patient. He was clinically diagnosed with imiquimod-induced localized vitiligo-like lesions.

Imiquimod is an immune-response modifier that is generally well tolerated but has minor side effects like erythema, burning, blistering and excoriation.\[13\] Its mechanism of action in human papilloma virus (HPV) infection is by enhancing the host’s innate and cellular immune response against the virus; it also stimulates peripheral blood monocytes, macrophages and dendritic cells to produce certain cytokines (interferon alfa, interleukins 12, 6 and 8, tumor necrosis factor alfa, nitric oxide).\[14,15\]

We found 10 previous reports in English of Imiquimod-induced hypopigmented macules [Table 1]. There appear to be no specific criteria to differentiate among “depigmentation,” “hypopigmentation,” “vitiligo” or “vitiligo-like lesions” and these names were chosen at will by authors of the respective reports. Moreover, among the 10 patients previously reported, only one had agreed for a biopsy and the histopathologic examination findings were consistent with vitiligo.\[14\] Besides, family history of vitiligo or other autoimmune disorders was reported in only one case. Thus, the reported hypopigmented macules were most probably secondary to imiquimod application. For this reason, we felt “imiquimod-induced hypopigmented macules” would be a better name for this side effect.
Concerning the pathomechanism of this side effect, many hypotheses were suggested. Imiquimod application induces antigen presentation that activates Langerhans cells. Consequently, destruction and apoptosis of the melanocytes can occur and this was confirmed by TUNEL assay.[16] Moreover, vitiligo pathogenesis involves pro-inflammatory cytokines such as interferon alfa, interleukin 6 and 8, tumor necrosis factor alfa and nitric oxide.[12] These cytokines can be induced by imiquimod application and may play a role in the development of hypopigmentation.[17] Third, the occurrence of these hypopigmented imiquimod-induced lesions has been exclusively reported in the genital area that has thin skin and this may also contribute to its development.

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Conflicts of interest
There are no conflicts of interest.

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Sarcoidosis is a multisystem disorder of unknown etiology histologically characterized by non-caseating epithelioid cell granulomas. Primary localized cutaneous amyloidosis shows deposition of amyloid in apparently normal skin with no evidence of systemic amyloidosis. The association of systemic sarcoidosis and amyloidosis has been reported. However, the association of macular amyloidosis, a clinical subtype of primary localized cutaneous amyloidosis with cutaneous sarcoidosis is rare.

A 54-year-old woman presented with a history of hyperpigmentation of the skin of her upper back and the extensor aspect of her forearms for 7–8 months. The pigmentation started with a burning sensation followed by the development of raised skin colored lesions over 3–4 months. There were similar lesions on the shins. Clinical examination revealed multiple, skin-colored, discrete papules and plaques on a background of hyperpigmentation on the sun exposed areas of the upper back and the extensor aspects of forearms. The skin underlying and surrounding these lesions showed rippled pigmentation [Figure 1a and b]. Similar lesions were present on the shins. In addition, three, discrete, dull red, 1 cm × 1 cm papules were present on the chest. Systemic examination was non-contributory. Skin biopsy from hyperpigmentation of the upper back showed homogeneous, eosinophilic amyloid deposits in the papillary dermis [Figure 2]. Biopsy from a papular lesion with underlying pigmentation showed naked epithelioid cell granulomas and giant cells with a few lymphocytes in the superficial and mid-dermis, within the areas where amyloid was deposited. Melanophages were also seen in the papillary dermis [Figure 3]. The presence of the amyloid material was confirmed by Congo red stain.

Based on the above findings, the diagnosis of cutaneous sarcoidosis and cutaneous amyloidosis occurring at the same location was made. Complete hemogram, serum calcium, angiotensin converting enzyme levels and 24 h urine calcium levels were within normal limits. Mantoux test (with 5 units of PPD) was positive. Chest X-ray and electrocardiogram were normal. Pulmonary function test showed mild restriction of forced vital capacity.

Among the three known subtypes of primary localized cutaneous amyloidosis, macular and lichenoid are the most common presentations. The histopathology of macular amyloidosis typically reveals deposition of globular, amorphous eosinophilic material within the dermal papillae. Scattered apoptotic keratinocytes are also seen and this is believed to be the source of the amyloid material which reacts with anti-keratin antibody. The etiopathogenesis of this amyloid deposition remains unknown though...