Imiquimod-induced hypertrophic lupus erythematosus-like reaction

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Abstract

Imiquimod is a topical immunomodulator that acts as an inducer of interferon (IFN)-α expression through Toll-like receptor (TLR)7 signaling with indications for the treatment of non-hyperkeratotic actinic keratosis of the face or scalp, superficial basal cell carcinoma (BCC), and external genital and perianal warts. Imiquimod is also used off-label for nodular BCC, cutaneous T-cell lymphoma, pyogenic granuloma, and melanoma. Imiquimod-induced lupus-like reactions have been reported. However, hypertrophic lupus erythematosus (HLE) is a rare variant of cutaneous lupus and imiquimod-induced hypertrophic lupus has not been reported to date. We report a case of local induction of a plaque that resembled HLE clinically and histologically in an 82-year old woman following topical treatment with imiquimod.

Keywords: drug reaction, hypertrophic, imiquimod, lupus erythematosus

Introduction

Imiquimod is topical immunomodulator that acts as an inducer of interferon IFNα expression through TLR7 signaling with indications for the treatment of non-hyperkeratotic actinic keratosis of the face or scalp, superficial basal cell carcinoma and external genital and perianal warts. Imiquimod is also used off-label for nodular basal cell carcinoma, cutaneous T-cell lymphoma, pyogenic granuloma, and melanoma [1,2]. Imiquimod-induced lupus-like reactions have been reported [3]. Hypertrophic lupus erythematosus is a rare variant of cutaneous lupus characterized histologically by irregular epidermal hyperplasia associated with features of cutaneous lupus, including interface changes [4]. We report a case of local induction of a lesion that resembles HLE clinically and histologically in an 82-year-old woman following topical treatment with imiquimod.

Case Synopsis

An 82-year-old woman was referred to us by her primary care physician for evaluation and treatment of a hyperkeratotic plaque on her right cheek. The patient had a medical history of congestive heart

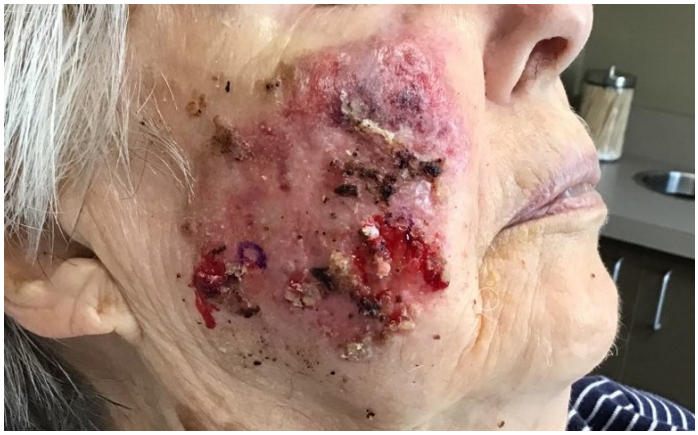

Figure 1. *Right cheek lesion.*

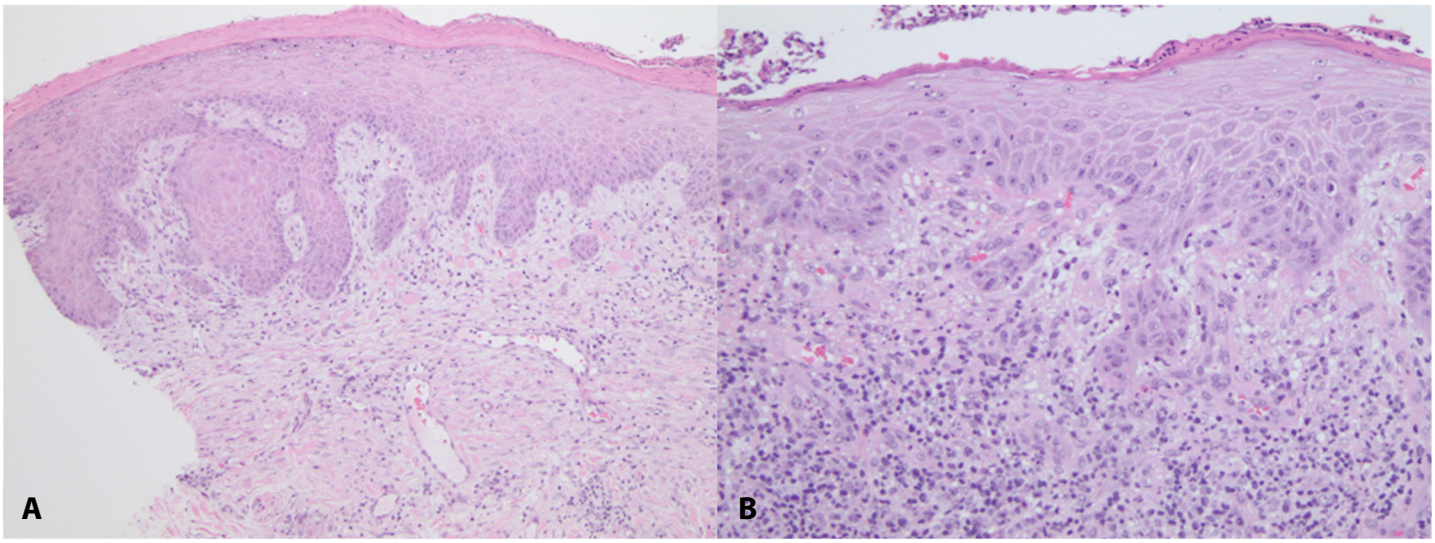

Figure 2. ***A)*** *Skin biopsy from the right cheek shows marked epidermal hyperplasia with overlying hyperkeratosis, parakeratosis, and focal scale crust. H&E, 100×.* ***B)*** *Skin biopsy specimen shows an interface pattern of lymphocytic inflammation along the dermal-epidermal junction and adnexal structure with superficial dermal fibrosis. Parakeratosis is present with the infiltrate extending into the deep dermis. H&E, 200×.*

failure, stroke, diabetes, dementia, rosacea, and onychomycosis. At presentation, the patient had a large, erythematous, crusted and bleeding plaque encompassing most of her right cheek (**Figure 1**).

A biopsy done about 18 months prior to presentation showed an irritated seborrheic keratosis. Repeat biopsies performed four and five months after the initial biopsy showed actinic changes, actinic keratoses, and possible basal cell carcinoma. She was prescribed imiquimod 5% cream daily for treatment of the actinic keratoses and possible basal cell carcinoma by another dermatologist. The patient completed a 4-week course of daily imiquimod prior to her visit with us. Previous treatments for the hyperkeratotic skin lesion included mupirocin 2% topical ointment and fluorouracil 5% topical cream. The patient's medications at the time of presentation included ciclopirox 8% nail solution, atorvastatin 20mg, cyclobenzaprine 10mg, donepezil 10mg, doxycycline monohydrate 100mg, enalapril maleate 5mg, furosemide 40mg, memantine 10mg, metformin 10mg, metoprolol succinate 100mg, ondansetron 4mg, potassium chloride 10mEq and warfarin 5mg, all orally.

Differential diagnosis of the hyperkeratotic plaque included basal cell carcinoma, squamous cell carcinoma, drug eruption, granuloma faciale, sarcoidosis and an infectious process. Two biopsies of the right cheek were performed by us and H&E staining as well as immunohistochemistry for CD123 were performed. H&E staining showed irregular epidermal hyperplasia and parakeratosis with a slight increase in superficial mucin. The inflammatory infiltrate extended into the deep dermis. No eosinophils were seen. CD123 immunohistochemistry detected increased plasmacytoid dendrocytes in clumps, findings consistent with HLE (**Figures 2, 3**).

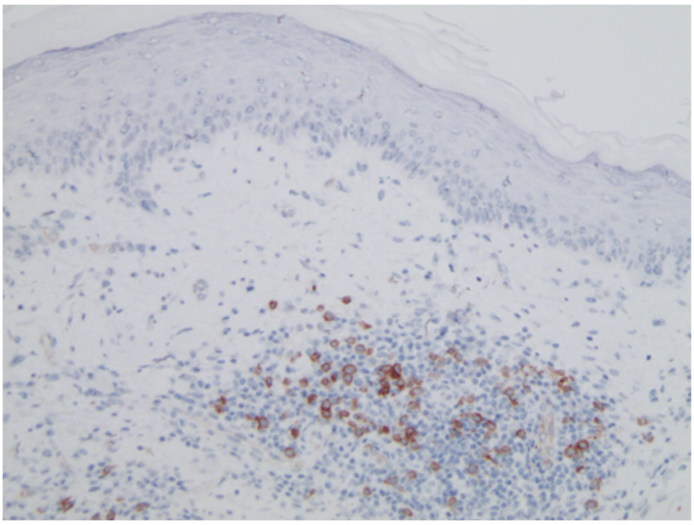

Figure 3. *An immunohistochemical stain for CD123 shows clusters of positive-staining dendritic cells within the inflammatory infiltrate, 200×.*

A diagnosis of imiquimod-induced HLE was made and the patient was started on topical mupirocin and halcinonide 0.1% cream two times a day with marked improvement in three weeks. The imiquimod had been discontinued prior to the patient being seen.

Case Discussion

Imiquimod, a member of the imidazoquinolinone family, targets TLR7 receptors on plasmacytoid dendritic cells, and Langerhans cells IFNα, TNF, interleukins 2, 6, 8, and other proinflammatory cytokines [5,6]. Imiquimod can induce cutaneous reactions including erythema, pain, and erosions as well as pemphigus-like acantholysis, vitiligo, and lupus-like changes [1]. The pathogenesis of imiquimod-induced lupus-like changes is unknown to date. However, it is postulated that histopathologic induction of lupus following imiquimod is related to TLR activation, TNF, and autoimmunity [7,8]. Increased expression of TLR7 receptors contributes to the development of lupus erythematosus and it is known that patients with systemic lupus erythematosus have increased blood levels of IFNα which correlate to disease activity [8,9]. Furthermore, reports of lupus-like lesions at the injection sites of subcutaneous IFNα can be found [10]. A histological clue to distinguishing an imiquimod-induced lupus-like reaction from cutaneous lupus erythematous is the absence of mucin [1]. Our case shows minimally increased mucin while showing histological features of HLE and the characteristic clumps of CD123 plasmacytoid dendrocytes reported in cutaneous lupus and HLE. [4].

Conclusion

We present a case of clinically and histologically hypertrophic lupus erythematosus-like reaction in imiquimod-treated skin. This reaction is rare and not previously reported in the literature.

Potential conflicts of interest

The authors declare no conflicts of interest.

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