SHORT COMMUNICATIONS

Imiquimod-Induced Cutaneous Lupus-Like Reaction: A Potential Histologic Pitfall Highlighting the Importance of Clinicopathologic Correlation

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Although controversial, the use of imiquimod for the treatment of primary melanoma in-situ (MIS) and residual MIS after surgical excisions has become more common. This is especially true in patients with multiple medical comorbidities, treatment of cosmetically sensitive areas and when surgical intervention would lead to significant functional impairment.[1] Recognizing imiquimod-induced lupus-like reactions on histology is important and necessitates good clinicopathologic correlation given the potential ramifications of unnecessary laboratory workup and the need for systemic medications can be avoided. We report a case of lupus erythematous-like reaction in a patient being treated with imiquimod for residual MIS of the face.

An 84-year-old woman with a history of multiple skin cancers and dementia was found to have an invasive melanoma of the right nasal side wall with a Breslow depth of 2.3mm. The patient underwent wide local excision with 2cm margins, sentinel lymph node biopsy negative and repair with a full thickness graft. The final clinical staging of melanoma was IIA. However, margins were positive for MIS. The patient was subsequently treated with topical 0.1% tretinoin daily for two weeks followed by imiquimod 5% cream 5 days a week for 12 weeks. Thereafter, the patient developed a pink erythematous patch with overlying scale (Figure 1). A scouting biopsy for residual MIS at the edge of the graft at 12 weeks showed a lichenoid interface dermatitis with features resembling a mixed connective tissue disease (Figure 2a & 2b) without residual MIS, which resolved after completion of topical imiquimod.

Figure 1. Faint pink erythematous patch with overlying scale after 2-week pretreatment with tretinoin 0.1% cream and 12-week field treatment with imiquimod 5% cream.

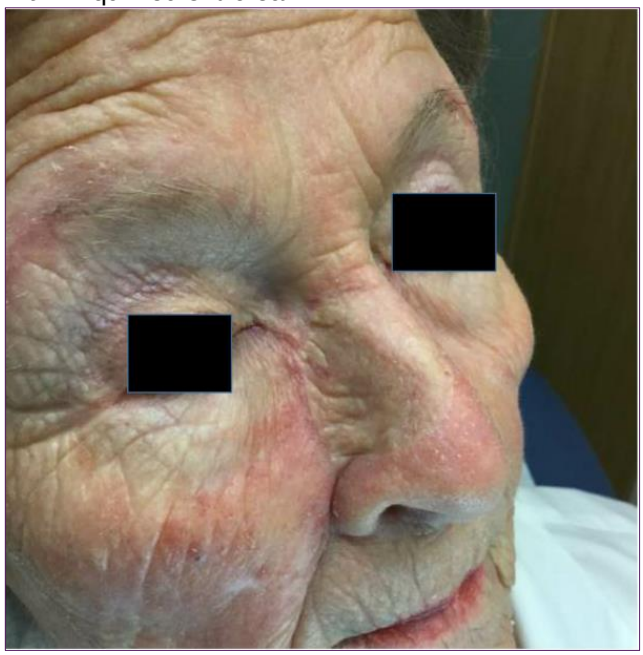
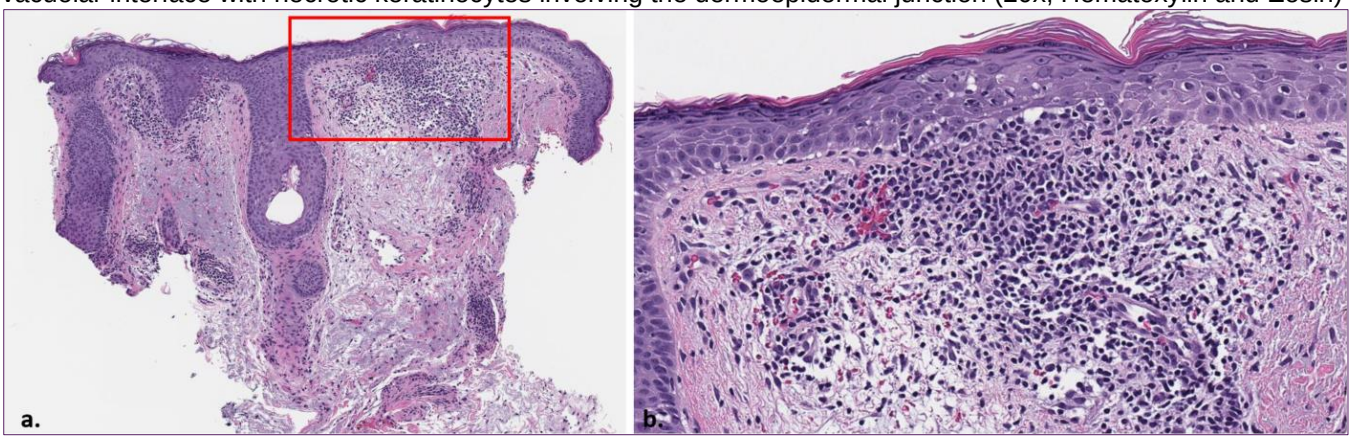


Figure 2. (A) Vacuolar interface dermatitis with lichenoid infiltrate (10x, Hematoxylin and Eosin). **(B)** Scattered vacuolar interface with necrotic keratinocytes involving the dermoepidermal junction (20x, Hematoxylin and Eosin)



Imiquimod is a toll-like receptor 7 agonist approved for superficial basal cell carcinoma, actinic keratosis and external genital warts. Common cutaneous reactions expected from treatment include erythema, pain, and erosions. In some instances, patients can have flu-like symptoms of fatigue and fever most pronounced when treating mucosal surfaces.

On histologic examination, our patient's imiquimod therapy induced a lupus-like interface reaction with adnexal vacuolar change, periadnexal lymphocytic infiltrates and colloid bodies that mimics cutaneous lupus.[2] However, cutaneous lupus demonstrates dermal mucin deposition and increased thickness of the basement membrane, which distinguishes the two diagnoses on histologic examination.

Overall, imiquimod is thought to induce lupus erythematous-like microscopic findings via local upregulation of interferon alpha and/or direct pro-apoptotic activity via B-cell lymphoma 2(Bcl-2) with subsequent activation of caspases.[2] To date, there are 3 cases in the literature addressing this phenomenon in patients aged 75 to 91 years old for the treatment of actinic keratosis and lentigo maligna.[2,3] However, with better long term efficacy data the use of imiquimod for the treatment of residual MIS will continue to increase making the potential prevalence of a lupus-erythematous like reaction more common. Hence, this case highlights the importance of clinicopathologic correlation and good communication between the dermatologist and dermatopathologist to arrive at the correct diagnosis.

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