Lichenoid Drug Reaction From Isotretinoin Therapy

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Lichenoid drug reactions induce lesions that are clinically and histologically almost indistinct from idiopathic lichen planus. Fortunately, most such eruptions are not induced by medications used to treat idiopathic disease. We describe a patient with the vulvovaginal-gingival variant of lichen planus who developed a lichenoid drug reaction after receiving isotretinoin for her condition.

Lichenoid drug reactions (LDRs) result after the patient ingests, inhales, or has contact with offending chemicals and drugs.[1] Typically, medications such as gold, antimalarials, thiazide diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, penicillamine, and nonsteroidal anti-inflammatory agents are most suspect.[1,2] Clinically, lesions may be identical to idiopathic lichen planus, or they may demonstrate increased eczematization, dyspigmentation, and hypertrophy. The histologic distinction of drug-induced lichen planus from idiopathic lichen planus may be difficult; however, the former demonstrates parakeratosis, spongiosis, a deep perivascular infiltrate, upward movement of dyskeratotic cells, dermal eosinophils, and plasma cells.[3]

The efficacy of isotretinoin for acne vulgaris and other acneform eruptions is well documented.[4] Side effects include cheilitis, xerosis, conjunctivitis, palmar/plantar desquamation, epistaxis, paronychia, and reversible alopecia.[5,6] More specific cutaneous reactions also have been described; however, to our knowledge, isotretinoin has not been reported to induce an LDR.

Case Report

A 50-year-old white woman presented with a 4-year history of painful vaginal and oral ulcerations with progressive dyspareunia. The patient's oral lesions improved after receiving methylprednisolone for a shoulder injury. She took no medications and was allergic to sulfa drugs. Erosions and ulcerations were present on the buccal mucosa and on the mucosa of the upper and lower gums. No blisters were noted, but some reticulation was seen. The vulva was diffusely erythematous with erosions and desquamation. Periurethral stenosis was present and a speculum examination was not possible.

Results of a vaginal biopsy performed at an outside location revealed an ulcerated epithelium with an interface inflammatory infiltrate. Occasional plasma cells were present, and the changes were considered compatible with ulcerative lichen planus. Eosinophils were not noted.

The patient was given prednisone 60 mg/d, which dramatically improved her oral lesions and lessened the vulvar discomfort. After several weeks, isotretinoin 1 mg/kg per day was added to her therapy, and the steroids were reduced. Aside from moderate cheilitis and dry eyes, she tolerated the medication well. The oral lesions gradually resolved, and vulvar involvement subsided.

After taking the isotretinoin for 3 months, our patient began to develop poorly demarcated areas of mild erythema and bilateral scaling on the arms and legs (Figure 1). This was initially believed to represent retinoid dermatitis and was treated with emollients. The condition continued to progress, however, and the lesions eventually became better demarcated with overlying scale and delicate striations.

Results of a biopsy of the lesion revealed an interface inflammatory infiltrate with a saw-toothed epidermis, hypergranulosis, dyskeratotic cells, and numerous plasma cells. These features were compatible with an LDR (Figure 2). Results of immunofluorescence testing demonstrated colloid bodies with IgA and IgM and linear fibrin along the basement membrane. The isotretinoin therapy was discontinued, and the lesions resolved over a period of several weeks. The patient's mucosal lesions continue to improve with topical steroid use. She refused rechallenge with isotretinoin.

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Comment

The pathogenesis of LDRs remains unclear. Certain medications, such as penicillamine and angiotension-converting enzyme inhibitors, are believed to alter cell surface molecules, making them more antigenic and eliciting an LDR.[7] It is also possible for patients to latently develop lichen planus.[1] The number of medications capable of causing an LDR is large and increasing.[2]

Vitamin-A derivatives have been successfully used to treat various cutaneous conditions including lichen planus.[8-14] Specifically, oral isotretinoin is useful for cutaneous and mucosal involvement.[9,11] Giustin et al[12] used 0.1% isotretinoin topically on 20 patients with oral lichen planus and reported significant improvement compared with placebo. They proposed that normalization of keratinocyte antigen expression or suppression of the inflammatory infiltrate might be operative. Treatment failures using oral isotretinoin for lichen planus also have been described.[15]

Isotretinoin administration has been reported to cause numerous cutaneous conditions (Table) aside from those typically associated with the hypervitaminosis A-type state.

Our patient may be best classified as having the vulvovaginal-gingival form of lichen planus initially,[14] and then having an activation of an LDR at nonmucosal sites. Some patients in this classification have responded well to etretinate administration without reported side effects such as those experienced by our patient. The histologic features of her biopsy specimens supported a diagnosis of LDR and was confirmed by the resolution of the lesions after the medication was discontinued.

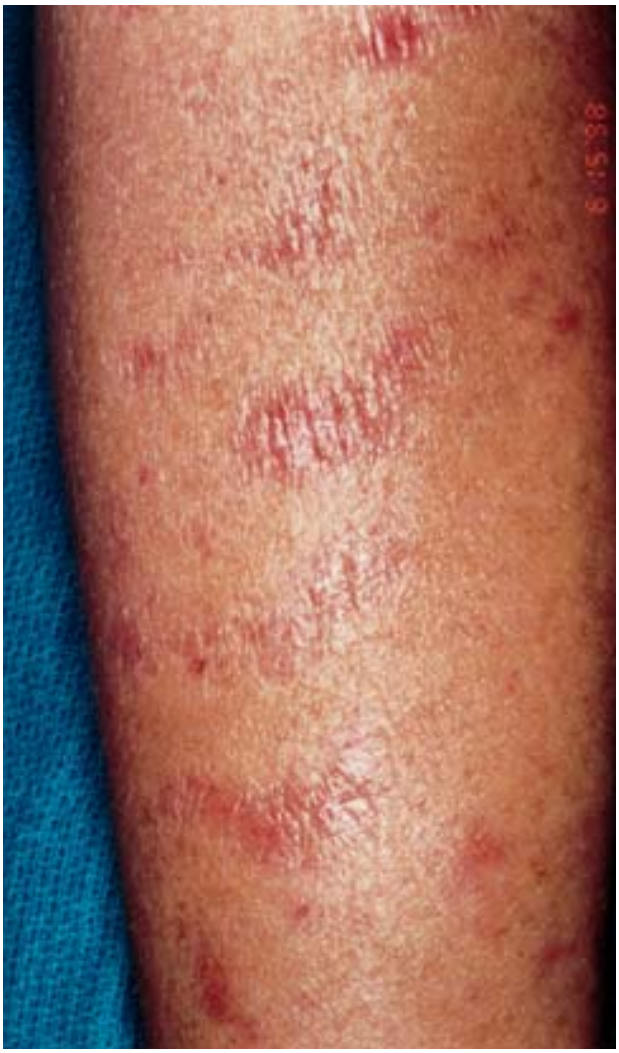

Figure 1. Poorly demarcated erythematous patches on the lower leg.

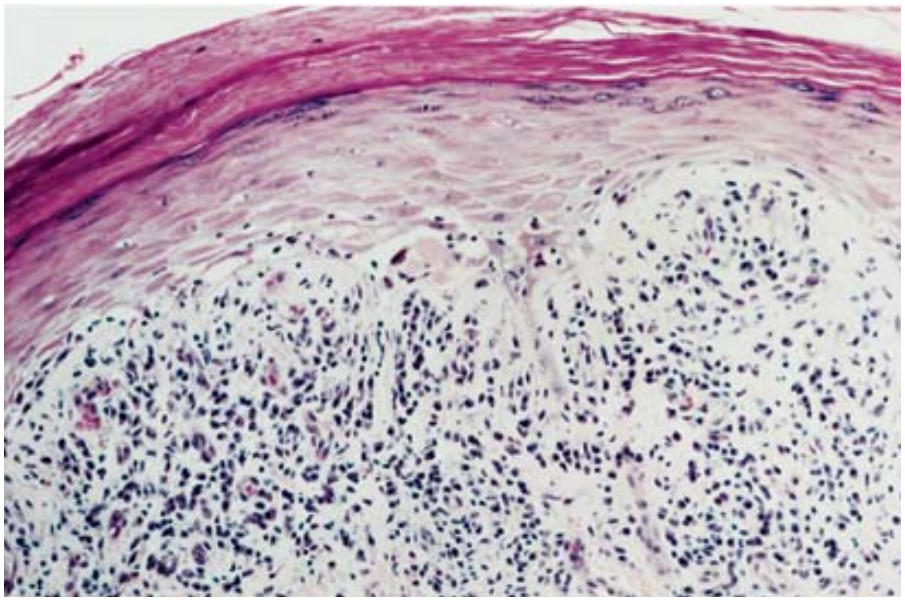

Figure 2. Interface changes with numerous plasma cells compatible with a lichenoid drug reaction (H&E, original magnification ×250).

Reported Cutaneous Reactions to Isotretinoin Administration

Erythema multiforme[16]

Erythema nodosum[17]

Facial calcified cysts[16]

Fixed drug reaction[16]

Hyperpigmentation[16]

Leukoderma[16]

Mycosis fungoides–like drug reaction[18]

Nummular eczema[19]

Onycholysis[16]

Osteoma cutis[16]

Pili torti[20]

Pityriasis rosea–like drug reaction[5]

Pyoderma gangrenosum[21]

Pyogenic granulomas[6]

Urticaria[16]

UVA-induced photoallergy[22]

UVB-induced photoallergy[23]

Varicella-zoster infection[16]

To our knowledge, an LDR from isotretinoin administration has not been previously reported. It is interesting to note that our patient continued to experience mucosal healing even after discontinuing the drug. This may be due to the extended half-life of isotretinoin.

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