Keratosis lichenoides chronica successfully treated with isotretinoin and methotrexate

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INTRODUCTION

Keratosis lichenoides chronica (KLC) is a rare mucocutaneous eruption, with just greater than 70 cases reported in the literature. KLC is characterized clinically by hyperkeratotic papules arranged in a distinctive linear and reticular pattern distributed on the trunk and extremities. This eruption can sometimes be associated with oral and genital ulcers and inflammatory ophthalmologic disease.

The pathophysiology of KLC is not well understood. Treatment can be challenging, as KLC is notoriously resistant to many therapies. Here, we present a patient with KLC who had a marked response to a combination of isotretinoin and methotrexate.

CASE REPORT

A 24-year-old woman presented with a 20-month history of a cutaneous eruption, papillary conjunctivitis with eyelid margin ulceration, and oral and vulvar ulcers. She was taking azathioprine, colchicine, infliximab, and methylprednisolone for presumed Behcet disease; however, there was no improvement on this regimen. She was not taking any other medications. Her medical and family histories were unremarkable, as was her review of systems.

Physical examination revealed numerous 1- to 3-mm pink-red scaly papules on the face, upper chest, back, flexor arms and wrists, and popliteal fossa. The lesions coalesced in linear and reticular configurations (Fig 1). There were tender, 1- to 2-cm red subcutaneous nodules involving the bilateral lower legs. The scalp, palms and soles, and nails were unaffected. On the upper and lower mucosal lips, buccal mucosa, tongue, and left labia majora were multiple 3- to 10-mm shallow ulcers (Fig 2). Both eyelids were mildly edematous with crusted ulceration along the inferior gray lines, and there were dense papillae on the tarsal conjunctive superiorly and inferiorly. The bulbar conjunctivae were unaffected and corneas were clear, and there was no evidence of active or prior intraocular inflammation (Fig 3).

Results of laboratory evaluation, which included antinuclear antibodies, Ro, La, double-stranded DNA, Smith, rheumatoid factor, antineutrophil cytoplasmic antibodies, and rapid plasma reagin, were normal. Erythrocyte sedimentation rate and C-reactive protein level were not elevated. Skin and mucosal biopsies were performed (Fig 4). Results of direct immunofluorescence of perilesional skin and mucosa and indirect immunofluorescence were normal.

Skin biopsy found mild vacuolar interface change with necrotic keratinocytes and perivascular...
lymphocytic inflammation with areas of parakeratosis. Focal areas of epidermal atrophy and follicular plugging were also noted. Prominent mucin was absent. Biopsy of the buccal mucosa also found lymphocytic inflammation with vacuolar interface change. Together with the morphology, distribution, and pattern of the mucocutaneous lesions, the biopsy findings supported a diagnosis of KLC. Treatment with isotretinoin, 40 mg daily, resulted in a significant improvement in the cutaneous lesions, but there was persistence of the oral ulcers and blepharoconjunctivitis. Addition of methotrexate, 5 mg weekly, resulted in a marked improvement of both the oral and ocular lesions and allowed for rapid tapering and discontinuation of azathioprine, colchicine, infliximab, and methylprednisolone. The patient’s disease remained in remission on this regimen for 9 months.

DISCUSSION

There are currently no diagnostic criteria for KLC. However, characteristic clinical features have been described. The papules in KLC are typically pink-red to violaceous in color and have scale. They are arranged in linear or reticular patterns. A concurrent seborrheic dermatitis-like facial eruption is also often present. Behcet disease, which is also characterized by mucosal ulceration, typically presents with a papulopustular eruption, helping to differentiate these 2 etiologies. KLC is usually asymptomatic but can be pruritic. Although uncommon, mucosal involvement has been reported and includes oral ulceration, genital ulceration, and ocular involvement (including blepharitis, conjunctivitis, uveitis, and iridocyclitis). Nail changes including onychodystrophy and discoloration may be seen. Oral ulcers, eyelid margin ulceration, and papillary conjunctivitis were prominent features in our patient.

Histopathologic findings in KLC show a lichenoid, lymphocytic reaction pattern with focal basal vacuolar alteration. Perivascular and periappendageal lymphocytic infiltrate, sometimes with a few plasma cells, can be seen. Epidermal changes including alternating areas of atrophy and acanthosis with focal parakeratosis, follicular plugging, and sometimes neutrophilic debris can also be seen. Immunofluorescence is typically negative. Together these histologic features help differentiate KLC from lichen planus, which lacks parakeratosis and shows wedge-shaped hypergranulosis. Some investigators, however, consider KLC a variant of lichen planus. In Behcet disease, the typical papulopustular lesions show a predominantly neutrophilic infiltrate histopathologically. The negative direct immunofluorescence, lack of prominent mucin, and negative serologies argue against cutaneous lupus.
Management of KLC can be difficult and has not been studied in detail. A recent review of KLC suggested that oral retinoids and phototherapy, either alone or in combination, were the most effective forms of treatment. Of 30 patients who received oral retinoids, 6 of 30 (20%) had a partial response and 11 of 30 (36.6%) had a complete response. Our patient’s disease was refractory to treatment with azathioprine, colchicine, infliximab, and methylprednisolone, consistent with prior observations. Treatment with isotretinoin resulted in partial improvement in her cutaneous lesions. The addition of methotrexate led to near resolution of her cutaneous eruption, oral and genital ulcerations, and external ocular inflammation. The findings in this case illustrate classical findings in this rare inflammatory dermatosis and suggest that the combination of isotretinoin with methotrexate may be an effective therapeutic strategy for refractory KLC.

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