Cicatricial conjunctivitis secondary to discoid lupus erythematosus

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INTRODUCTION
Discoid lupus erythematosus (DLE) is the most common form of chronic cutaneous lupus (CCLE) and typically presents as well-demarcated, erythematous-to-violaceous, scaly plaques with evolving dyspigmentation and scarring. Although approximately 80% of lesions localize to sun-exposed areas such as the head, scalp, and ears, DLE can also affect mucosal sites, favoring the mouth.1,2 Involvement of ocular and periocular structures is less common and may be diagnostically challenging.3 Cicatricial conjunctivitis secondary to DLE is extremely rare, with few reported cases in the literature.4 Here we present a case of DLE with cutaneous and ocular involvement that eventuated in a unilateral cicatricial conjunctivitis.

CASE REPORT
A woman in her 70s with longstanding mild systemic lupus erythematosus (SLE) with manifestations including DLE of the scalp, positive dsDNA antibody, and clinically quiescent systemic disease presented for treatment of a recalcitrant scalp lesion. Examination of the scalp found a single red-purple scaly plaque with associated follicular plugging and alopecia, consistent with active DLE. She did not have any other classic DLE lesions on the head or neck. However, a lesion of uncertain etiology was noted on the right lower eyelid, characterized by a focal area of erythema involving the temporal aspect of the lid margin and surrounding palpebral conjunctiva with no disruption of eyelash architecture.

A biopsy of the right lower eyelid margin found atrophic lichenoid inflammation with basement membrane thickening, consistent with a lichenoid presentation of DLE. The patient was started on hydroxychloroquine with reduced activity, although not full remission, of her DLE. Her scalp lesion was managed with the addition of topical and intralesional steroids. However, she continued to have recurrent inflammation of her right lower eyelid with associated right-sided episcleritis over the next 3 years, ultimately having a focal area of symblepharon between the bulbar and palpebral conjunctiva (Fig 1). Because it was unclear whether the ongoing ocular inflammation was caused by active mucosal DLE, friction, and/or trauma from her existing eyelid biopsy scar, or another etiology, a diagnostic conjunctival biopsy in the symblepharon area was performed. Routine histopathology showed conjunctiva with partially attenuated stratified squamous epithelium, mild lichenoid infiltrate, rare perivascular lymphocytes and plasma cells, and mild fibrosis within the substantia propria (Fig 2). Direct immunofluorescence (DIF) found granular deposition of IgG and IgM at the basement membrane.
DISCUSSION

We present an unusual case of DLE presenting as unilateral cicatricial conjunctivitis, accompanied by striking clinical and pathologic findings. Diagnosis was challenging, requiring thoughtful interdisciplinary collaboration between the dermatology, ophthalmology, and pathology departments. To our knowledge, few cases of DLE with conjunctival involvement have been previously reported.5

In one series of 68 patients with CCLE, 24% were found to have mucosal involvement, with eyelid involvement noted in about 6%.5 Early DLE of the eyelids may present as a nonspecific blepharitis favoring the lower lid and/or may resemble several common skin conditions of the eyelids including allergic contact dermatitis, psoriasis, lichen planus, cutaneous neoplasm, or nonspecific conjunctivitis.3,4 Diagnosis can be challenging, and in a case series of 7 patients with periocular DLE, the median time from symptom onset to diagnosis was in excess of 3 years.3 As seen in our case, conjunctival DLE typically favors the lower lid and begins with focal lesions on the palpebral conjunctiva or lid margin. As lesions progress, scarring may occur, leading to permanent eyelash loss and symblepharon formation as noted in this case.5,6 Episcleritis, as seen in our patient, appears to be less common in primary DLE than in SLE2 but has been reported in both conditions.7 Of note, our patient is known to have DLE in the setting of SLE. Whereas SLE may cause direct visual impairment (eg, retinal vasculitis or optic neuritis/neuropathy), DLE can also seriously affect ocular function by disrupting the normal architecture of the eyelids, conjunctiva, and surrounding skin. Periocular lupus profundus can present with periocular swelling without other clinical features of lupus erythematosus skin disease and can be quite destructive.8

The presence of classic DLE on the scalp in this case provided important dermatologic clues to the etiology of the eye findings. However, we considered the full differential diagnosis for cicatricial conjunctivitis in this patient, including several autoimmune and inflammatory mucocutaneous conditions (eg, ocular cicatricial pemphigoid [OCP], lichen planus, DLE), drug reactions (eg, Stevens-Johnson syndrome), postsurgical changes and surface toxicity (eg, chemical burns, topical...
medications, protracted trauma), and several other conditions (eg, rosacea, infections, atopic keratoconjunctivitis).5 Because histopathologic features of some inflammatory conditions in this differential may overlap (Table I), conjunctival biopsy for routine histopathology and DIF can be a valuable tool to establish the correct diagnosis and treatment approach.

As seen in our patient, DIF in patients with DLE typically demonstrates granular deposition of IgG and IgM at the basement membrane (Fig 3). This finding is in contrast to the narrower, well-defined, linear deposits typically seen in OCP. Interestingly, a lupus band-like DIF pattern was observed in sun-protected bulbar conjunctival biopsies in 40% to 50% of patients with SLE and CCLE in one study, even in the absence of ocular signs and symptoms.9 This finding suggests that although DIF testing is useful in ruling out alternative diagnoses such as OCP, excellent clinicopathologic correlation is still paramount in reaching a final diagnosis. In our case, the clinical, histopathologic, and DIF findings taken together allowed us to render a final diagnosis of cicatricial conjunctivitis secondary to DLE.

Overall, cicatricial conjunctivitis secondary to DLE tends to run a milder course than OCP and may respond favorably to topical and intralesional steroids.2,5 In more severe cases of conjunctival DLE, the treatment approach is similar to that of recalcitrant DLE occurring at other mucocutaneous surfaces, including antimalarials with or without systemic steroids and/or systemic immunomodulators. This patient experienced improvement in her ocular inflammation on hydroxychloroquine with the addition of ocular topical steroids with ongoing close monitoring. Because of multidisciplinary efforts between the dermatology, ophthalmology, and pathology departments to establish successfully a specific diagnosis in this challenging case, DLE-specific treatments are viable options should an escalation in therapy become necessary.

REFERENCES
1. Tebbe B, Orfanos CE. Epidemiology and socioeconomic impact of skin disease in lupus erythematosus. Lupus. 1997; 6(2):96-104.
2. Burge SM, Frith PA, Juniper RP, Wojnarowska F. Mucosal involvement in systemic and chronic cutaneous lupus erythematosus. Br J Dermatol. 1989;121(6):727-741.
3. Gupta T, Beaconsfield M, Rose GE, Verity DH. Discoid lupus erythematosus of the periiorbita: clinical dilemmas, diagnostic delays. Eye (Lond). 2012;26(4):609-612.
4. Arrico L, Abbouda A, Abicca I, Malagola R. Ocular complications in cutaneous lupus erythematosus: a systematic review

| Table I. Differential diagnosis of cicatricial conjunctivitis—inflammatory causes |
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| Ocular findings | Chronic blepharitis | Chronic conjunctivitis, cicatricial conjunctivitis, dry eye | Chronic conjunctivitis, cicatricial conjunctivitis, dry eye, keratitis, corneal ulceration |
| Dermatologic clues | Attention to scalp, face, ears, sun-exposed areas, and mouth may reveal typical DLE lesions elsewhere. | Attention to the hair/scalp (eg, lymphocyte-mediated scarring alopecia), skin (eg, lichenoid papules), nails (eg, pterygium, anonychia), oral mucosa (eg, Wickham striae), and genital mucosa (eg, inflammation at posterior fourchette) may reveal lichen planus lesions elsewhere. | Attention to oral, nasal, and genital mucosa to evaluate for blisters, erosions, and scarring. |
| DIF10 | Granular deposition of IgG and IgM along the BMZ, cytoid bodies with IgM and IgA | Shaggy deposition of fibrinogen along the BMZ in 55% to 75% of oral mucosal cases; scattered, clumped cytoid bodies with IgM and IgA; cytoid bodies with IgG, C3, and fibrinogen occasionally | Linear deposition of IgG, C3, IgA along the BMZ |
| Autoantibodies | Check antinuclear antibodies, consider extractable nuclear antigen | No specific autoantibody | BP230 (BPAG1), BP180 (BPAG2), B4 integrin subunit, laminin-5, laminin-6, type VII collagen (290 kd) |

BMZ, Basement membrane zone; DIF, direct immunofluorescence.
with a meta-analysis of reported cases. J Ophthalmol. 2015;2015:254260.
5. Thorne JE, Jabs DA, Nikolskaia O, Anhalt G, Nousari HC. Discoid lupus erythematosus and cicatrizining conjunctivitis: clinicopathologic study of two cases. Ocul Immunol Inflamm. 2002;10(4):287-292.
6. Donzis PB, Insler MS, Buntin DM, Gately LE. Discoid lupus erythematosus involving the eyelids. Am J Ophthalmol. 1984;98(1):32-36.
7. Zuber TJ, Pearlstein MV, Hwang CJ, Efekhari K, Lugo-Somolinos A, Googe PB. Periorbital swelling and episcleritis may be a sign of cutaneous lupus erythematosus. Clin Case Rep. 2019;7(7):1422-1425.
8. Magee KL, Hymes SR, Rapini RP, Yeakley JW, Jordon RE. Lupus erythematosus profundus with periorbital swelling and proptosis. J Am Acad Dermatol. 1991;24(2):288-290.
9. Frith P, Burge SM, Millard PR, Wojnarowska F. External ocular findings in lupus erythematosus: a clinical and immunopathological study. Br J Ophthalmol. 1990;74(3):163-167.
10. Nicolas MEO, Kalaaji AN. Mayo Clinic Atlas of Immunofluorescence in Dermatology: Patterns and Target Antigens. United States: CRC Press; 2006.