Discoid lupus erythematosus precipitated by topical diphencyprone immunotherapy for alopecia areata

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INTRODUCTION

Discoid lupus erythematosus (DLE) is a subset of chronic cutaneous lupus erythematosus. We present a patient whose scalp DLE was triggered by topical application of diphencyprone (DCP) immunotherapy for chronic alopecia areata (AA).

Abbreviations used:

AA:	alopecia areata
alopecic LE:	alopecia of systemic lupus erythematosus
DCP:	diphencyprone
DIF:	direct immunofluorescence
DLE:	discoid lupus erythematosus
ILK:	intralesional triamcinolone injections
SLE:	systemic lupus erythematosus

CASE REPORT

A 16-year-old Chinese boy presented in May 2004 for multifocal nonscarring alopecia on the scalp. AA was the diagnosis and he received intralesional triamcinolone injections (ILK), achieving more than 90% regrowth of hair by July 2004. However, his AA relapsed in August 2004.

Concurrently, he had indurated erythematous plaques on his face and chest in August 2004. Biopsy of the facial plaques showed basal vacuolar alteration along the follicular epithelium and thickened basement membrane. Direct immunofluorescence (DIF) found granular deposits of IgG, IgA, IgM, C3, and C1q along the basement membrane zone. Autoantibody screen was positive for antinuclear antibody of 1:100 (speckled pattern) and anti-topoisomerase of 1. Double-stranded DNA was negative. The diagnosis was DLE, and he was treated with hydroxychloroquine until lesions became inactive in April 2006.

During the treatment period for DLE, he continued to receive ILK injections for AA, which relapsed and remitted over different areas on the scalp. By December 2005, there were no new patches, and residual ones showed greater than 80% to full regrowth of hair. Unfortunately, his AA recurred in May 2008.

In August 2009, an alopecic patch on the right occipital scalp was hardened and atrophic. Biopsy from it found an infiltrate of lymphocytes around a hair bulb without involvement of the rest of the hair follicle. Some lipoatrophy in the absence of subcutaneous inflammation was present. There was preservation of hair follicle numbers and sebaceous glands and absence of thickening of the basement membrane or basal vascular alteration (Fig 1, *A* and *B*). DIF showed a strong continuous granular deposition of IgM and weak discontinuous C3 deposition along basement membrane zone and follicular epithelium. Extractable nuclear antigen panel was negative. Clinically and histologically, the diagnosis was consistent with AA, complicated by intralesional steroid-induced lipoatrophy. A repeat autoimmune screen in October 2017 found antinuclear antibody of 1:320 (speckled), negative extractable nuclear antigen, and negative double-stranded DNA. He continued to receive ILK for his AA through May

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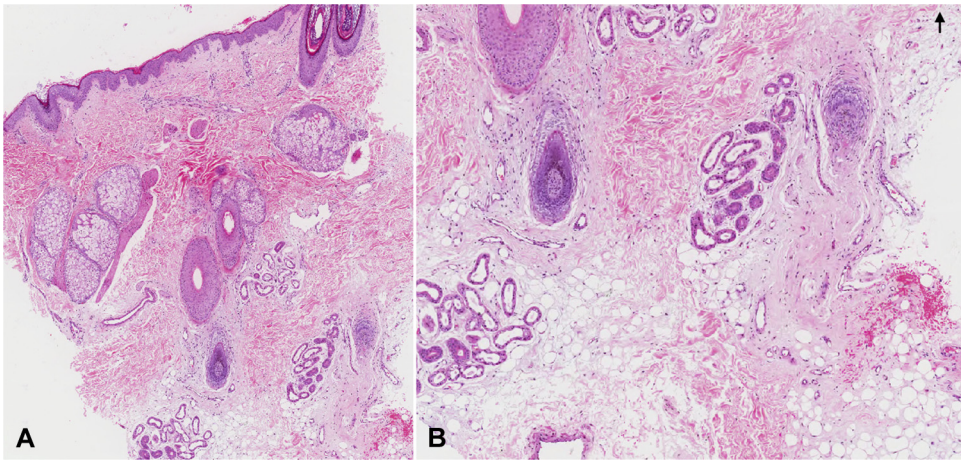

Fig 1. Hematoxylin-eosin stains of scalp biopsy from 2009 consistent with AA. **A**, There is a mild peribulbar infiltrate of lymphocytes around hair bulbs. The epidermis and follicular epithelium are intact and do not exhibit basal vascular change. Sebaceous glands are preserved, and there is lack of inflammation affecting other parts of the hair follicle apart from the hair bulbs. These findings are in keeping with the diagnosis of AA. **B**, There is a mild peribulbar infiltrate of lymphocytes in association with lipoatrophy with lack of subcutaneous inflammation.

2018 with 2 courses of oral prednisolone. Although the AA patches over the occipital and parietal areas achieved full regrowth by 2015, there were recurring and remitting patches over the vertex. By 2018, his AA progressed to involve 15% of scalp surface area. Throughout these years, he did not display any symptoms or signs of systemic lupus erythematosus (SLE).

Topical immunotherapy with DCP was started to treat his AA in August 2018. After 11 weekly sessions, the alopecic patches became erythematous and indurated with visible telangiectasia and atrophy (Fig 2). A repeat scalp biopsy found basal vacuolar alteration along the epidermis and hair follicle in association with a superficial and deep perivascular, perifollicular and perieccrine infiltrate of lymphocytes with occasional plasma cells (Fig 3, *A* and *B*). Sebaceous glands were present but diminished in size. There was increased dermal mucin on alcian blue, and basement membrane was focally thickened around a hair follicle Fig 4, *A* and *B*). DIF showed bright granular deposits of IgG, IgM, and C3 along the basement membrane zone. These findings supported the diagnosis of scalp DLE, likely precipitated by DCP. DCP was immediately discontinued. He was treated with hydroxychloroquine and ILK, which led to resolution of DLE and regrowth of hair.

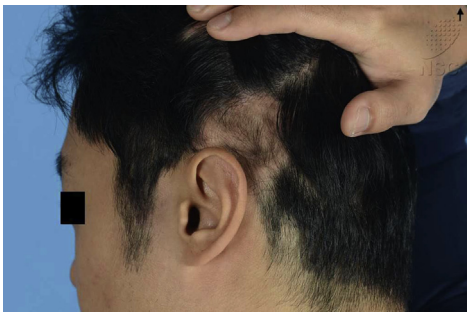

Fig 2. An erythematous, indurated and atrophic plaque on the scalp of our patient after 11 cycles of weekly DCP in 2018.

DISCUSSION

DCP is the likely trigger for a DLE flare in our patient, as his lesions emerged only within the areas of treatment after application of DCP and resolved after DCP was discontinued. DCP is a potent topical sensitizing agent that induces a low-grade localized dermatitis reaction, and contact dermatitis has been reported as a trigger for DLE flares.[1,2]

Trauma[3] can precipitate or exacerbate DLE in susceptible patients. Damage to the epidermal keratinocytes and increased exposure of intracellular autoantigens is postulated to activate antinuclear autoantibodies. Koebnerization from DCP or needling from repeated ILK injections could have precipitated DLE in our patient. However, we expect the DLE lesions to have appeared earlier or persisted with the ILK injections, if this were the case.

It is prudent to consider the diagnosis of early-stage DLE. However, the diagnosis of AA is favored over DLE because of the presence of inflammation localized around hair bulbs in the absence of more extensive inflammation affecting the rest of the hair

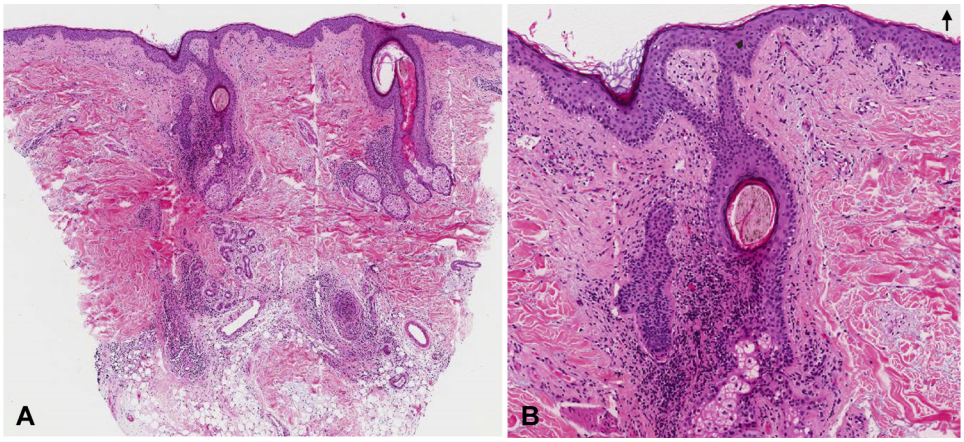

Fig 3. Hematoxylin-eosin stains of the post-DCP scalp biopsy from 2018 consistent with DLE. **A**, Superficial and deep perivascular, perifollicular, and periadnexal infiltrate in association with basal vacuolar alteration of the epidermis and hair follicles. Sebaceous glands are present but diminished in size. These findings are consistent with the diagnosis of scalp DLE (low power). **B**, There is a perifollicular infiltrate of lymphocytes in association with basal vacuolar alteration. Original magnifications: **A,** ×40; **B,** ×100.

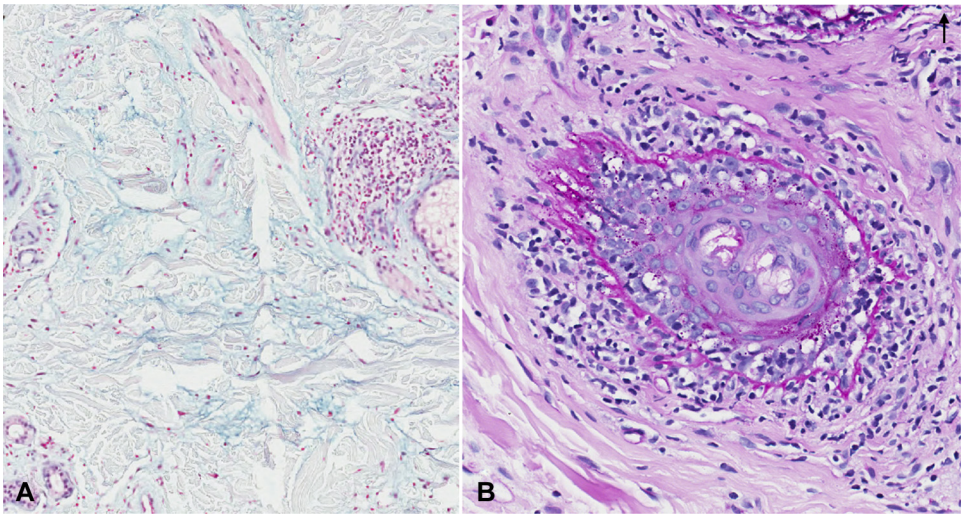

Fig 4. **A**, Increase in dermal mucin as seen on alcian blue. **B**, Focal thickening of the basement membrane of a hair follicle on periodic acid–Schiff.

follicle, lack of basement membrane thickening or basal vacuolar alteration, and presence of normal sebaceous glands. Furthermore, the alopecic patches regrew without residual scarring over the years, favoring AA as the initial diagnosis.

The diagnosis of patchy nonscarring alopecia of SLE (alopecic LE) was entertained in this patient. Alopecic LE may mimic AA clinically and may be histologically difficult to distinguish in some instances.[4] Both may present with peribulbar inflammation, follicular miniaturization and increase in catagen/telogen hairs, prompting the proposal of the term *alopecia areata-like pattern* to incorporate such disparate entities with similar histopathologic features (Thomson/Kolivras, personal communication, May 12, 2020). However, almost all reported cases of alopecic LE to date have been reported in patients with active SLE.[5] Our patient did not have SLE clinically or laboratory during his long follow-up. Histopathologically, interface dermatitis was not seen in the earlier scalp biopsy, whereas biopsies of patients with patchy nonscarring alopecia of SLE showed interface change along the dermoepidermal junction in 87.5% and along the follicular epithelium in 40.6%.[6] Our patient had a classic relapsing-remitting course of nonscarring hair loss, with good regrowth of hair in between, which is characteristic of AA. Therefore, favor a diagnosis of AA over

alopecic LE. Patients with AA have an increased incidence of lupus erythematosus, and the 2 conditions are not mutually exclusive. In a recent meta-analysis, the odds ratio of patients with AA having lupus was 4.7 (95% confidence interval, 3.7-6.1).[7]

Continual review and periodic screening for coexisting autoimmune conditions in AA patients is important, as delayed diagnosis can lead to irreversible scarring.

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