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Journal

Dermatology Online Journal, 24(9)

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Publication Date

2018

DOI

10.5070/D3249041418

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Seven-year itch: a perplexing case of lichen planus-lupus erythematosus overlap syndrome

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Abstract

Lichen planus-lupus erythematosus overlap syndrome is a rare disorder characterized by clinical and histopathological features of both lichen planus (LP) and lupus erythematosus (LE). Cutaneous lesions commonly affect the distal arms, legs, face, and trunk and these plaques are often large, scaly, painful, and atrophic, often exhibiting hypopigmentation or a red to blue-violet color. We report a case of LP-LE overlap syndrome diagnosed in a man previously believed to have atypical lichen planus who presented with an exacerbation of exuberant pruritic erythematous scaly plaques. The patient had six separate skin biopsies all of which displayed features of LP. Because the clinical symptoms did not correlate to the histopathological picture, a seventh skin biopsy with direct immunofluorescence (DIF) was performed and immunologic markers measured. The DIF demonstrated early lupus bands; serologic testing exhibited elevated ANA and anti-SSA. These findings established the diagnosis of LP-LE overlap syndrome. The patient was started on hydroxychloroquine with short-term trials of oral prednisone during disease flares, which took place in the first three months of treatment.

Keywords: lichen planus, cutaneous lupus erythematosus, lichen planus-lupus erythematosus overlap syndrome, LP, LE

Introduction

Lichen planus-lupus erythematosus overlap syndrome is a rare disorder characterized by clinical and histopathological features of both lichen planus

(LP) and lupus erythematosus (LE). Whereas LP and LE are both well-established individual entities, less than 50 cases of LP-LE overlap syndrome have been reported in the literature [1]. Cutaneous lesions commonly affect the distal arms, legs, face, and trunk. Plaques are often large, scaly, painful, and atrophic with hypopigmentation and/or a red to blue-violet color. However, presentation is heterogeneous among case reports. There is disagreement as to whether LP-LE overlap syndrome should be recognized as a distinct disorder, an intermediate form of either condition, or a coexistence of LE and LP lesions in the same patient. Cases have been reported in which patients have separate lesions consistent with each disease; alternatively, there is at least one case report of genuine overlap within a single lesion [2]. Histological analysis may reveal characteristics of



Figure 1. There are well-demarcated, erythematous plaques with overlying scale on the chest and abdomen.



Figure 2. *The ear helix and conchal bowl display erythematous scaly gray plaques.*

each disease or both simultaneously. Therefore, direct immunofluorescence (DIF) may be essential in confirming the diagnosis. We report a case of LP-LE overlap syndrome diagnosed in a man previously believed to have atypical lichen planus who presented with an exacerbation of exuberant pruritic skin eruptions. The uniqueness of this case lies in the necessity of multiple biopsies to obtain the diagnosis of LP-LE overlap syndrome.

Case Synopsis

A 70-year-old man presented to the dermatology clinic with an exacerbation of a pruritic skin eruption present on-and-off for seven years. Symptoms were previously mild and tolerable with topical corticosteroids. However, recently the cutaneous lesions had become more diffuse and pruritic. He had asymptomatic involvement of the oral mucosa. On review of systems, he suffered from low back pain and his pruritus was severe, preventing him from

sleeping. His medical history was significant for hypertension, hyperlipidemia, atrial fibrillation, diabetes mellitus, and benign prostatic hyperplasia. His medications included simvastatin, metformin, lorazepam, lisinopril, finasteride, and dabigatran, all of which he had been taking chronically. He had known allergies to hydrochlorothiazide, beta-blockers, and Percocet, to which he had not recently been exposed.

Dermatologic examination revealed erythematous plaques with scale on the scalp and ears, and numerous well-demarcated, erythematous plaques on the chest, abdomen, back, and inguinal folds (Figures 1, 2). The mid-lower back had a solitary thick annular lichenified plaque on an erythematous base with silvery scale. The extremities displayed a scattering of annular and centrifugal erythematous papules and plaques without scale. There was extensive cheilitis of the lips with multiple erosions and white lacy plaques on the lateral and anterior aspects of the tongue (Figure 3). No nail pitting was present.

Basic laboratory examinations were notable for elevations in glucose, creatinine, and microalbumin with a reduction in eGFR as a result of longstanding diabetes mellitus. Rheumatologic markers were



Figure 3. *There is extensive cheilitis of the lips. The tongue displays multiple erosions and white lacy plaques on the right lateral aspect.*

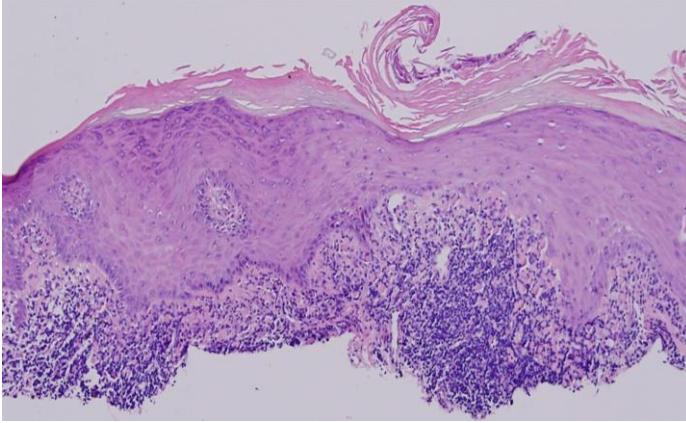


Figure 4. Skin biopsy of the lip vermilion border: histopathology exhibits compact orthohyperkeratosis, band-like lichenoid infiltration, saw-tooth rete pattern, and many Civatte bodies. H&E, 100 \times .

significant for positive antinuclear antibodies, elevated Anti-SSA (>8.0 IU), positive anti-cardiolipin IgM and IgA, borderline anti-histone antibody, and low complement C3 (49.6mg/dl). Tests for the following antibodies were negative: anti-Smith, anti-dsDNA, anti-SSB, anti-smooth muscle, anti-RNP, and rheumatoid factor. Complement C4 and CH50 were within normal limits.

The patient had three previous skin biopsies between 2011 and 2014 consistent with LP. Given the patient presented to our office with different lesion morphologies, three more biopsies were taken with careful consideration of the location. These sites were lower lip cheilitis, erythematous papule on the chest, and thick scaly plaque on the lower back (Figures 4, 5). All three exhibited compact hyperkeratosis, patchy lichenoid infiltrate, and many necrotic keratinocytes consistent with the previous diagnosis of LP. Because the clinical symptoms were not consistent with LP, another biopsy was performed and sent for histopathology and direct immunofluorescence (DIF). **It wasn't until the patient's seventh biopsy that the pathology returned with histological features suggestive of LE (Figure 6).** The DIF exhibited granular deposition of C3 and IgM at the basement membrane zone correlating to an evolving lupus band.

Altogether, the findings established the diagnosis of LP-LE overlap syndrome. Having previously failed topical corticosteroids, phototherapy, and antipruritics, the patient was started on

hydroxychloroquine 200mg twice daily with short-term bursts of oral prednisone during disease flares in the first three months of treatment.

Case Discussion

The rarity of LP-LE overlap syndrome coupled with an atypical presentation and numerous skin biopsies consistent with LP made for a challenging case to diagnose. There are cases in which LP can be mistaken for LE, especially in patients with only oral or scalp lesions. On biopsy of clinically ambiguous lesions, histopathological features of one or both processes can often be found, obscuring the diagnosis and complicating determination of prognosis and treatment. As in this case, the diagnosis of LE or LP-LE overlap syndrome may require multiple biopsies to be performed or for other constitutional signs of LE to be present.

Upon formulating the differential diagnosis during **the patient's early visits, lichenoid drug eruption was high on the differential.** The patient was on chronic treatment with an ACE inhibitor and a statin, both of which are potential causative agents. However, the pathology did not align with a lichenoid drug eruption; there were no eosinophils, no vacuolar alterations, and no spongiotic dermatitis. The initial pathology showing lichenoid infiltration and civatte bodies was diagnostic for LP; however, this did not **correlate with the patient's cutaneous**

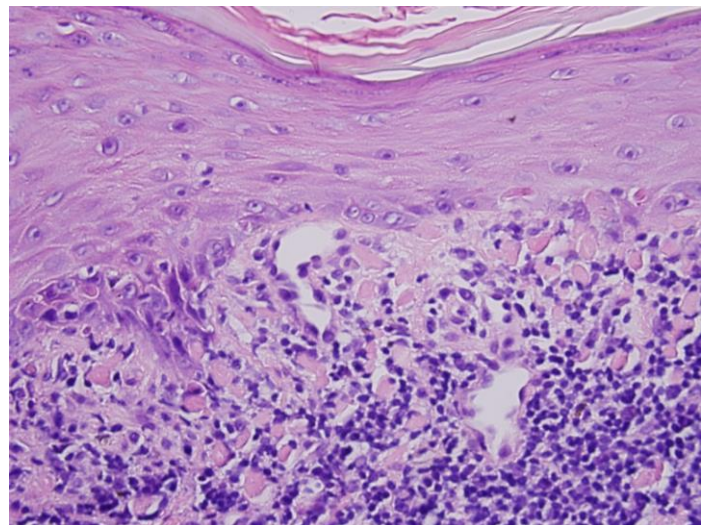


Figure 5. High-power view of a skin biopsy of the lip vermilion border: histopathology exhibits effacement of the basement membrane, lichenoid infiltration, and numerous necrotic keratinocytes. H&E, 400 \times .

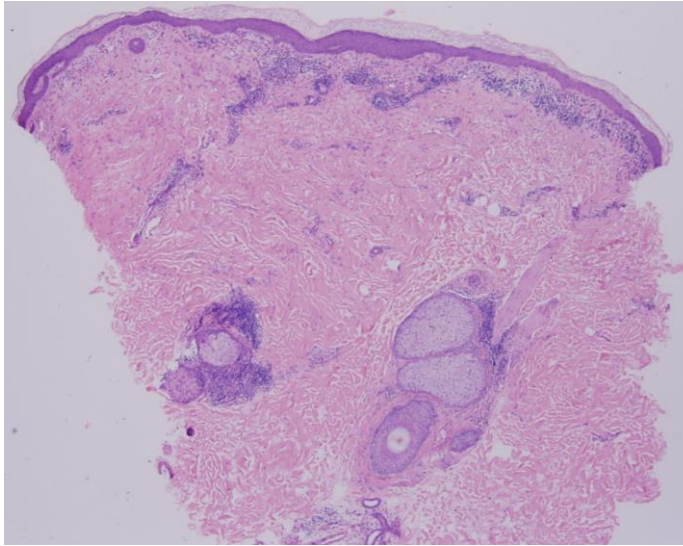


Figure 6. Skin biopsy of plaque on the chest: histopathology displays an interface dermatitis with superficial and deep perivascular and periadnexal lymphohistiocytic infiltrate characteristic of cutaneous lupus erythematosus. H&E, 10 \times .

manifestations. On repeat biopsy (the patient's seventh and last biopsy), the pathology exhibited periadnexal and perivascular infiltration consistent with cutaneous LE.

DIF has become an essential tool in helping to diagnose LP-LE overlap syndrome as granular or homogeneous bands of immunoglobulin in the basement membrane zone have been demonstrated in lesional and non-lesional mucosa in systemic LE (100% and 71%, respectively) as opposed to only rarely in LP (4%), [3]. The DIF in this case displayed an evolving lupus band consistent with LE. Two academic dermatopathologists were consulted on this case and agreed with the final diagnosis of LP-LE overlap syndrome.

A review of existing case reports on LP-LE overlap syndrome was performed. A PubMed search of "lichen planus-lupus erythematosus overlap syndrome" yielded thirty-three results. Of those, sixteen publications were relevant and applicable. Thirty-one patients were presented in these case reports. The clinical presentation and antibody findings of each of these patients are summarized in Table 1 [1, 5, 7-20].

Following diagnosis confirmation, the patient was worked up for systemic manifestations of LE. Although he did have low back pain, the

rheumatology consultant attributed this to degenerative joint disease. His history of nephropathy correlated to his long-standing diabetes. The patient did not exhibit any non-cutaneous signs of SLE, although it is difficult to make a concrete determination of this given his comorbidities. Conversion of cutaneous LE into systemic LE has been documented at a conversion frequency of 5-10%, although this may be an underestimate [4]. In order to avoid missing this diagnosis, patients diagnosed with atypical LP may benefit from repeat biopsies with DIF analysis and rheumatologic markers in order to rule out LE or confirm LP-LE overlap syndrome [3].

It is important to note, spontaneous remission of cutaneous LP occurs in 64% to 68% of cases within one year. Therefore, the diagnosis of LP-LE overlap should be considered in patients with longstanding LP that is refractory to treatment [3]. Some authors suggest that many cases of LP-LE overlap syndrome are missed as a result of variable clinical and histopathological presentations [5]. Recognizing this clinical entity in a timely manner can prevent iatrogenic worsening of disease: treatment for LP can include narrowband UVB and PUVA whereas cutaneous LE is strongly associated with photosensitivity, and abnormal reactivity to UV light is a factor in the pathogenesis of the disease [3, 6]. A proposed explanation is that UV rays induce keratinocyte apoptosis, which results in the initiation of an autoimmune reaction cascade [6]. Our patient was provided phototherapy when he was diagnosed with atypical LP. He did not exhibit worsening of cutaneous manifestations at the time of phototherapy as he was on concurrent treatment with oral prednisone owing to flare and severe pruritus. However, once his diagnosis was adjusted accordingly, he was transitioned to the appropriate treatment of hydroxychloroquine.

Conclusion

We report a rare case of a patient diagnosed with LP-LE overlap syndrome. After six separate skin biopsies consistent with LP, **it was not until the patient's seventh biopsy that the pathology returned with histological features of LE.** This illustrated the

importance of continuing to work-up patients whose skin manifestations do not correlate with the pathological findings. Additionally, it can be beneficial to take multiple biopsies from different locations and to send a DIF. Rheumatologic markers

such as ANA, Anti-SSB, and complement can be helpful. Physicians should have a high suspicion of LP-LE overlap syndrome in patients with atypical LP who have had symptoms for over a year, especially if not improved with treatment.

Table 1. Summary of clinical and antibody findings in patients with LP-LE overlap syndrome reported in previous case studies.

Diagnosis [Reference]	Age at diagnosis	Sex	Clinical presentation	Antibodies
LP-LE overlap [7]	36	F	Thick scaling scarring plaques on extremities & trunk. Recurrent ulcerations on ankles and feet.	ANA positive 1:160 speckled pattern
LP-LE overlap [8]	17	F	Extensive atrophic, erythematous, & hyperpigmented plaques involving her scalp, face, and extremities.	Not discussed
LP-LE overlap [9]	34	F	Violaceous, thickened, scaly lesions on scalp, arms, malar and auricular regions. Buccal and lip mucosa showed white papules with a reticular pattern. Erythematous, well-defined, mildly raised plaque on left lower eyelid.	ANA positive anti-dsDNA positive
LP-LE overlap [1]	26	M	Erythematous, slightly scaly, irregularly bordered, infiltrated large plaques with central atrophy on back. Butterfly type rash involving nose and malar region and erythema on ears and neck. Widespread violaceous lichenoid papules on upper and lower extremities.	ANA negative anti-dsDNA negative; Normal complement levels
LP-LE overlap [10]	24	F	Multiple plaques on scalp, neck, back and lips and painful ulceration in the mouth.	ANA negative anti-dsDNA negative; Normal complement levels; TSH elevated
LP-LE overlap [11]	40	F	Multiple red, flat, painful lesions on both extremities and back. Raw, painful lesions in the oral cavity associated with a burning sensation.	ANA positive in a speckled pattern 1:1000 Anti-dsDNA negative; Anti-histone antibodies negative; ESR 40 mm/h Elevated T3, T4 with normal TSH
LP-LE overlap [13]	42	F	Rough, white patches on buccal mucosa.	ANA positive Anti-dsDNA positive
LP-LE overlap [15]	35	F	Scaly annular and pigmented lesions all over the body.	ANA positive Anti-Ro positive
LP-LE overlap [16]	45	F	Plaques showing central atrophy and erythematous vesicular borders over both dorsa of feet and buttocks, and follicular and papular lesions over buttocks and lumbar area.	Normal levels

Table 1 (continued). Summary of clinical and antibody findings in patients with LP-LE overlap syndrome reported in previous case studies.

Diagnosis [Reference]	Age at diagnosis	Sex	Clinical presentation	Antibodies
LP-LE overlap [18]	59	F	Multiple well-defined flat papulo-squamous scaly violaceous plaques, mostly in the forearms, in the anterior neck, scalp, ears, shoulders, elbows, ears, buttocks, hands and fingers and under the chin. Ulcerated plaques inside the mouth.	Routine blood tests were within normal limits; no rheumatologic work-up performed
LP-LE overlap [19]	53	F	Violaceous erythema around the nostrils and the upper lips and atrophic scaly erythema on the cheeks and neck.	ANA positive 1:40 speckled & homogenous anti-dsDNA positive C3 and C4 levels slightly decreased
LP-LE overlap [5]	50	F	Patchy hair loss and patchy depigmentation mainly on the back and hands. Butterfly type rash mainly on the nose, malar region, and forehead.	Autoantibody screens, including anticardiolipins, were negative
LP-LE overlap [20]	49	M	Well-demarcated erythematous squamous plaques on the back, arms, hands, and feet.	ANA negative ESR 30 mm/hr Rheumatoid factor negative
LP-LE overlap [17]	71	F	Erythematous eruption on the face, scalp, trunk and upper extremities	ANA negative anti-histone negative anti-SS-A & SS-B negative anti-dsDNA negative C3 and C4 levels normal
LP-LE overlap [12]	41	F	Livid red to violet atrophic ulcerative patches with telangiectasia and bullae: acral extremities, trunk, face, nails	ANA negative
LP-LE overlap ¹²	49	M	Verrucous atrophic erythematous to violaceous plaques with telangiectasia; palms, soles, dorsal hands, and feet, nails, trunk, penis	ANA negative
LP-LE overlap [12]	72	F	Erythematous atrophic patches with hypopigmentation & hyperpigmentation pigmentation & telangiectasia: face	ANA positive: 1:80 speckled
LP-LE overlap [12]	45	F	Atrophy & telangiectasia of proximal nail folds & nailbeds with loss of nail plates: nails only	ANA negative
LP-LE overlap [12]	40	F	Atrophic erythematous to violaceous patches with hypopigmentation of distal phalanges & nailbeds & loss of nail plates; lower lip & oral mucosa also involved	ANA negative
LP-LE overlap [12]	46	M	Erythematous atrophic areas with poikiloderma, mild follicular plugging, & nail dystrophy: nails, extremities, lip, face, scalp; oral mucosa also involved	ANA positive: 1:40 homogenous
LP-LE overlap [12]	23	M	Atrophic, erythematous areas with hypopigmentation, telangiectasia, & anonychia: nail beds only	ANA negative

Table 1 (continued). Summary of clinical and antibody findings in patients with LP-LE overlap syndrome reported in previous case studies.

Diagnosis [Reference]	Age at diagnosis	Sex	Clinical presentation	Antibodies
LP-LE overlap [12]	58	M	Atrophic erythematous to violaceous areas with hypopigmentation, telangiectasia, scaling: dorsal hands, fingers, nails, extremities, neck	ANA negative
LP-LE overlap [12]	44	F	Erythematous atrophic plaques: arms, face, trunk	ANA positive: 1:40 homogenous
LP-LE overlap [12]	63	M	Atrophic violaceous to erythematous scaling plaques: dorsal hands, proximal nail folds, fingers, face, scalp	ANA negative
LP-LE overlap [12]	63	M	Atrophic violaceous scaling, plaques: face	ANA negative
DLE + LP [14]	45	F	LE-like lesions on back, breasts, arms, lichenoid papules on wrists, mucosal lesions in mouth	ANA positive ESR 18 mm/h
DLE [14]	47	F	LE-like lesions on face, verrucous lesions on arms and vulva, mucosal lesions in mouth	ANA positive ESR 21 mm/h Disturbed liver functions
DLE + LP [14]	29	M	LE-like lesions on faced forearms, lichenoid papules on wrists, mucosal lesions in mouth	ESR 32 mm/h Positive rheumatoid factors
DLE [14]	30	M	LE-like lesions on face and scalp, mucosal lesions on mouth and lower lip	ANA positive
DLE [14]	46	F	LE-like lesions on face, verrucous lesions on arms	ESR 13 mm/h
DLE + LP [14]	41	M	LE-like lesions on scalp, lichenoid papules on penis, mucosal lesions in mouth	ESR 13 mm/h Positive rheumatoid factors Disturbed liver functions

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