Involvement of scalp and nails in lupus erythematosus

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Lupus erythematosus (LE) is a systemic autoimmune disorder associated with polyclonal B-cell activation resulting in diverse patterns of autoantibody production and a heterogeneous clinical expression constituting a spectrum extending from limited cutaneous disease to life-threatening systemic manifestations. For daily clinical practice, the characteristics of cutaneous lupus erythematosus (CLE) have been well defined in terms of morphology, and clinical and laboratory criteria are available for the classification as systemic lupus erythematosus (SLE). The many different types of skin lesions encountered in patients with LE have been classified into those that are histologically specific for LE and those that are not. While LE non-specific skin lesions on their own do not enable a diagnosis of LE, they can be important reflections of underlying SLE disease activity. This also applies to the involvement of the scalp and nails. Finally, it must be kept in mind that LE patients may also develop drug-related, or other unrelated common disorders of the hair and nails that do not reflect LE disease activity.

**Key words:** alopecia; cutaneous lupus erythematosus; discoid lupus erythematosus; effluvium; hair; lupus hair; nails; Raynaud’s phenomenon; SLE; splinter haemorrhage

## Hair and scalp involvement in lupus erythematosus

### Discoid LE of the scalp

The typical skin lesion of LE-specific disease on the scalp is discoid lupus erythematosus (DLE). Scalp involvement occurs in 60% of DLE patients, and is the only area involved in approximately 10%.\(^1\) Patients with systemic LE may also have discoid lesions, including the scalp, although less frequently. Nevertheless, because of the high specificity of the discoid lesion, it has been included in the criteria for the classification of systemic lupus erythematosus (SLE). Five to 10% of patients presenting with DLE lesions will subsequently develop clear-cut evidence of systemic disease, with the extent and distribution of the DLE lesions determining the risk: patients with lesions both above and below the neck (generalized DLE) have a higher rate of immunological abnormalities and risk for progression to SLE compared to patients with DLE lesions restricted to the head and neck area (localized DLE). Patients with only DLE of the scalp uncommonly progress to involvement with SLE.\(^2\)

In general, DLE lesions can be precipitated by sunlight exposure, though less frequently than acute cutaneous lupus erythematosus (ACLE) and subacute cutaneous lupus erythematosus (SCLE) lesions. In over 50% of patients with DLE standardized UV testing did not induce skin lesions.\(^3\) Particularly, DLE lesions in the hair-bearing scalp and external auditory canal are examples where this form of cutaneous LE is usually not related to light exposure. The appearance of DLE lesions may follow any form of trauma of the skin. In one series, DLE lesions were initiated by trauma in 11%, sunburn in 5%, infection in 3%, and exposure to cold in 2%.\(^4\) DLE lesions have also been noted to occur following exposure to X-ray, diathermy, and chemical burns, and have arisen in scars associated with herpes zoster.

Early DLE lesions of the scalp consist of scaling erythematous or violaceous papules which expand to form round or irregularly shaped plaques with variable atrophy, follicular plugging, telangiectasis, and mottled areas of hyper- and hypopigmentation, which are particularly conspicuous on dark skin, while advanced lesions are scarring (Figure 1). Permanent alopecia resulting from inflammatory follicular destruction occurred in 34% of patients...
in one series. Rarely, as a late sequel, squamous cell carcinoma may arise in chronic smouldering DLE lesions. This has also been reported on the scalp.

DLE lesions are histologically characterized by vacuolar interface alteration involving the hair follicles and epidermis accompanied by a patchy, superficial, and deep perivascular and periadnexal lymphocytic infiltrate (Figure 2) (see also ‘Overview of common, rare and atypical manifestations of cutaneous lupus erythematosus and histopathological correlates’ in this issue). Laminated keratin fills dilated follicular ostia corresponding to the clinical follicular plugging. Minimal lymphocyte exocytosis into the basal layer keratinocytes of the follicular epithelium and interfollicular epidermis may be present, while apoptotic keratinocytes are often found both at the dermal-epidermal junction and within the outer follicular epithelium. Basal layer epithelial destruction with pigmentary incontinence is typical, and melanophages are commonly found in the papillary dermis of older lesions. Basement membrane zone thickening, initially consisting of a fine fibrillar reduplication of basal lamina recognizable only in special stains (e.g. periodic acid-Schiff [PAS]), progresses to form a broad homogenous band of cosinophilic basement membrane material. Increased dermal mucin is usually present both superficially and deep and is best detected in Alcian blue-stained sections. At times, lesions of DLE may manifest follicular interface dermatitis while sparing the interfollicular epidermis; for these cases the term folliculotropic DLE has been proposed.

Direct immunofluorescence studies demonstrate dense granular deposition of immunoglobulin (most commonly IgG, but IgM and IgA may also be present) and complement factor C3 at the dermal-epidermal junction in 75% of cases (Figure 3). Occasionally, globular IgM deposits on cytoid bodies within the epidermis and papillary dermis may also be seen. In contrast to lichen planopilaris they tend to be few in number and are not grouped.

Clinically non-inflammatory alopecic patches of LE

Alopecic patches without clinically appreciable inflammation may also occur and be difficult to differentiate from pseudopelade or alopecia areata, unless the presence of other, more typical lesions of cutaneous LE suggests the diagnosis of LE.

On histopathological examination, clinically non-inflammatory alopecia patches of LE lack superficial inflammation, but deeper inflammation is usually present. Generally, perifollicular lymphocytic infiltrates or infiltrates within remnant fibrous tracts are found, while the late-stage, ‘burnt-out’ lesions of the pseudopelade state demonstrate absence of hair follicles and fibrosis with a loss of elastic fibers, reflecting true scar formation. The PAS stain may be helpful in demonstrating basement membrane thickening which may occur in chronic lesions of LE. Occasionally, direct immunofluorescence studies of such a lesion may demonstrate a telogen follicle with linear deposition of immunoreactants (Figure 4).

Differential diagnosis

The differential diagnosis of DLE of the scalp is principally that of other causes of inflammatory scarring alopecia or pseudopelade. The term pseudopelade is reserved to designate a slowly progressive, multifocal, cicatricial alopecia usually of the centro-parietal scalp region, without clinically evident inflammation or folliculitis. Regardless of detailed clinical and histopathological studies strongly supporting the idea that pseudopelade is a distinct entity, some authorities prefer to consider pseudopelade as an end stage of several well-recognized disorders, including lichen planopilaris and DLE. Usually, DLE can be differentiated from lichen planopilaris by the histopathological features
of interface alteration, pattern, and density of the lymphocytic infiltrate, and dermal fibrosis, as well as on the basis of immunofluorescence studies.12–14

LE non-specific hair and scalp involvement

In addition to the focal and scarring form of alopecia associated with the DLE lesion, SLE patients may experience a diffuse, non-scarring, and transient hair loss associated with exacerbations of their lupus disease process. This diffuse hair loss seen in SLE is usually the result of a telogen effluvium. The telogen effluvium is in all probability the result of both severe catabolic effects and elevated levels of circulating proinflammatory cytokines of the lupus disease flare on hair growth cycling.10 Occasionally, patients with severe systemic disease may also experience dystrophic anagen effluvium.10

In anagen effluvium, episodes of severe illness result in a temporary shutdown of the hair matrix, producing a narrowed segment of hair shaft (Pohl–Pinkus constriction), analogous to Beau’s lines in the fingernails, that is prone to intrafollicular fracture.
Another form of transient alopecia in chronically active SLE patients, probably closely related in causation to telogen effluvium, are thin, weakened hairs or lupus hairs, especially at the periphery of the scalp (Figure 5). It is hypothesized that with the induction of a negative nitrogen balance, normal hair growth is interrupted leading to the production of thin, weakened hairs which easily fragment above the surface of the scalp. In any case, the pathomechanisms leading to generalized hair loss in SLE do not result in scarring. With the onset of quiescence of the SLE disease process, hair regrowth can be expected, and the alopecia disappears.

Yet another form of hair loss in SLE that is fairly common but has received little attention in the literature is patchy, non-scarring alopecia. This form of hair loss occurs in patients with severe disease, in which the underlying diagnosis of SLE is not in doubt. Patches of partial hair loss are scattered on the scalp, associated with mild erythema but no evidence of scarring. Gentle traction reveals that hairs remaining in the alopecic patches are almost all telogen hairs, or dystrophic anagen hairs. Also in these cases, when the underlying disease is brought under control, complete hair regrowth occurs. Histopathologically, a peribulbar infiltrate of lymphoid cells is found surrounding anagen hair bulbs, many of which are miniaturized. The inflammatory infiltrate may be denser than that found in alopecia areata. The percentage of catagen and telogen hair is greatly increased. Pigment incontinence and a mild inflammatory infiltrate are frequently found in the fibrous streamers below telogen hairs. These histological findings are similar to those found in alopecia areata, and a diagnosis of LE may not be possible on histological grounds alone. Only the especially dense inflammatory infiltrate, presence of dermal mucin, and further clinical and serological findings would support a diagnosis of LE.

Rarely, vascular lesions may be present on the scalp. These too are largely confined to patients with SLE and fall into the categories of immunologically mediated inflammatory vasculitic lesions or pauci-inflammatory microthrombotic lesions triggered by underlying procoagulant and/or hyperviscosity states associated with LE (antiphospholipid antibody syndrome). The histological presentation is either a severe pandermal vasculitis with associated thrombosis and resultant cutaneous infarction, or bland luminal thrombi occluding vessels in the deeper reticular dermis or subcutis with necrosis of the epidermis and dermis, while the superficial vascular plexus merely shows compensatory ectasia. Both cutaneous vasculitis and thrombotic vasculopathic lesions may be a harbinger of more serious extracutaneous organ involvement.

**Differential diagnosis**

It should also be remembered that LE patients not infrequently develop other unrelated conditions of the hair that are not the direct result of LE disease activity. These primarily include drug-related hair

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**Table 1  Scalp involvement in lupus erythematosus (LE)**

<table>
<thead>
<tr>
<th>Histologically LE specific scalp involvement:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Discoid LE of the scalp</td>
</tr>
<tr>
<td>• Clinically non-inflammatory alopecic patches of LE</td>
</tr>
<tr>
<td>• LE-related pseudopelade state</td>
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</tbody>
</table>

**Differential diagnosis:**

| Other causes of inflammatory scarring alopecia, e.g. lichen planopilaris and variants |
| Pseudopelade (diagnosis of exclusion)  |

<table>
<thead>
<tr>
<th>Histologically LE non-specific hair and scalp involvement:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diffuse telogen effluvium</td>
</tr>
<tr>
<td>• Dystrophic anagen effluvium (Pohl-Pinkus constrictions)</td>
</tr>
<tr>
<td>• Lupus hair</td>
</tr>
<tr>
<td>• Patchy, non-scarring alopecia</td>
</tr>
<tr>
<td>• Vasculopathic lesions of the scalp</td>
</tr>
</tbody>
</table>

**Differential diagnosis:**

| Alopecia areata                                           |
| Drug-related disorders of hair (dyschromia, alopecia)     |
| Other unrelated, common disorders of hair, e.g. androgenetic alopecia |

**Source:** modified from Trüeb.40

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Figure 5  Lupus hair.
alterations, and other unrelated, common causes of hair loss, such as androgenetic alopecia.

Antimalarial therapy (chloroquine, hydroxychloroquine) has long been recognized as a cause of altered pigmentation, especially of normally blonde or reddish hair, resulting in greyness of scalp hair, eyelashes, eyebrows, and beard, while cytotoxic, immunosuppressive agents (azathioprine, cyclophosphamide, and methotrexate) and systemic retinoids (acitretin, isotretinoin), used in the treatment of LE, may cause reversible alopecia. Quinacrine (mepacrine) has been observed to cause a severe lichenoid drug eruption in some individuals resulting in an irreversible scarring alopecia. On an unusual occasion, alopecia areata has been observed in SLE patients. This is an unusual occurrence and no causal relationship between SLE and this type of alopecia has been established. In all probability it represents either a coincidental finding or this finding has been confused with patchy, non-scarring alopecia of SLE. We observed patchy, non-scarring alopecia with vitiligo-like depigmentation in a case of paraneoplastic subacute cutaneous lupus erythematosus (Figure 6). Following successful surgical removal of the tumor (peripheral adenocarcinoma of the lung) skin lesions resolved in this case.

DLE of the nail

DLE can localize to the nail unit, but is never restricted to it. Focal lesions of DLE occurring over the nail fold can produce nail plate dystrophy with longitudinal ridging, which may be broken off in the distal part or partially split (Figure 7). In hypertrophic LE, nail bed hyperkeratosis is associated with gross palmoplantar hyperkeratosis extending on the dorsa of the digits to surround the nails, which again are longitudinally ridged.

In chilblains LE, a chronic unremitting variant seen predominantly in women, red-purple patches develop on the fingers (Figure 8) and toes that are precipitated by cold, damp climates. Such lesions are reminiscent of simple chilblains or pernio lesions, which is why the term ‘perniotic LE’ has also been used to describe them. As the lesions evolve, however, they take on the typical appearance of DLE lesions, both clinically and histopathologically. One may hypothesize whether such patients have simple pernio that in the predisposed individual produces an isomorphic response that results in a DLE lesion. Chilblains LE patients often have typical DLE lesions elsewhere.

Lupus erythematosus unguium mutilans is the term used for a rare form of destructive nail involvement associated with decalcification and atrophy of the distal phalanges. The nail area shows a cyanotic tinge, adherent scales, and only debris of the nail plate. Subungual friable yellowish-brown material may lift up the nail plate. Some...
nails may be entirely destroyed leaving the nail bed exposed as a deep red, shiny area.\(^{24}\)

Histopathologically, LE of the perionychium shows hyperkeratosis, liquefaction degeneration of the basal cell layer, and a predominantly lymphocytic infiltrate in the superficial dermis with oedema and ectatic capillaries in the papillary dermis, while LE of the nail bed causes hyperorthokeratosis with a corresponding granular cell layer, thinning of the spinous cell layer, and oedema of the basal cells which exhibit ill-defined borders. Hyaline bodies are observed in the superficial dermis.\(^{25}\)

**Differential diagnosis**

The differential diagnosis of LE specific nail involvement is principally that of other causes of chronic inflammatory periungual disease with resultant nail plate dystrophy. Usually, DLE involving the nail can be diagnosed on the basis of coexisting typical DLE lesions elsewhere, so that (in contrast to the scalp) nail biopsies are usually not indicated.

**LE non-specific nail involvement**

Although a wide spectrum of nail abnormalities has been described in systemic LE, none is sufficiently distinctive to be useful in the diagnosis of disease. Nevertheless, examination of the nail unit may supply important information in patients with collagen vascular diseases, including LE. Nail changes were detected with a frequency of 31% in one series of patients with SLE. They were associated with active disease in the majority of affected patients. Patients with nail changes had a significantly higher incidence of Raynaud’s phenomenon and oral ulcerations, but no increased incidence of other skin manifestations, or of vasculitis.\(^{26}\) Direct immunofluorescence of proximal nail fold changes in SLE shows the typical immune deposit pattern of LE (lupus band) at the dermal-epidermal junction.\(^{27}\)

Punctate or striate leuconychia, nail pitting or ridging, and onycholysis in patients with SLE are the consequence of altered keratinization of the nail matrix. Onycholysis refers to the detachment of the nail plate from its bed. This was reported as the most frequent nail abnormality.\(^{26}\) In another series, nail dyschromia in the form of diffuse, dark blue-black hyperpigmentation intermixed with longitudinal pigmented bands was found in approximately 52% of black SLE patients, without relationship to disease activity, or to antimalarial therapy.\(^{28}\)

Nail fold erythema, red lunulae, and nail fold hyperkeratosis with ragged cuticles and splinter haemorrhages (Figure 9) can also be observed in patients with SLE. In one series, red lunulae were found in 19.6% of patients with LE.\(^{29}\) Although rarely described in the literature, they seem not to be uncommon, and have been associated with the
presence of periungual erythema, or chilblains. A case was reported in which painful red lunulae of the fingernails were the presenting sign of SLE. The appearance of Beau’s lines suggested inflammation of the nail matrix area. Multiple subungual splinter haemorrhages have also been observed in antiphospholipid syndrome secondary to SLE (see also review on ‘Dermatological manifestations of Hughes’ antiphospholipid syndrome’ in this issue).

Vasculopathic lesions of the nail unit with blood vessel infarction leading to focal necrosis of the nail fold and cuticular haemorrhages are common features of SLE. They result either from small vessel necrotizing vasculitis, or from the formation of vaso-occlusive platelet thrombi in the smaller vessels of patients with antiphospholipid antibodies. Less frequently, digital gangrene may occur secondary to prolonged ischaemia. The cutaneous manifestations of vasculitis are the putative manifestations of circulating immune complexes which histologically produce a leucocytoclastic vasculitis. Direct immunofluorescence examination of lesional biopsies generally demonstrates fibrinogen, complement, and granular IgG deposition around blood vessels.

In addition to vasculitis and thrombi formation, SLE patients frequently experience Raynaud’s phenomenon that is characterized by paroxysmal triphasic colour changes involving the fingers and/or toes. Initially, there is a vasospastic phase with blanching of the digits (Figure 10), followed by a cyanotic phase with purplish discoloration, then by a reperfusion erythema upon rewarming. The frequency of Raynaud’s phenomenon is environmentally dependent, being more frequent in SLE patients living in cold climates, and ranging from 18% of SLE patients seen in southern California to 44% in patients examined in Baltimore, USA. There is no correlation between the severity of Raynaud’s phenomenon and SLE disease activity. Formation of pterygium inversum unguis (ventral pterygium) may be seen in LE associated with Raynaud’s phenomenon. It is characterized by a distal extension of the hyponychial tissue which anchors to the undersurface of the nail, thereby eliminating the distal groove.

Differential diagnosis

The differential diagnosis of LE non-specific nail involvement in LE focuses primarily on other connective tissue diseases with vascular involvement of the proximal nail fold (scleroderma, dermatomyositis, mixed connective tissue disease, rheumatoid arthritis). These show different microscopic nail fold capillary patterns (i.e. capillary density, morphological changes), as described elsewhere.

Again it should be remembered that LE patients not infrequently develop other unrelated conditions of the nails that are not the direct result of LE disease activity. These primarily include drug-related nail alterations, and the more common causes of onycholysis.

Antimalarials have long been recognized as a cause of altered pigmentation of the nails in the form of diffuse hyperpigmentation or transverse bands of pigmentation. Other drugs occasionally used in the treatment of LE that may cause nail pigmentation are cyclophosphamide, gold and gold compounds, and methotrexate. Drugs that may cause onycholysis include clofazimine, gold and gold compounds, ibuprofen, indometacin, isotretinoin, methotrexate, and piroxicam.

Onycholysis occurs very frequently in fingernails, less so in toenails. It is usually symptomless, and it is mainly the appearance of the nail which concerns the patient. There are many additional causes of onycholysis, of which the most important are trauma (accidental, occupational, self-inflicted) and Candida albicans (which can be isolated in 74% of cases), which account for a predominance of female patients varying from the age of 25 years onwards and peaking at the 50- to 60-year-old
Table 2 Nail involvement in lupus erythematosus (LE)

<table>
<thead>
<tr>
<th>Histologically LE specific nail involvement:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Discoid LE of the nail unit</td>
</tr>
<tr>
<td>• Hypertrophic LE</td>
</tr>
<tr>
<td>• Chilblains LE</td>
</tr>
<tr>
<td>• Lupus erythematosus unguium mutilans</td>
</tr>
<tr>
<td>Differential diagnosis:</td>
</tr>
<tr>
<td>• Other causes of chronic inflammatory periungual disease with nail plate dystrophy, e.g. lichen planus</td>
</tr>
<tr>
<td>Histologically LE non-specific nail involvement:</td>
</tr>
<tr>
<td>• Leuconychia (punctate, striate)</td>
</tr>
<tr>
<td>• Nail pitting, ridging (Beau’s lines)</td>
</tr>
<tr>
<td>• Onycholysis</td>
</tr>
<tr>
<td>• Nail dyschromia (diffuse, longitudinal)</td>
</tr>
<tr>
<td>• Nail fold erythema</td>
</tr>
<tr>
<td>• Red lunulae</td>
</tr>
<tr>
<td>• Nail fold hyperkeratosis, ragged cuticles, and splinter haemorrhages</td>
</tr>
<tr>
<td>• Vasculopathic lesions of the nail unit (vasculitis, microthrombotic)</td>
</tr>
<tr>
<td>• Pterygium inversum unguis (in Raynaud’s phenomenon)</td>
</tr>
<tr>
<td>Differential diagnosis:</td>
</tr>
<tr>
<td>• Other connective tissue diseases with vascular involvement of the proximal nail fold, i.e. scleroderma, dermatomyositis, mixed connective tissue disease, rheumatoid arthritis (nail fold capillary microscopy)</td>
</tr>
<tr>
<td>• Drug-related disorders of the nails (dyshchromia, onycholysis)</td>
</tr>
<tr>
<td>• Other unrelated, common disorders of the nails, e.g. onycholysis of other origin (accidental, occupational, self-inflicted, C. albicans, onychomycosis, psoriasis, eczema)</td>
</tr>
</tbody>
</table>

Source: modified from Trüeb.40

age group. Onychomycosis as a cause of onycholysis mainly affects toenails following trauma. Other frequent causes of onycholysis are common dermatological disorders, such as psoriasis and eczema. When onycholysis occurs in the fingernails of males, then it occurs more frequently in those who have distinctive jobs relating to the waterborne environment, for example barbers (occupational hazard).

Nail fold capillary microscopy

In all collagen vascular diseases, the proximal nail fold is an important site of alterations, and careful investigation of this nail constituent is an essential part of the patient’s clinical evaluation. In these patients, irregular capillary loops are frequently visible even without a magnifying lens. Nail fold capillary microscopy is a simple and non-invasive technique that can give useful information for early diagnosis of collagen vascular diseases. Several instruments have been developed for in vivo examination of the nail fold capillary bed,37 though common dermatoscopes (x10) are useful and inexpensive instruments for ordinary screening. More sophisticated instruments that permit higher magnifications (x40) and photographic documentation are advisable for long-term follow-up of the microangiopathic alterations of the nail fold capillary bed. Nail fold examination in SLE shows a normal density of capillary loops but a marked deformation of the individual capillaries. While the vessel dilation is minimal, the arrangement of the capillary loops is tortuous and can be corkscrew shaped. Occasionally, meandering loops that may resemble glomerular tufts are observed. Similar abnormalities have also been described in DLE38,39 (see also the article on ‘Diagnostic algorithm for Raynaud’s phenomenon and vascular skin lesions in systemic lupus erythematosus’ in this issue).

Treatment

There is no ideal treatment for the alopecias related to LE. However, high-potency topical or intraleisonal corticosteroids may both halt the progression of DLE lesions of the scalp, and speed the resolution of patchy, non-scarring alopecia. Long-term single-agent or combined antimalarial therapy, as indicated by the severity of the disease, is of value for patients who have non-scarring hair loss due to the underlying LE process. Owing to the high risk of irreversible scarring alopecia, DLE of the scalp is best treated early and aggressively as outlined above. Hair pieces and wigs often offer the best solution for those patients with permanent alopecia. As long as disease activity is present, the trauma of plastic surgery procedures, such as alopecia reduction and hair transplantation, may carry the risk of an isomorphic response (Koebner’s phenomenon).2

Treatment measures of acral lesions are aimed at keeping the digits warm by physical measures and the discontinuance of exacerbating factors such as smoking and the intake of oral contraceptives. Vasodilating agents and/or inhibitors of platelet aggregation such as nifedipine and low-dose aspirin, respectively, are often used to improve digital blood flow. The small number of hypertrophic DLE that do not respond to single-agent or combined antimalarial therapy, may respond to treatment with systemic isotretinoin, while potent topical corticosteroids under occlusion may lead to some improvement in chilblains LE.2

References

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