Histologic Findings in Cutaneous Lupus Erythematosus

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Christian A. Sander, Amir S. Yazdi, Michael J. Flaig, Peter Kind

Lupus erythematosus (LE) is a chronic inflammatory disease that can be clinically divided into three major categories: chronic cutaneous LE (CCLE), subacute cutaneous LE (SCLE), and systemic LE (SLE). In general, LE represents a spectrum of disease with some overlap of these categories. Classification is based on clinical, histologic, serologic, and immunofluorescent (see Chap. 22) features. Consequently, histologic findings alone may not be sufficient for correct classification. In addition, these categories can be subdivided into numerous variants affecting different levels of the skin and subcutaneous tissue.

Chronic Cutaneous Lupus Erythematosus

Discoid Lupus Erythematosus

Discoid LE (DLE) is the most common form of LE. Clinically, the head and neck region is affected in most cases. On the face, there may be a butterfly distribution. However, in some cases, the trunk and upper extremities can be also involved. Lesions consist of erythematous scaly patches and plaques.

Histologically, in DLE the epidermis and dermis are affected, and the subcutaneous tissue is usually spared. However, patchy infiltrates may be present. Characteristic microscopic features are hyperkeratosis with follicular plugging, thinning, and flattening of the epithelium and hydropic degeneration of the basal layer (liquefaction degeneration) (Fig. 21.1). In addition, there are scattered apoptotic keratinocytes (Civatte bodies) in the basal layer or in the epithelium. Particularly in older lesions, thickening of the basement membrane becomes obvious in the periodic acid-Schiff stain. In the dermis, there is a lichenoid or patchy lymphocytic infiltrate with accentuation of the pilosebaceous follicles. There is interstitial mucin deposition and edema, and usually no eosinophils and neutrophils are present.

Hypertrophic lesions have acanthosis and hyperkeratosis of the epidermis (Weedon 2002). Direct immunofluorescence is an important test that should be performed in this subtype. Usually, there is deposition of IgG and IgM in 50%–90% of cases. The differential diagnosis includes drug reaction, dermatomyositis, graft-vs-host disease, and mycosis fungoides. Jessner's lymphocytic infiltration of the skin usually does not involve the epidermis as hydropic degeneration of the basal layer and scattered apoptotic keratinocytes do not occur. Otherwise, the dermal infiltrate is identical to LE. Consequently, Jessner's lymphocytic infiltration of the skin is regarded as a variant of LE by some authors. In a drug reaction there are frequently eosinophils that are not

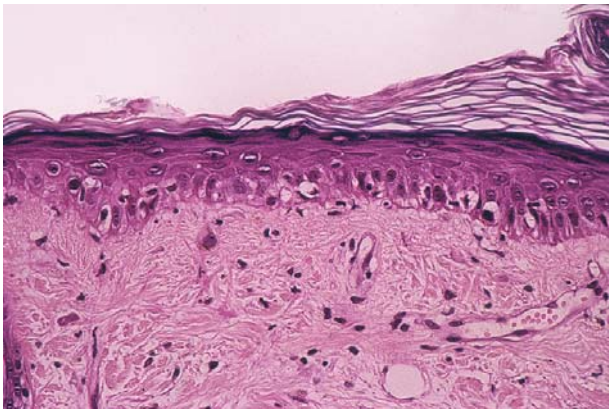

Fig. 21.1. Discoid lupus erythematosus. Hydropic degeneration of the basal layer

seen in DLE. In graft-vs-host disease, there is usually not a prominent lymphocytic infiltrate involving the dermis. Early-stage dermatomyositis can be histologically difficult to distinguish from DLE because it can exhibit identical changes. Consequently, clinical features should be considered for diagnosis. In mycosis fungoides, lymphocytes frequently exhibit nuclear atypia.

Subacute Cutaneous Lupus Erythematosus

The term "subacute cutaneous lupus erythematosus" was coined in 1977 by Gilliam (Gilliam 1977) and further characterized by Sontheimer et al. (Sontheimer et al. 1979) in 1979. The authors introduced a previously undescribed variant of LE with skin lesions at the neck, shoulders, upper thorax, and arms. Clinically, recurrent annular polycyclic or papulosquamous lesions involve the upper trunk, extensor regions of the arms, and face and neck region.

The histopathologic features of SCLE are almost identical to those of DLE (Fig. 21.2). In individual cases, in particular in early lesions, differentiation by histopathologic features alone may be difficult or impossible. However, usually in SCLE there are more prominent changes at the dermoepidermal interface such as hydropic degeneration of the basal epithelial layer. Forming clefts or vesicles, epidermal atrophy, and dermal edema may be also more prominent as in DLE, and there may be extravasation of erythrocytes and dermal fibrin deposits. Apoptotic keratinocytes (Civatte bodies) in the epidermis may be numerous. In addition, the lymphocytic infiltrate is more confined to the upper dermis and bandlike compared with DLE.

Compared with DLE, SCLE has less hyperkeratosis, atrophy of pilosebaceous units, follicular plugging, and thickening of the basal layer (Bangert et al. 1984, Jerdan et al. 1990). The lupus band test result is positive in approximately 60% of cases.

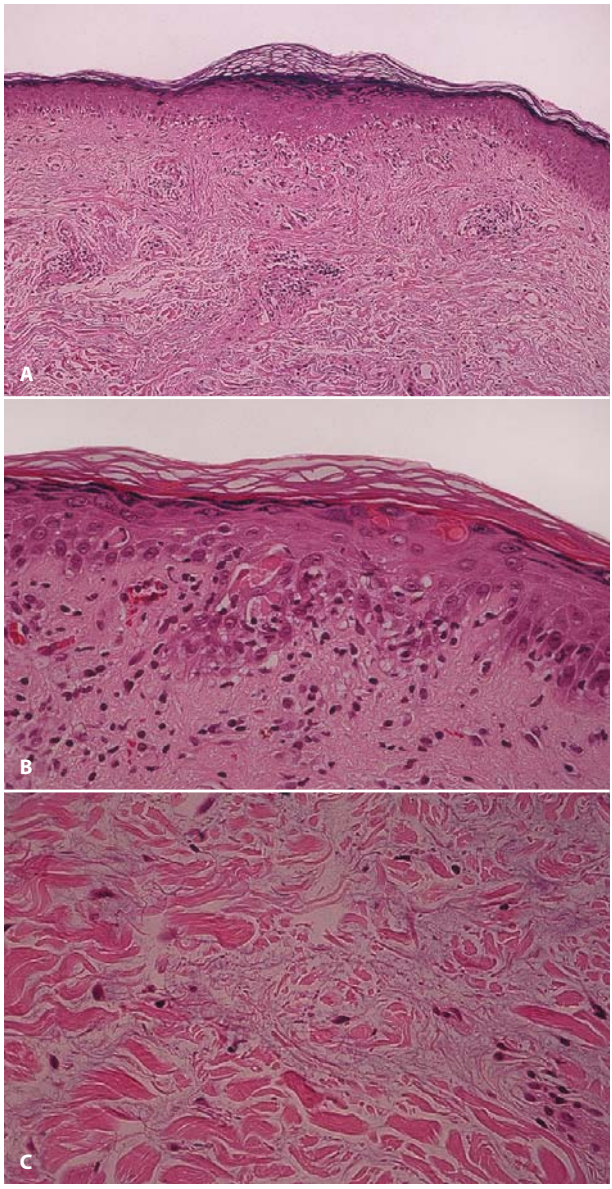

Fig. 21.2A–C. Subacute cutaneous lupus erythematosus.
B Hydropic degeneration of the basal layer and apoptotic keratinocytes in the epidermis.
C Mucin deposition in the dermis

Systemic Lupus Erythematosus

Clinically, in SLE there are erythematous patches. In early lesions, histopathologic changes of SLE can show indifferent changes that may be unspecific, including discrete vacuolar degeneration of the basal layer, edema, and a discrete lymphocytic infiltrate in the upper dermis. Well-established lesions show prominent vacuolar

degeneration of the basal membrane, edema, extravasation of erythrocytes, and a lymphocytic infiltrate in the upper dermis. Neutrophils are sometimes present in early lesions at the dermoepidermal junction. Fibrinoid material may be present in the dermis around vessels and between collagen strands. In individual cases, distinction from leukocytoclastic vasculitis is impossible because all of the signs of leukocytoclastic vasculitis may be present, including nuclear dust, fibrinoid necrosis of vessel walls, neutrophilic infiltrate, and extravasation of erythrocytes. Eosinophils may be present in some drug-induced cases. Mucin can be present in larger amounts in the dermis and can be verified by using special stains (Alcian blue). The subcutaneous fat is frequently involved, with changes that are similar to those seen in LE profundus (see the following section).

The differential diagnosis includes polymorphous light eruption that usually does not exhibit larger amounts of mucin. Leukocytoclastic vasculitis does not show prominent mucin deposition or vacuolar degeneration of the basal layer.

Variants of Lupus Erythematosus

Lupus Erythematosus Tumidus

LE tumidus (LET) usually affects sun-exposed areas such as the face, back, and V area of the neck. Clinically, there are erythematous, succulent, edematous, nonscarring plaques (Kuhn et al. 2000). Histologically, LET is characterized by patchy lymphocytic infiltrates in the dermis. Mucin deposits are observed between the collagen fibers. The epidermis and the subcutaneous tissue are usually not involved (Kuhn et al. 2003).

Direct immunofluorescence depends on the duration of the lesion. In long-lasting lesions, usually there is deposition of IgG and IgM along the basement membrane (Kind et al. 1992). The differential diagnosis includes polymorphous light eruption, Jessner's lymphocytic infiltration of the skin, and pseudolymphoma (reactive lymphocytic infiltrate). Furthermore, reticular erythematous mucinosis (Steigleder et al. 1974) is regarded by Ackerman as a variant of LE.

Lupus Erythematosus Profundus

LE profundus is a variant of LE described by Kaposi (Kaposi 1883) in 1883 and in more detail by Irgang in 1940 (Irgang 1940). LE profundus is a panniculitis, also termed "lupus panniculitis". Clinically, LE profundus has a predilection for the face, neck, proximal extremities, trunk, and lower back (Tuffanelli 1985).

Histologically, the epidermis and dermis may be involved, with vacuolar degeneration and dermal lymphocytic infiltration (Fig. 21.3). However, the key feature is the prominent lobular panniculitis. There is a diffuse lymphocytic infiltrate with nuclear dust (Sanchez et al. 1981), and fat necrosis may develop later on in hyalinization of adipose lobules. Areas with fat necrosis have plasma cells, histiocytes, and neutrophils. Eosinophils may be present in approximately 25% of cases (Peters et al. 1991). Vascular involvement includes arteries and veins with endothelial cell hypertrophy, edema, and, in some cases, thrombosis or calcification. Perivascular fibrosis (onion-skin configuration) can be observed in the surroundings of vessels.

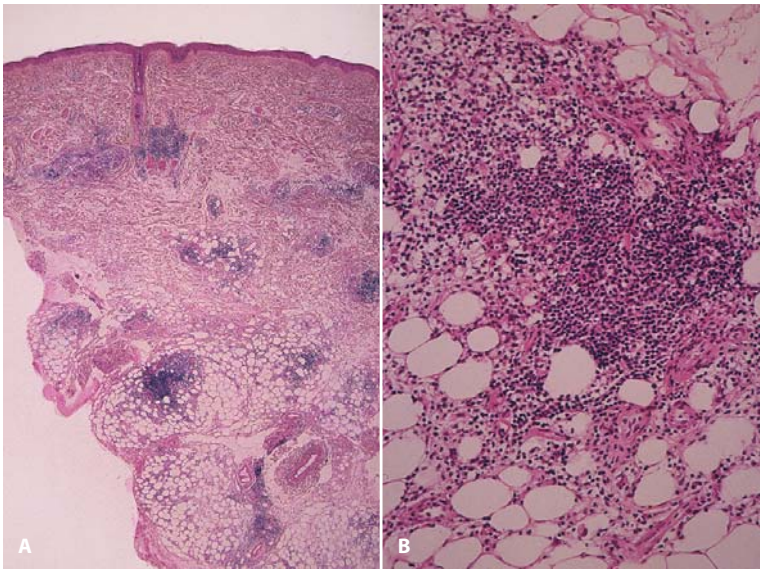

Fig. 21.3A, B. Lupus erythematosus profundus. Patchy lymphocytic infiltrates in the dermis and subcutaneous tissue

Another characteristic feature is the presence of reactive lymphoid follicles. Lymphoid follicles are rare in panniculitis but may be seen in rare cases of erythema nodosum, erythema induratum, and morphea (Harris et al. 1979). These entities are also part of the differential diagnosis of LE profundus. However, erythema induratum is usually on the calves of women, a location that is not common in LE profundus. In morphea, there are thickened collagen bundles, which are not present in LE profundus. Erythema nodosum usually does not display the histologic changes in the epidermis that may be seen in LE profundus. Another important differential diagnosis is subcutaneous panniculitis-like T-cell lymphoma, which is a cytotoxic T-cell malignancy. The neoplastic cells infiltrate the subcutaneous tissue and rim individual fat cells. Angioinvasion and necrosis may be prominent. T-cell receptor gene rearrangement studies are useful in diagnosis, as benign panniculitis does not show a monoclonal population (Sander et al. 2001).

Neonatal Lupus Erythematosus

NLE is a rare disease presenting in the neonatal period that resolves in the first 6 months of life. Associated disorders include transient thrombocytopenia, leukopenia, and a congenital heart block. Affected are children of mothers suffering from SLE. Clinically, children exhibit lesions as seen in SCLE. The causative agents are maternal IgG antinuclear antibodies (usually anti-Ro/SSA, less frequently anti-La/SSB, α-fodrin, and U1-RNP).

Histologic changes are similar to those of SCLE. However, infiltration at the dermoepidermal interface and vacuolar degeneration of the basal layer are more pronounced, sometimes with formation of clefts and edema of the dermis.

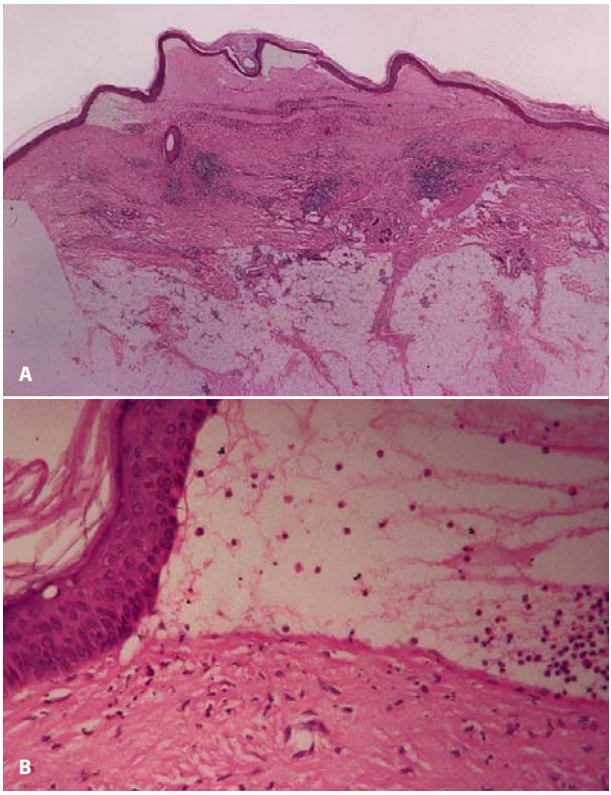

Fig. 21.4A, B. Bullous lupus erythematosus. Blister formation

Bullous Lupus Erythematosus

In BLE, patients present with blisters that can resemble dermatitis herpetiformis or bullous pemphigoid. Histologically, BLE can present with two different variants: in one variant the infiltrate consists of neutrophils and in the other of mononuclear cells. There is a pronounced neutrophilic infiltrate in the dermis with the formation of papillary dermal abscesses, resembling dermatitis herpetiformis or linear IgA bullous disease. In addition, there is blister formation and dermal edema. Nuclear dust is seen in the papillary dermal abscesses. In the second variant, there is a mononuclear infiltrate with formation of blisters believed to represent a long-standing lesion of LE (Fig. 21.4).

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