JOURNAL OF MULTIDISCIPLINARY SCIENCES AND INNOVATIONS

VOLUME 04, ISSUE 11
MOPNTHLY JOURNALS

ISSN NUMBER: 2751-4390
IMPACT FACTOR: 9,08

CLINICAL AND MORPHOLOGICAL STAGES OF LICHEN SCLEROSUS ET ATROPHICUS AND IMMUNOHISTOCHEMICAL MARKERS OF PROGRESSION

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Abstract: Lichen sclerosus et atrophicus is characterized by a staged restructuring of the epidermis and dermis, including an early inflammatory interface dermatitis and a late scleroatrophic stage. Immunohistochemical (IHC) markers of endothelial activation and hypoxia (CD31, VEGF) and apoptosis (CD95/Fas) reflect the dynamics of morphogenesis and can be used for early detection of the risk of squamous cell carcinoma of the vulva and penis. The review systematizes current data on the histopathological patterns of LS, vascular and apoptotic progression mechanisms, as well as differential diagnosis with morphea and precancerous lesions.

Keywords: lichen sclerosus, morphogenesis, immunohistochemistry, CD31, VEGF, CD95, angiogenesis, apoptosis, squamous cell carcinoma.

Introduction

Lichen sclerosus (LS) is classified as a chronic inflammatory–dystrophic dermatosis characterized by progressive remodeling of the skin and mucous membranes with the development of sclerosis and atrophy. Despite the accumulation of clinical and morphological data, the mechanisms of disease morphogenesis, the sequence of stage-related transformations, as well as the patterns of vascular and immunohistochemical changes remain insufficiently elucidated. Meanwhile, morphological staging and the spectrum of molecular markers largely determine the clinical course of LS, the rate of its progression, and the likelihood of oncological complications, which underscores the particular importance of their systematic investigation [1, 2].

The morphological evolution of LS predictably proceeds through stages reflecting a shift from inflammatory to sclerotic processes. At the early (presclerotic) stage, features of vacuolar interface dermatitis predominate. Histologically, hydropic degeneration of basal layer keratinocytes, a dense band-like lymphocytic infiltrate in the upper dermis, edema and dilation of blood vessels, as well as initial fibrinoid changes in the stromal matrix are observed [3, 4]. These features often lack sufficient specificity, making early lesions difficult to verify until more characteristic signs of papillary sclerosis develop.

With disease progression, a late stage forms, characterized by marked epidermal atrophy combined with hyperkeratosis, homogenization and hyalinization of collagen fibers in the papillary dermis, reduction of elastic structures and skin appendages, as well as a pronounced decrease in the vascular network. Thus, the histological picture reflects a gradual transition from an inflammatory pattern to a scleroatrophic variant, which is of fundamental importance for assessing disease activity and prognosis.

Microvascular density (MVD) and endothelial status are considered key parameters in the early morphogenesis of LS. During the phase of active inflammation, increased angiogenic activity is observed, manifested by elevated expression of VEGF and endothelial markers CD31/CD34. These changes are interpreted as reactive vascular remodeling in response to local tissue injury and hypoxic stimuli within the dermis [1, 5]. As the process becomes chronic and scleroatrophic changes progress, a tendency toward a decrease in MVD is noted, reflecting progressive reduction of the microcirculatory bed and the development of tissue ischemia.

In parallel with vascular alterations, apoptotic processes in the epidermis and dermis intensify in the late stages of LS. Increased apoptosis of keratinocytes and fibroblasts contributes to epidermal atrophy and deepening stromal sclerosis [2]. The expression of CD95 (Fas), as a marker of apoptotic pathway activation, increases with prolonged disease duration, consistent with the concept of a shift from a predominantly inflammatory pattern to a dystrophic–sclerotic one. For assessing the risk of malignization, disturbances in cell cycle regulation and proliferation are of particular importance: aberrant p53 expression patterns in LS lesions, combined with altered proliferative activity assessed by Ki-67, are associated with the development of differentiated vulvar intraepithelial neoplasia (VIN) and HPV-independent squamous cell carcinoma [6].

Thus, immunohistochemical evaluation of angiogenesis and apoptosis markers, supplemented by analysis of proliferation and tumor suppressor indicators, makes it possible to objectively determine the stage and activity of LS, identify early signs of precancerous transformation, and more accurately stratify patients according to oncological risk.

The clinical and morphological similarity between lichen sclerosus and localized scleroderma (morphea) is обусловлено the commonality of dystrophic–sclerotic changes in the dermis and epidermal atrophy, which often leads to diagnostic difficulties in clinical practice, especially at early stages of the disease. In such cases, dermoscopy plays an important role, allowing the identification of features that closely correlate with the histological structure of lesions: LS is more typically characterized by follicular plugs, superficial sclerosis, and whitish structureless areas, whereas morphea is dominated by deep reticular sclerosis accompanied by relative reduction of the vascular pattern and less pronounced follicular changes [7, 8].

Equally important is the differentiation of LS from early neoplastic processes, since long-standing lesions may serve as a background for the development of differentiated vulvar intraepithelial neoplasia and early squamous cell carcinoma. Their distinction requires a comprehensive assessment of morphological features (basal layer atypia, parakeratosis, impaired epithelial maturation and stratification) in combination with immunohistochemical algorithms involving p53 and p16, which increase the sensitivity of detecting precancerous changes and help verify the HPV-independent pathway of carcinogenesis [6].

Prospects for further research are associated with the development of quantitative approaches to the morphological and immunohistochemical assessment of LS, including microvascular density morphometry, digital pathology methods, and the creation of integrated activity scales and prognostic models for squamous cell carcinoma risk based on panels of angiogenesis and apoptosis markers combined with p53 typing. Such approaches may improve the accuracy of early diagnosis, prognostic stratification, and patient monitoring in clinical practice [1].

Conclusion

Lichen sclerosus represents a stage-dependent process in which the sequential transition of inflammatory, vascular, and dystrophic–sclerotic changes shapes the clinical and morphological diversity of the disease and determines its outcomes. The early phase is characterized by active inflammation and reactive angiogenic remodeling, whereas in later stages dermal hyalinosis, epidermal atrophy, and microcirculatory reduction predominate, accompanied by increased apoptosis and progressive tissue ischemia. This morphological evolution explains the persistence of clinical manifestations, the tendency toward scarring, and the likelihood of long-term lesion persistence in the absence of adequate therapy.

Immunohistochemical verification of stage-related changes significantly expands diagnostic and prognostic capabilities. Evaluation of angiogenesis and endothelial activation markers (CD31, VEGF) allows objective assessment of early morphogenetic activity, while the apoptosis marker CD95 reflects the intensification of dystrophic mechanisms in the late phase. Supplementing this panel with indicators of cellular proliferation and tumor suppression (Ki-67, p53) provides a basis for early identification of unfavorable disease trajectories and subclinical signs of precancerous transformation. In practical terms, this enables more accurate patient stratification according to complication risk, selection of optimal follow-up intervals, and timely performance of targeted biopsies in suspicious lesions.

Therefore, the integration of stage-specific morphology with immunohistochemical profiling forms a modern, pathogenetically grounded model of lichen sclerosus, allowing not only a better understanding of disease progression mechanisms but also improved effectiveness of early diagnosis, prevention of scarring deformities, and reduction of oncological complications.

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