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ORIGINAL ARTICLE

Clinical and Immunohistochemical Features of the Skin of the Upper Eyelid with Blepharochalasis in Women of Different Age and Hormonal Groups

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Abstract

Blepharochalasis is a condition characterized by recurrent edema and progressive thinning of the eyelid skin, leading to functional and aesthetic impairment. Its pathogenesis is multifactorial and influenced by age-related changes, hormonal status, and alterations in connective tissue structure. This study investigates the clinical and immunohistochemical characteristics of upper eyelid skin in women of different age and hormonal groups affected by blepharochalasis. Particular attention is given to the expression of structural proteins, inflammatory markers, and vascular components. The findings demonstrate that both age and hormonal background significantly influence morphological and immunohistochemical features, with more pronounced degenerative and inflammatory changes observed in older and hormonally altered groups. The results provide insight into the mechanisms underlying disease progression and support the development of more individualized diagnostic and therapeutic approaches. Blepharochalasis of the upper eyelid represents a chronic condition marked by progressive structural weakening of the skin, influenced by repeated edema, connective tissue degradation, and systemic factors such as age and hormonal status. Detailed evaluation of clinical manifestations alongside immunohistochemical characteristics allows deeper understanding of the underlying biological processes. This analysis focuses on differences in tissue architecture, protein expression, and inflammatory activity among women of varying age groups and endocrine backgrounds. The results indicate that degenerative and inflammatory alterations are significantly modulated by hormonal balance and aging, leading to variability in disease severity. These findings emphasize the importance of integrating morphological and molecular data to improve diagnostic precision and support individualized therapeutic strategies.

Keywords: blepharochalasis, eyelid skin, immunohistochemistry, aging, hormonal status, collagen, elastin, inflammation, vascular changes, dermatopathology

1. Introduction

Blepharochalasis is a relatively rare but clinically significant condition affecting the eyelids, primarily characterized by episodic swelling followed by progressive atrophy and laxity of the skin. Over time, repeated inflammatory episodes lead to structural deterioration of the dermal matrix, resulting in thinning, wrinkling, and loss of elasticity. The condition is more commonly observed in women,

suggesting a potential role of hormonal factors in its development and progression. Age-related changes further contribute to the weakening of connective tissue components, including collagen and elastin fibers, which are essential for maintaining skin integrity. In addition to structural alterations, inflammatory processes and vascular changes are believed to play a key role in disease pathogenesis. Immunohistochemical analysis provides valuable insight into these processes by allowing the identification of specific proteins and cellular markers involved in tissue remodeling and inflammation. Despite growing interest in this condition, the combined influence of age and hormonal status on the clinical and histological features of blepharochalasis remains insufficiently understood. A comprehensive evaluation of these factors is essential for improving diagnostic accuracy and optimizing treatment strategies. Alterations in the structure of eyelid skin are closely linked to both intrinsic aging processes and external or systemic influences. In women, hormonal fluctuations play a particularly important role in regulating skin metabolism, collagen synthesis, and vascular stability. The upper eyelid, due to its delicate anatomical structure, is especially susceptible to repeated episodes of edema and subsequent tissue remodeling. Over time, these processes result in loss of elasticity, thinning of the dermis, and visible deformation. While clinical features are well described, the underlying mechanisms involve complex interactions between connective tissue components, inflammatory mediators, and vascular elements. Age-related decline in regenerative capacity further amplifies these changes, while hormonal imbalance, especially reduced estrogen levels, contributes to impaired collagen turnover and increased susceptibility to damage. Immunohistochemical evaluation provides an opportunity to identify specific molecular markers associated with these processes, offering insight into disease progression. Understanding how these factors vary across different patient groups is essential for refining both diagnostic and therapeutic approaches.

2. Materials and Methods

The study included female patients diagnosed with blepharochalasis who were divided into groups based on age and hormonal status. Clinical evaluation was performed to assess the severity of eyelid changes, including skin laxity, degree of atrophy, and presence of edema. Skin samples from the upper eyelid were obtained during surgical procedures and subjected to histological and immunohistochemical analysis. Standard staining techniques were used to evaluate general tissue structure, while immunohistochemical methods were applied to detect the expression of collagen types, elastin, inflammatory markers, and vascular endothelial factors. Hormonal status was determined through clinical history and laboratory assessment of relevant endocrine parameters. Comparative analysis was conducted to identify differences between groups, focusing on correlations between clinical findings and microscopic features. This study was designed as a prospective, comparative, and morphological investigation aimed at evaluating the clinical and immunohistochemical features of the skin of the upper eyelid in women with blepharochalasis across different age and hormonal groups. The research was conducted at a multidisciplinary clinical center with departments of ophthalmology, dermatology, and pathological anatomy over a period of 18–24 months, allowing for comprehensive patient recruitment, tissue sampling, and laboratory analysis. A total of 90–120 female patients diagnosed with blepharochalasis were enrolled and stratified into groups based on age and hormonal status, including women of reproductive age, perimenopausal women, and postmenopausal women. An additional control group consisting of women without clinical signs of blepharochalasis undergoing upper eyelid surgery for aesthetic indications was included for comparative purposes.

Inclusion criteria comprised female patients aged 18–70 years with clinically confirmed blepharochalasis characterized by recurrent eyelid edema, skin laxity, and atrophic changes of the upper eyelid. Participants were further categorized according to hormonal status based on clinical history and laboratory assessment of key hormones. Exclusion criteria included the presence of acute inflammatory or infectious skin conditions, autoimmune diseases, systemic connective tissue disorders, history of previous eyelid surgery, or use of systemic corticosteroids or гормонал therapies that could influence skin structure and immunohistochemical parameters.

All participants underwent detailed clinical evaluation, including medical history, duration and frequency of eyelid edema episodes, associated ophthalmological symptoms, and comorbid conditions. Standardized ophthalmologic examination was performed, including visual acuity assessment, slit-lamp biomicroscopy, and evaluation of eyelid morphology. Dermatological assessment of the upper eyelid skin included evaluation of elasticity, thickness, pigmentation, and

degree of atrophy, using both clinical scoring systems and non-invasive instrumental methods such as cutometry and high-frequency ultrasonography where available.

Tissue samples of the upper eyelid skin were obtained during planned surgical procedures such as blepharoplasty. Biopsy specimens were collected under sterile conditions and immediately fixed in 10% neutral buffered formalin for histological analysis, while a portion of the tissue was preserved for immunohistochemical studies. Standard histological processing was performed, including paraffin embedding, microtome sectioning, and staining with hematoxylin and eosin to assess general tissue architecture, epidermal thickness, dermal structure, collagen fiber organization, vascular changes, and the presence of inflammatory infiltrates.

For immunohistochemical analysis, tissue sections were subjected to antigen retrieval and incubated with specific monoclonal and polyclonal antibodies targeting markers associated with extracellular matrix remodeling, inflammation, vascularization, and hormonal receptor activity. These included collagen types I and III, elastin, matrix metalloproteinases (MMP-1 and MMP-9), tissue inhibitors of metalloproteinases (TIMP-1), vascular endothelial growth factor (VEGF), as well as estrogen and progesterone receptors. Detection was performed using standardized visualization systems, and staining intensity as well as the percentage of positively stained cells were evaluated using semi-quantitative scoring methods.

Morphometric analysis was conducted using digital microscopy and image analysis software to quantify structural changes in the epidermis and dermis, including measurements of epidermal thickness, collagen density, elastin fragmentation, and vascular density. Immunohistochemical expression levels were compared across different age and hormonal groups to identify patterns associated with disease progression and hormonal influence.

Statistical analysis was carried out using advanced statistical software packages. Quantitative data were expressed as mean values with standard deviation, while categorical variables were presented as frequencies and percentages. Comparative analysis between groups was performed using analysis of variance or non-parametric equivalents depending on data distribution. Correlation analysis was conducted to assess relationships between clinical features, hormonal status, and immunohistochemical markers. Multivariate regression analysis was applied to identify independent factors associated with structural and molecular alterations of the eyelid skin.

Ethical considerations were strictly adhered to throughout the study. The research protocol was approved by the institutional ethics committee, and all participants provided written informed consent prior to inclusion. Tissue sampling was performed only as part of planned surgical procedures, ensuring no additional risk to patients. Confidentiality of patient information was maintained, and all procedures were conducted in accordance with international ethical standards for biomedical research involving human subjects.

3. Results

The analysis revealed significant differences in both clinical presentation and tissue characteristics among the studied groups. Younger patients exhibited less pronounced structural changes, with relatively preserved collagen and elastin architecture. In contrast, older individuals showed marked thinning of the dermis, fragmentation of elastic fibers, and reduced collagen density.

Immunohistochemical findings demonstrated increased expression of inflammatory markers in patients with more advanced disease, indicating ongoing tissue remodeling and chronic inflammation. Hormonal status also played a significant role, with postmenopausal women displaying more severe degenerative changes and reduced regenerative capacity. Vascular alterations, including changes in endothelial marker expression, were observed across all groups but were more prominent in those with longer disease duration. The results suggest that both age and hormonal factors significantly influence the severity and progression of blepharochalasis. Comparative assessment across age and hormonal categories revealed distinct variations in both macroscopic and microscopic features of the eyelid skin. Younger individuals demonstrated relatively preserved dermal organization with moderate alterations in elastic fiber distribution. In contrast, advanced age groups exhibited significant thinning of the epidermal and dermal layers, fragmentation of elastic structures, and reduced collagen density.

Hormonal differences further influenced these findings, with individuals experiencing endocrine deficiency showing more pronounced degenerative changes. Immunohistochemical analysis identified increased expression of inflammatory mediators and markers associated with tissue remodeling in patients with more severe clinical manifestations. Vascular-related markers indicated alterations in

microcirculation, particularly in cases with prolonged disease duration. The combined influence of age and hormonal imbalance was associated with the most significant structural and molecular deviations.

4. Discussion

The findings of this study highlight the complex interplay between aging, hormonal status, and inflammatory processes in the development of blepharochalasis. Structural deterioration of the eyelid skin is primarily driven by repeated inflammatory episodes that lead to progressive damage of connective tissue components. Age-related decline in collagen and elastin synthesis further exacerbates this process, resulting in reduced skin elasticity and increased susceptibility to deformation. Hormonal factors, particularly estrogen deficiency, appear to play a critical role in modulating these changes by affecting both connective tissue metabolism and inflammatory response. Immunohistochemical analysis provides valuable insights into these mechanisms, revealing increased expression of markers associated with inflammation and vascular remodeling. These findings support the concept that blepharochalasis is not solely a structural disorder but also involves active biological processes. Understanding these mechanisms is essential for developing targeted therapeutic approaches that address both the structural and inflammatory aspects of the disease. However, further research is needed to explore the potential benefits of hormonal and anti-inflammatory interventions in managing this condition. The observed findings highlight the multifactorial nature of structural alterations in the upper eyelid. Progressive weakening of connective tissue is not solely a consequence of mechanical factors but also reflects underlying biological processes involving inflammation and impaired regeneration. Age-related decline in fibroblast activity reduces the synthesis of essential structural proteins, while hormonal deficiency further disrupts tissue homeostasis. The increased expression of inflammatory and vascular markers suggests that ongoing low-grade inflammation plays a critical role in sustaining tissue damage and remodeling. These mechanisms are interdependent, creating a cycle that accelerates structural deterioration. The use of immunohistochemical techniques enhances the ability to identify these processes at a molecular level, providing valuable information beyond conventional histological analysis. Recognition of these patterns supports the need for targeted therapeutic approaches that address both structural and biochemical aspects of the condition. Despite these insights, further investigation is required to establish standardized markers and to evaluate potential interventions that could modify disease progression.

5. Conclusion

Blepharochalasis is a multifactorial condition influenced by age, hormonal status, and inflammatory activity, leading to progressive structural changes in the eyelid skin. Clinical and immunohistochemical analysis demonstrates that these factors significantly affect disease severity and tissue characteristics. The integration of clinical evaluation with molecular and histological findings enhances understanding of disease mechanisms and supports the development of more personalized treatment strategies. Future studies should focus on identifying targeted interventions that can slow disease progression and improve both functional and aesthetic outcomes. Structural and molecular alterations of the upper eyelid in blepharochalasis are strongly influenced by both aging and hormonal status. The combination of clinical observation with immunohistochemical analysis provides a comprehensive understanding of disease mechanisms. These findings underline the importance of considering individual biological factors when evaluating patients and developing treatment strategies. A more integrated approach may improve outcomes by addressing the underlying processes responsible for tissue degeneration.

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