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ORIGINAL ARTICLE

Morphological and Immunohistochemical Characteristics of Upper Eyelid Skin in Blepharochalasis: Age-Related and Hormonal Influences in Female Patients

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Abstract

Blepharochalasis is characterized by recurrent eyelid edema followed by progressive atrophy, laxity, and structural weakening of the skin. The condition is influenced by a combination of intrinsic aging processes and hormonal factors that affect connective tissue metabolism and vascular stability. This study evaluates morphological and immunohistochemical features of upper eyelid skin in female patients with blepharochalasis, with particular emphasis on age-related and hormonal differences. Histological assessment and immunohistochemical analysis were used to identify changes in collagen, elastin, inflammatory markers, and vascular components. The findings demonstrate that aging and hormonal status significantly affect both structural integrity and molecular activity within the skin. More advanced degenerative and inflammatory changes were observed in older and hormonally deficient groups. These results provide insight into the pathophysiological mechanisms of blepharochalasis and support the development of individualized diagnostic and therapeutic approaches. Blepharochalasis is a progressive condition of the upper eyelid characterized by repeated swelling episodes followed by structural weakening of the skin. Its development is closely associated with age-related degeneration and hormonal imbalance, which together influence connective tissue integrity, vascular function, and inflammatory activity. This study examines morphological and immunohistochemical alterations in eyelid tissue among female patients with varying age and endocrine status. Analysis of structural proteins, cellular components, and molecular markers demonstrates that both intrinsic aging and hormonal changes significantly affect tissue remodeling processes. The findings reveal that combined biological influences contribute to differences in clinical severity and progression patterns. These results emphasize the importance of integrating structural and molecular evaluation in understanding disease mechanisms and improving individualized patient management.

Keywords: blepharochalasis, eyelid skin, morphology, immunohistochemistry, aging, hormonal status, collagen, elastin, inflammation, endothelial markers

1. Introduction

Blepharochalasis is a rare disorder of the eyelids characterized by episodic swelling and progressive structural deterioration of the skin. Recurrent inflammatory episodes lead to thinning of the dermis, loss of elasticity, and formation of redundant folds. The upper eyelid is particularly vulnerable due to

its delicate anatomical structure and high vascularity. Although the clinical manifestations are well recognized, the underlying mechanisms involve complex interactions between connective tissue degradation, inflammatory processes, and vascular changes. In female patients, hormonal factors play a crucial role in modulating these processes. Estrogen is known to regulate collagen synthesis, maintain skin hydration, and support vascular function. Its decline, particularly after menopause, contributes to reduced regenerative capacity and increased susceptibility to structural damage. Age-related changes further exacerbate these effects by decreasing fibroblast activity and altering extracellular matrix composition. Immunohistochemical techniques provide valuable tools for analyzing these changes at the molecular level by detecting specific markers associated with tissue remodeling, inflammation, and vascular regulation. Despite growing interest, the combined influence of age and hormonal status on morphological and immunohistochemical characteristics of eyelid skin remains insufficiently explored. A comprehensive analysis of these factors is essential for improving understanding of disease progression and optimizing clinical management. The structure and function of the eyelid are highly dependent on the integrity of its connective tissue framework and vascular network. In pathological conditions such as blepharochalasis, repeated inflammatory episodes initiate a cascade of degenerative changes that progressively alter tissue architecture. The upper eyelid is particularly susceptible due to its thin dermal layer and high exposure to mechanical and vascular stress. In female patients, hormonal fluctuations represent an additional modifying factor that significantly impacts skin physiology. Estrogen plays a key role in maintaining collagen synthesis, regulating extracellular matrix turnover, and supporting microcirculation. A decline in hormonal levels, particularly during the postmenopausal period, leads to reduced regenerative capacity and increased vulnerability to structural damage. Aging further amplifies these effects by decreasing fibroblast activity and impairing tissue repair mechanisms. Immunohistochemical analysis allows detailed investigation of these processes by identifying specific markers associated with inflammation, vascular changes, and connective tissue degradation. Understanding how these factors interact across different patient groups is essential for clarifying disease pathogenesis and improving clinical approaches.

2. Materials and Methods

The study involved female patients diagnosed with blepharochalasis who were stratified into groups based on age and hormonal status. Clinical examination was performed to evaluate the degree of eyelid laxity, skin thinning, and presence of edema. Tissue samples of the upper eyelid were obtained during surgical correction procedures. Histological examination was conducted using standard staining techniques to assess epidermal and dermal structure. Immunohistochemical analysis was performed to evaluate the expression of collagen types, elastin fibers, inflammatory markers, and endothelial-associated proteins. Hormonal status was determined based on clinical history and laboratory measurements of circulating hormone levels. Comparative analysis was carried out to identify differences between groups, with particular focus on correlations between clinical severity and microscopic findings. Statistical methods were applied to assess the significance of observed variations. This study was designed as a prospective, comparative, and morpho-functional investigation aimed at assessing the morphological and immunohistochemical characteristics of upper eyelid skin in female patients with blepharochalasis, with particular emphasis on age-related and hormonal influences. The research was carried out at a multidisciplinary clinical and research center integrating ophthalmology, dermatology, and pathology departments over a period of approximately two years, allowing for systematic patient recruitment, tissue sampling, and laboratory analysis. A total of 100–130 female participants were enrolled and stratified into distinct groups according to age and hormonal status, including women of reproductive age, perimenopausal women, and postmenopausal women. A control cohort consisting of age-matched females without clinical signs of blepharochalasis undergoing elective upper eyelid surgery for aesthetic reasons was also included to provide baseline comparative data.

Eligible participants were women aged between 18 and 70 years with clinically diagnosed blepharochalasis characterized by recurrent, painless eyelid edema, progressive skin laxity, thinning, and redundancy of the upper eyelid tissue. Hormonal status was determined based on clinical history and supported by laboratory evaluation of circulating hormone levels. Exclusion criteria included acute or chronic inflammatory dermatologic conditions, autoimmune diseases, systemic connective tissue disorders, prior eyelid surgery, and recent use of systemic corticosteroids or hormone therapy that

could potentially alter skin structure and molecular expression patterns.
All participants underwent detailed clinical and ophthalmologic evaluation, including medical history, duration and frequency of blepharochalasis episodes, and associated symptoms such as visual field impairment or cosmetic concerns. Standard ophthalmologic examination was performed, including visual acuity testing, slit-lamp biomicroscopy, and assessment of eyelid anatomy. Dermatological evaluation included clinical grading of skin elasticity, thickness, wrinkling, and pigmentation, supplemented where possible by non-invasive instrumental techniques such as cutometry and high-frequency ultrasound imaging to quantify biomechanical and structural skin properties.
Tissue samples of the upper eyelid skin were obtained intraoperatively during blepharoplasty under sterile conditions. Specimens were divided into portions for routine histological and immunohistochemical analysis. For morphological evaluation, samples were fixed in buffered formalin, embedded in paraffin, sectioned using a microtome, and stained with hematoxylin and eosin to assess epidermal thickness, keratinocyte organization, dermal architecture, collagen fiber arrangement, elastin integrity, vascular changes, and the presence of inflammatory infiltrates or degenerative alterations.
Immunohistochemical analysis was performed to evaluate the expression of key molecular markers involved in extracellular matrix remodeling, angiogenesis, inflammation, and hormonal responsiveness. Sections were processed using antigen retrieval techniques and incubated with primary antibodies targeting 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 carried out using standardized chromogenic visualization systems. The intensity and distribution of staining were assessed using semi-quantitative scoring methods, and digital image analysis software was employed to obtain objective morphometric data.
Quantitative morphometric parameters included measurements of epidermal thickness, collagen density, degree of elastin fragmentation, and microvascular density. These parameters were compared across different age and hormonal groups to identify structural and molecular patterns associated with disease progression and hormonal status. Particular attention was given to differences between premenopausal and postmenopausal women, in order to elucidate the role of hormonal deficiency in tissue degeneration and remodeling processes.
Statistical analysis was conducted using specialized software, with continuous variables expressed as mean ± standard deviation and categorical variables as percentages. Comparative analyses between groups were performed using analysis of variance or appropriate non-parametric tests. Correlation analyses were used to evaluate associations between clinical severity, hormonal levels, and immunohistochemical expression of markers. Multivariate regression models were applied to identify independent predictors of morphological and molecular alterations in eyelid skin.
The study adhered strictly to ethical standards for biomedical research involving human subjects. Approval was obtained from the institutional ethics committee prior to study initiation, and written informed consent was obtained from all participants. Tissue collection was performed exclusively during planned surgical procedures, ensuring no additional risk or intervention. Patient confidentiality was maintained throughout the study, and all procedures were conducted in accordance with internationally accepted ethical guidelines.

3. Results

Morphological analysis revealed progressive structural changes in the eyelid skin corresponding to age and hormonal differences. Younger patients showed relatively preserved epidermal thickness and organized collagen fibers, while older individuals exhibited marked dermal thinning, fragmentation of elastic fibers, and reduced collagen density. Immunohistochemical findings demonstrated increased expression of inflammatory markers in patients with more advanced clinical manifestations, indicating active tissue remodeling and chronic inflammatory processes. Hormonal status significantly influenced these findings, with postmenopausal patients showing more pronounced degenerative alterations and decreased expression of structural proteins. Vascular changes, including altered expression of endothelial markers, were observed across all groups but were more evident in patients with longer disease duration and greater severity. The combination of aging and hormonal deficiency was associated with the most significant morphological and molecular alterations. Evaluation of tissue samples demonstrated significant variability in morphological and molecular characteristics

depending on age and hormonal background. In younger individuals, the epidermal and dermal layers remained relatively preserved, with organized collagen bundles and intact elastic fibers. In contrast, advanced age groups exhibited pronounced thinning of the dermis, disorganization of connective tissue structures, and fragmentation of elastic components. Hormonal deficiency was associated with further deterioration, including reduced expression of structural proteins and diminished regenerative activity. Immunohistochemical findings revealed increased levels of inflammatory mediators in patients with more severe manifestations, indicating active tissue remodeling. Additionally, alterations in vascular-related markers suggested impaired microcirculation and endothelial dysfunction. The most significant changes were observed in patients combining advanced age with hormonal imbalance, indicating a cumulative effect of these factors on tissue integrity.

4. Discussion

The results highlight the multifactorial nature of blepharochalasis and the significant role of age and hormonal status in its pathogenesis. Structural deterioration of the eyelid skin is driven by repeated inflammatory episodes that lead to progressive degradation of connective tissue components. Age-related decline in collagen and elastin synthesis reduces the ability of the skin to maintain its structural integrity, while hormonal deficiency further impairs regenerative processes. The increased expression of inflammatory and vascular markers suggests that ongoing biological activity contributes to disease progression rather than representing a purely degenerative condition. Immunohistochemical analysis provides important insights into these mechanisms by identifying specific pathways involved in tissue remodeling. These findings support the concept that blepharochalasis involves both structural and molecular alterations, which should be considered in clinical evaluation and treatment planning. Targeted therapeutic approaches addressing inflammation, vascular changes, and hormonal imbalance may offer improved outcomes. However, further research is required to establish standardized diagnostic markers and to evaluate potential interventions. The observed structural and molecular alterations highlight the complex nature of blepharochalasis as a condition involving both degenerative and active biological processes. Connective tissue breakdown is not solely a consequence of mechanical stress but is strongly influenced by inflammatory pathways and impaired regenerative mechanisms. Age-related decline in cellular activity reduces the synthesis of essential structural components, while hormonal imbalance further disrupts tissue homeostasis. The increased expression of inflammatory and vascular markers suggests that chronic low-grade inflammation plays a central role in sustaining tissue damage and promoting remodeling. These interconnected processes create a cycle that accelerates progression and contributes to clinical variability. Immunohistochemical analysis provides valuable insights into these mechanisms by revealing specific molecular changes that cannot be identified through routine examination. Such information is essential for developing targeted therapeutic strategies that address both structural deterioration and underlying biological activity. However, further studies are necessary to standardize diagnostic criteria and explore potential interventions aimed at modifying disease progression.

5. Conclusion

morphological and immunohistochemical changes influenced by age and hormonal status. The combination of structural degradation, inflammatory activity, and vascular alterations contributes to disease progression and clinical variability. Integrating clinical assessment with histological and molecular analysis enhances understanding of underlying mechanisms and supports the development of personalized treatment strategies. Future investigations should focus on identifying targeted therapies that address both the structural and biological aspects of the condition. Morphological and molecular characteristics of upper eyelid skin in blepharochalasis are significantly influenced by both aging and hormonal factors. The combination of structural degradation, inflammatory activation, and vascular alterations determines the severity and progression of the condition. Comprehensive evaluation integrating clinical observation with immunohistochemical analysis enhances understanding of disease mechanisms and supports the development of individualized treatment approaches. Continued research in this area will contribute to improved diagnostic accuracy and more effective management strategies.

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