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Eyelid Margin Inflammation: Pathophysiology, Diagnosis and Management Approaches

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ABSTRACT

Introduction and Purpose: Eyelid margin inflammation is a commonly reported syndrome of ophthalmic complaints. It is a chronic, multifactorial disorder of the eyelid margins that significantly impacts the visual function and quality of life of patients across all age groups. Establishing the epidemiology is challenging, and the diagnosis relies primarily on a physical examination combined with a thorough ophthalmological assessment, potentially supplemented by additional tests. The condition is recurrent, often necessitating long-term treatment. Successful management requires close collaboration between the specialist and the patient, which demands commitment and patience. Eyelid margin inflammation manifests through various symptoms, such as burning, itching, dryness, or a feeling of sand in the eyes. This condition is characterized by a wide range of symptoms with varying severity, contributing to the complexity of its diagnosis and treatment. This review examines the diagnostic approaches and treatment strategies for eyelid margin inflammation, focusing on the most common underlying factors.

Materials and Methods: A comprehensive survey of articles published in scientific journals was conducted via the online research platforms PubMed and Google Scholar. Articles were searched by entering keywords in the appropriate configuration: "eyelid rim inflammation", "Meibomian gland dysfunction", "demodex".

Description of current knowledge: Studies have indicated that the approach to diagnosing and managing eyelid margin inflammation is largely contingent on the underlying cause and the intensity of the patient's symptoms.

Keywords: "eyelid rim inflammation", "Meibomian gland dysfunction", "demodex".

Introduction: Eyelid margin inflammation, often referred to as blepharitis, is a common ophthalmic condition characterized by chronic inflammation of the eyelid margins [1]. It occurs in all age groups, with a higher incidence in middle-aged and older people. Individuals with meibomian gland dysfunction and seborrheic inflammation tend to be of more advanced age [2]. Eyelid margin inflammation manifests itself with discomfort, burning, a feeling of lingering sand under the eyelids. Dilation of blood vessels on the anterior surface of the eyelid margin with scaling at the base of the eyelashes is observed. It is often accompanied by inflammation of the conjunctiva, cornea, intra-particular abscesses at the base of the eyelashes and a disorder of tear film secretion, which leads to the development of dry eye syndrome [3][4]. The complexity of the condition is compounded by the poor correlation between subjective complaints and observable physical symptoms, combined with unclear pathophysiological mechanisms that can make accurate diagnosis and effective treatment difficult [5]. Blepharitis is a widespread condition, with prevalence estimates ranging from 12% to 47% in various populations [6] [7]. Causes of blepharitis can be allergic factors, infections, Meibom's gland dysfunction, environmental factors or systemic diseases.

Etiopathogenesis: Eyelid margin inflammations are divided into:

-anterior eyelid margin inflammation, most common in young people. It can be inflammatory (bacterial, viral, parasitic) or non-inflammatory (seborrheic, toxic, allergic)

-posterior eyelid rim inflammation, characteristic of the elderly with an inflammatory (microbial, Meibom's gland inflammation) or non-inflammatory (rosacea, allergy, psoriasis) basis

-mixed forms

Anterior blepharitis tends to be more characterized by inflammation of the anterior lid margin and base of the eyelashes, which can be accompanied by excessive scaling, crusting, and redness of the eyelid margins [7].

Anterior inflammation of the eyelid margins

Anterior eyelid margin inflammation predominantly affects the area around the base of the eyelashes. This type of inflammation is most commonly attributed to either staphylococcal or seborrheic factors. In general, the underlying etiology is an infectious agent. Anterior blepharitis tends to be more characterized by inflammation of the anterior lid margin and base of the eyelashes, which can be accompanied by excessive scaling, crusting, and redness of the eyelid margins. In cases of staphylococcal etiology, an abnormal cellular response to the cell wall components of Staphylococcus aureus is believed to contribute to the inflammation, including the accompanying red eye symptoms and peripheral corneal infiltrates observed in some patients. This form of inflammation tends to be more prevalent and severe in individuals with atopic dermatitis. Seborrheic dermatitis, on the other hand, is associated with generalized seborrheic dermatitis, in which the lesions frequently localize to the hairy skin areas.

Posterior inflammation of the eyelid margins

Posterior eyelid inflammation is caused by the malfunction of Meibomian glands [8], which are responsible for secreting the fatty component of the tear film and forming its protective outer layer. In this condition, the openings of the terminal tubules leading the secretion of the Meibomian glands become obstructed, typically due to the activity of bacterial lipases. This

results in the formation of free fatty acids, which raise the melting temperature of the sebum and reduce its fluidity, thereby hindering its expulsion from the glandular tubules. Prolonged obstruction leads to inflammation and hyperkeratinization of the tubular epithelium [9]. This phenomenon leads to reduced phospholipid content in the tear film, resulting in excessive tear evaporation and the development of dry eye syndrome symptoms [10]. The lesions associated with posterior eyelid inflammation resemble the ocular manifestations observed in rosacea, leading to the understanding that these lesions represent the ophthalmic expression of the disease or its localized precursors [11].

The role of demodex in the etiopathogenesis of eyelid rim inflammation

Demodex, a microscopic mite that lives on human skin and eyelashes, has been identified as an important contributor to some forms of eyelid inflammation. Demodex folliculorum longus (in anterior eyelid rim inflammation) and Demodex folliculorum brevis (in posterior eyelid rim inflammation). The mites feed on sebum and epithelial cells lining the hair follicles and Meibom's glands, respectively. In large numbers, Demodex can lead to mechanical blockage of the openings of the Meibom's glands, as well as an inflammatory response to their presence and associated bacterial proliferation. It is noteworthy that the incidence of Demodex infestation increases with age and may be an important contributor to the development of posterior eyelid inflammation in the elderly. Elimination of the Demodex mite was associated with amelioration of symptoms in patients with treatment-resistant eyelid margin inflammation [12].

Conditions associated with chronic inflammation of the eyelid margins

Unstable pre-corneal tear film and dry eye syndrome occur in about 30-50% of patients and are associated with an imbalance between the aqueous and lipid components of the tear film, leading to excessive evaporation of tears from the ocular surface. Multiple or recurrent chalazions often accompany posterior blepharitis. Corneal epithelial diseases and recurrent corneal epithelial erosions can be exacerbated by posterior eyelid margin inflammation. Skin diseases such as rosacea, seborrheic dermatitis and acne vulgaris can also be associated with eyelid rim inflammation. Bacterial keratitis is associated with diseases of the surface of the eye, which can develop secondary to chronic eyelid rim inflammation. Allergic conjunctivitis and keratitis often coexist with staphylococcal eyelid rim inflammation. Long-term contact

lens wear can cause posterior eyelid margin disease, potentially due to inhibition of eyelid movement or effects on normal secretion by Meibom's glands. Eyelid margin inflammation significantly affects the incidence of bacterial keratitis associated with contact lens wear. Abnormal growth and loss of eyelashes can also be observed as pathology coexisting with eyelid margin inflammation.

Diagnostics

Symptoms

Subjective and physical symptoms that may be reported by patients with eyelid margin inflammation include redness, swelling, and irregular thickening of the eyelid margins, often accompanied by shedding of scales, crusts, debris at the base of the eyelashes [13] [14] [6], irritation, burning, tearing, itching, scaly eyelids, eyelid sticking, intolerance to contact lenses, photophobia, and increased blinking frequency. Anterior blepharitis is often associated with staphylococcal infection or seborrheic dermatitis, while posterior blepharitis is primarily linked to Meibomian gland dysfunction [6][15][14]. Clinicians should inquire about the timing of symptom exacerbation, the duration of the condition, whether one or both eyes are affected, and any circumstances that worsen the condition. Additionally, information about current and previous general and topical medications, such as antihistamines and those with anticholinergic effects, as well as the patient's ophthalmic history, including any surgeries, trauma, or presence of chalazia, should be obtained.

Physical examination

The initial ophthalmological examination should begin with visual acuity, in the best possible correction and measurement of intraocular pressure. This should be followed by a thorough evaluation of the skin of the cheek area, forehead, nose, chin and possibly other involved areas. The slit-lamp examination evaluates the tear film, the anterior margin of the eyelids, the eyelashes, the posterior margin of the eyelids after eyelid inversion, the condition of the conjunctiva and the cornea.

Additional examinations

Cultures may be indicated in patients with recurrent inflammation and severe inflammation, and in those who do not respond to treatment. Obtaining cultures from the eyelid margins is recommended. Microscopic analysis of the eyelashes can detect the presence of Demodex mites [16]. An eyelid biopsy to rule out cancer may be indicated in cases of highly asymmetrical lesions, refractory lesions, and recurrent chalazions in one location that do not respond well to treatment. When sebaceous gland cancer is suspected, consultation with a pathomorphologist is indicated.

Subsequent medical assessments

The subsequent medical assessment should encompass: obtaining an updated history since the last appointment, conducting visual acuity testing, performing an external examination, and carrying out a biomicroscopic evaluation. If corticosteroid therapy has been prescribed, the patient should be re-evaluated in a few weeks to determine the clinical response to treatment, measure intraocular pressure, and assess the patient's adherence to the prescribed regimen.

Long-term targets

Advise the patient about the chronic and recurrent character of the condition. Convey that, while the severity of symptoms can often be mitigated, complete resolution is uncommon. Patients presenting with eyelid inflammatory lesions that raise concern for potential neoplastic processes should be referred to the appropriate medical specialists for further assessment and management.

Prevention and non-pharmacological management: Consistent implementation of eyelid hygiene routines, undertaken on a daily or multi-weekly basis, commonly mitigates the symptoms of persistent eyelid margin inflammation [17]. Eyelid margin inflammation is more common in people who have struggled with the condition in the past, which is why daily eye hygiene is so important [18]. Management of eyelid margin inflammation involves maintaining proper eyelid hygiene. This includes applying warm compresses to the eyelids, massaging the lids to express pathological secretions from the Meibomian glands, and mechanically cleaning the eyelid margins using a cotton swab soaked in a dilute shampoo solution or specialized eyelid hygiene wipes [3]. Patients can perform a massage perpendicular to the eyelid margin to express Meibomian gland secretions. Additionally, rubbing the eyelids along the margin helps remove any dried secretions that have accumulated

on the eyelashes. Applying warm compresses and massaging the eyelids once or twice a day, at a convenient time for the patient, is usually satisfactory. Expressing the contents of the Meibom's glands can be particularly beneficial, but should be done carefully. Long-term use of warm compresses in conjunction with eyelid cleansing is recommended, as discontinuation of treatment can lead to recurrence of symptoms. For individuals who wear makeup, it is recommended to thoroughly remove it before going to bed. Patients are advised to refrain from using makeup, as this practice can contribute to the development and recurrence of eyelid margin inflammation [19]. Applying eyeliner within the eyelid margin should be avoided. Sharing cosmetic products with others is inadvisable, as this can contribute to the spread of bacteria. Patients with a history of eyelid margin inflammation should refrain from using the same eye makeup cosmetics that were utilized before or during the infection, as this may lead to recurrence of the condition [20]. The optimal course of action is to properly discard the old makeup products and replace them with new ones.

Research examining the efficacy of oral omega-3 fatty acid supplementation in patients with moderate to severe anterior blepharitis found no significant beneficial impact on eyelid margin inflammation. However, common clinical practice recommends omega-3 fatty acid supplementation in eyelid margin inflammation. The proposed rationale is that omega-3 fatty acids may help reduce the inflammatory response, though this has not been conclusively supported by high-quality evidence [1][21][6].

Pharmacological management: The duration, intensity of therapy should be considered individually based on the severity of inflammation and the response to the implemented treatment. Common pharmacotherapy includes topical antibiotics in the form of ointments (bacitracin, erythromycin, chloramphenicol) and steroid preparations in the form of drops and artificial tear preparations. Topical antibiotics can help reduce the bacterial load on the eyelid margin associated with blepharitis [1][21]. In selected cases, oral antibiotic therapy should be prescribed. Oral doxycycline(50-100mg twice a day for a week and then once a day for 6-24 weeks), other tetracyclines and azithromycin(500mg/day for 3 days, 3 cycles at weekly intervals) may be ordered. They are intended not only to have a bactericidal effect, but also, as in the case of tetracyclines, to reduce the secretion of staphylococcal lipases. It is believed that the use of azithomycin is more effective in the anterior form of eyelid rim inflammation. Topical corticosteroid preparations are often useful in managing more severe or recalcitrant

cases of eyelid margin inflammation, as they can help reduce inflammation [21]. Prolonged use of topical corticosteroids, however, carries the risk of developing ocular hypertension and glaucoma, so their use should be reserved for short-term management of particularly severe inflammation [22] [23] [21] [6]. It is worth mentioning that there are reports of a lack of conclusive evidence regarding the effectiveness of eyelid margin inflammation therapy, such as topical corticosteroid therapy or oral antibiotic therapy [24]. Artificial tear products can help alleviate the symptoms of dryness and discomfort associated with eyelid margin inflammation [23] [25] [22] [21]. Topical cyclosporine and/or insertion of punctal plugs may assist in addressing a concurrent deficiency in the aqueous layer of the tear film [26]. A study examining individuals with meibomian gland dysfunction found that the group treated with topical cyclosporine 0.05% experienced a decrease in the number of blocked meibomian gland openings after 3 months, although there was no statistically significant improvement in subjective symptoms [27].

Summary: Blepharitis is a chronic, multifactorial ocular condition affecting both pediatric and adult populations. It is characterized by inflammation of the eyelid margins, which can result from various factors including bacterial infections, Meibomian gland dysfunction, or allergic reactions. The disease can be classified into distinct subtypes: anterior, posterior, and mixed. Patients with blepharitis commonly experience symptoms such as itching, burning, eyelid redness, foreign body sensation, tearing, and occasionally, visual disturbances. In some instances, cutaneous changes like peeling of the eyelid epidermis may also occur. Diagnosis is primarily based on comprehensive physical examination and observation of clinical signs, occasionally supplemented by microbiological testing. The management of eyelid margin inflammation involves a combination of daily eyelid hygiene practices, pharmacological interventions, and for Meibomian gland dysfunction, the use of warm compresses and eyelid massage. In select cases, lubricating eye drops may be incorporated to alleviate dry eye symptoms. Eyelid margin inflammation represents a chronic and recurrent condition that necessitates long-term management. Emphasizing patient education and close collaboration between the patient and healthcare provider is crucial to effectively control symptoms and prevent potential complications.

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Statement of the authors' contribution

Grzegorz Szcześniak: Conceptualization, Writing-rough preparation

Aleksandra Kiełczewska: Methodology, Investigation Resources

Anna Kiełczewska: Formal analysis, Visualisation, Writing-review and editing

All authors have read and approved the published version of the manuscript.

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11

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