УДК:617.77-002:616-056.3]-06-07 DOI: 10.31655/2307-3373-2024-4-66-72

BLEPHARITIS — ALLERGIC AND NOT ONLY

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Abstract. Blepharitis is a very common disease in ophthalmology, dermatology, and allergist practice. It can be acute or chronic. Acute blepharitis is most often caused by viruses (Herpes simplex and Varicella zoster) and bacteria (Staphylococcus). Chronic blepharitis is a symptom of allergies, metabolic syndromes most often associated with liver disease, autoimmune diseases, fungal infections, and Demodex. The liver is a vital organ that supports immunity, metabolism, digestion, stores vitamins, and is responsible for detoxification. Therefore, liver dysfunction can also cause skin lesions around the eyes. Stress, through the activation of the pituitary-hypothalamic-adrenal system, promotes cell activation and the release of biologically active cytokines, which in turn is a factor in skin damage. Clinically, blepharitis is manifested by redness, itching, and swelling of the eyelids, sometimes the formation of scales on the eyelids. As a rule, both eyes are affected and the disease has a recurrent course. In most cases, blepharitis does not pose a threat to the patient's life, but it reduces the quality of life and is dangerous for the development of such complications as conjunctival lesions and the formation of corneal marginal ulcers.
The article presents clinical cases of patients with chronic blepharitis who had similar symptoms but differed in etiology and treatment regimens.

Key words: blepharitis, contact dermatitis, toxic blepharitis.

Blepharitis is an acute or chronic inflammation of the eyelids that is one of the most common reasons for visiting an ophthalmologist. Usually both eyes are affected. The eyelid edges become red, swollen, and scales appear. Patients often complain of itchy skin around the eyes [9]. In most cases, this disease is not life-threatening, but it can cause superficial keratopathy, corneal ulceration, and neovascularization. Blepharitis affects all age and ethnic groups [12].

Blepharitis is divided into anterior and posterior. Anterior blepharitis is a lesion of the eyelid margin with eyelashes. It is most often caused by a staphylococcal infection, which is manifested by plaque on the eyelashes, eyelash loss, and improper growth. In rare cases, eyelid ulceration, hard scales, corneal changes (erosion, infiltrates, scars, neovascularization and pannus, thinning, flictenules) are observed. Seborrheic blepharitis is manifested by the presence of scales on the eyelids, conjunctival injection and erosion. Changes in eyelashes are not common. Posterior blepharitis is a lesion of the meibomian glands located deep in the eyelids (meibomian blepharitis). It is often associated with rosacea [14].

Allergy is one of the main causes of blepharitis. Most often, it is a contact allergy to the ingredients of decorative (mascara, concealer, foundation) and care cosmetics (day and evening moisturizers), glue and degreaser after eyelash extension, household, pollen, and food allergens [11]. A frequent complication of allergic blepharitis is candidiasis (Malassezia and Candida), which does not allow for long-term remission of allergies without specific treatment [2; 12]. Blepharitis is also caused by autoimmune diseases, liver and gallbladder dysfunction, and diamine oxidase deficiency.

Malassezia is a type of saprophyte that may play a role in the development of chronic blepharitis. Malassezia is found on the skin of 90 % of the world's population [2]. But with a decrease in immunity, atopic dermatitis, irrational use of systemic or topical glucocorticoids, antibiotics, they begin to multiply actively, causing skin diseases. The irritating effect is not the fungi themselves, but their metabolites.

To date, no clear mechanism has been identified for the skin lesions around the eyes and diseases of the hepatobiliary system. However, some studies have been conducted that show a link between liver, intestinal, lung dysfunction, vascular endothelial damage and

skin lesions [8]. The liver is an important organ of our body involved in various metabolic processes related to detoxification. Liver dysfunction activates pro-inflammatory cytokines and the development of dermatitis. Also, hypercholesterolemia is associated with liver dysfunction and the production of cytokines (interleukin-1, interleukin-6 and TNFα) leads to the development of inflammation and skin lesions [5; 7].

Stress is a trigger for the development of many diseases and causes exacerbation of chronic diseases. The mechanism linking stress and atopic dermatitis or blepharitis is not well understood today. However, the activation of the hypothalamic-pituitary-adrenal system and the sympathetic nervous system results in the release of hormones and peptides that bind to the corresponding receptors on cells through a number of pathways. The release of inflammatory factors (IL-1, IL-4, IL-5, IL-6, IL-18, and TNF) contribute to skin inflammation and affect skin repair [9]. Also, the expression of epidermal antimicrobial peptides decreases, which leads to increased sensitivity to infectious agents and increased water loss. Neuroendocrine factors can promote the production of cytokines and other effector molecules by interacting with resident cells and skin immune cells, ultimately resulting in damage to the skin barrier.

At the moment, the role of diamine oxidase in the development of urticaria, rhinitis, bronchial asthma, or even blepharitis is still under debate. Diamine oxidase is an enzyme that breaks down histamine and makes it safe for humans. In case of its deficiency, histamine intolerance develops, which can be clinically manifested not only by urticaria and abdominal pain, but also by headaches, tachycardia, hypotension, bronchospasm, rhinitis, sleep disturbance, and increased irritability. Very often, histamine is associated only with an allergic reaction, but this is not entirely true. Histamine's role in the body is to provide an immediate inflammatory response, alerting your body to any potential threats [2]. Histamine causes blood vessels to dilate so that white blood cells can quickly find and attack an infection or allergen – this is part of the natural immune response. Histamine is a neuroregulator, vasoactive substance, immunomodulator, biologically active inflammatory substance that has both pro-inflammatory and anti-inflammatory effects, and is involved in the process of digestion and the development of allergic reactions [1]. Histamine is produced in our body from an amino acid (histidine) and is stored in basophils and mast cells. Some bacteria in the human intestine are also capable of producing histamine. This biologically active substance enters our body with food. Histamine liberators are foods that contain a large amount of histamine or stimulate the body's cells to release histamine. They include: seafood, berries, fermented foods (cheese, wine, pickled vegetables), fish, citrus fruits, kiwi, coffee and strong tea, freshly prepared juices. Caffeinated beverages, energy drinks, and alcohol can block the activity of diamineoxidase.

Over the past year, 29 patients with signs of blepharitis, 26 of whom were women, visited our clinic. After a thorough history and additional examinations, it was found that the most common cause of blepharitis was allergy, which was diagnosed in 18 patients. In seven patients, it was the first episode of blepharitis. Two of them developed symptoms after eyelash lamination, and three patients developed symptoms after using decorative cosmetics. Twenty-two patients had symptoms of blepharitis not for the first time. Some patients also had complaints of nasal breathing disorders or urticaria, cough. Seventeen patients were found to be hypersensitive to pollen and household allergens, and had a history of allergic rhinitis, urticaria or atopic dermatitis with sensitization to pollen and household allergens. Four patients were diagnosed with non-infectious diseases of the liver and gallbladder, which caused blepharitis. In one patient, swelling of the upper eyelids and redness were caused by papillary thyroid cancer. Infection was the cause of chronic blepharitis in four patients.Eleven patients sought consultation with an ophthalmologist or dermatologist and received symptomatic treatment with a temporary effect. To reduce symptoms, they received recommendations to use H1-receptor blockers, systemic and topical glucocorticoids. However, some patients treated the disease on the advice of a pharmacist or friends.

Patients who had acute manifestations of blepharitis after eyelash lamination and use of decorative cosmetics are recommended to undergo treatment and patch testing to determine the cause of the complication [5; 6]. In this case, blepharitis can be caused by both contact allergy and irritation from chemicals. The irritation should decrease in 24–48 hours after the procedure, but if it is an allergy, the symptoms will increase. Clinical manifestations of blepharitis can last from several days to even several weeks, as some chemicals are excreted from the hair. One patient had a history of allergic rhinitis with sensitization to birch and timothy allergens, which could be a negative factor in the development of blepharitis [9].

ISSN 2307-3373

Photo 1
Blepharitis in the acute stage with scales on the upper eyelid

Photo 2
Blepharitis in partial remission with redness around the eyes

Clinical case 1

Patient N., aged 19 years, consulted an allergist with complaints of redness and itching, peeling of the skin of the upper eyelids (photo 1 and 2). To reduce the symptoms, she took citirizine in the morning and chloropyramine in the evening for several days, and applied methylprednisolone ointment to the upper eyelid and skin around the eyes in the evening. During the first days of treatment, the condition of the skin around the eyes improved, but after a week, the redness and peeling of the skin increased. From the anamnesis, it is known that this is not the first episode of the disease, but this time she notes a greater intensity of symptoms.Complaints first appeared at the age of 17 after a severe viral infection and antibiotics. Symptoms decreased after taking second-generation H1 receptor blockers and topical corticosteroids for short courses (5–7 days). There were no allergic reactions to household, pollen or food allergens. This exacerbation may be associated with the consumption of strawberries and citrus fruits. During the examination of the patient, we note a slight swelling, redness and dryness of the skin of the upper eyelid. There are also crusts on the scalp. The clinic performed a diagnostic examination of the scalp with a Wood's lamp and found that the crusts were highlighted in green. The results of this examination may indicate a fungal infection.

To confirm the diagnosis before starting treatment, the patient was recommended additional laboratory tests: determination of the level of total immunoglobulin E, specific immunoglobulin E to Malassezia spp, diamine oxidase, eyelid scraping and microscopic examination. To reduce the symptoms of blepharitis, the patient was recommended to follow a diet excluding histamine liberator products, long-acting H1-blockers (fexofenadine hydrochloride 120 mg twice daily), emollients on the upper eyelid and around the eyes, not to use topical corticosteroids, and consult an ophthalmologist before receiving the examination results.

Having received the results of the examination, we confirmed the diagnosis of fungal skin lesions of the eyelids and scalp, and also found a reduced level of diamine oxidase. The treatment regimen included clotremazole in the form of a cream for topical treatment and as part of shampoo, emollients, antihistamines, probiotics and a diet excluding histamine liberators. At the follow-up consultation in 7 days, the condition of the skin around the eyes was satisfactory, no itching.

Clinical case 2

A 61-year-old female patient complained of redness around the eyes and upper eyelid, swelling of the eyelid and under the eyes. Complaints for 3 days. The patient had a history of similar symptoms twice during the year. To reduce the symptoms, she used moisturizers and H1 receptor blockers. The patient also complains of constipation, indigestion, increased gas formation, and a bitter taste in the mouth. Objectively, we note redness and peeling of the skin around the eyes, cracks in the corner of the left eye (photo 3 and 4). The tongue is covered with a white coating. The abdomen is soft to palpation, slightly painful. There was no history of allergic reactions.

Consultation with an ophthalmologist, gastroenterologist, ultrasound examination of the abdominal cavi-

ISSN 2307-3373

Photo 3
Swelling of the upper eyelid and skin around the eyes, skin discoloration

Photo 4
Redness and swelling of the skin around the eyes

ty and thyroid gland are recommended. Laboratory tests: complete blood count, biochemical blood test (liver and kidney tests), C-reactive protein, total immunoglobulin E, eosinophilic cationic protein. To reduce the symptoms, emollients around the eyes, long-acting H1 receptor blockers (levocytirizine) in the morning for 10 days and first-generation blockers (hifenadine) in the evening for 5 days. The results of the examination of patient G. are presented in the table 1.

Table 1. Results of the patient's examination G.

Examination	Result
Complete blood count	N
Biochemical blood test	Gamma-glutamyltransferase – 64 IU/l↑ Direct bilirubin – 7 μmol/l Uric acid – 420 μmol/l↑ C-reactive protein – 4 mg/l
IgE	27mIU/ml
Eosinophilic cationic protein	18 ng/ml
Ultrasound examination of abdominal organs and thyroid gland	Thickening of the gallbladder wall (6 mm), bile "sludge". Increase in the size of the pancreas.
Consultation of ophthalmologist	No signs of acute infectious eye disease detected
Consultation of gastroenterologist	Chronic cholecystitis and pancreatitis in the acute stage

After receiving the results of the examinations and consultations, the patient was recommended second-generation H1-receptor blockers (fexofenadine) for 14 days, emollients to reduce redness and moisturize the skin of the upper eyelid, and treatment of chronic cholecystitis. At the follow-up visit, the patient's skin condition improved. The swelling has decreased. Currently, there are no clear markers of the interaction between liver function and skin lesions, but in some patients, cholecystitis or liver dysfunction causes exacerbation of not only chronic urticaria, atopic dermatitis, but also blepharitis.

Clinical case 3

Patient O, 26 years old, came to the clinic with complaints of redness, itching and swelling of the skin around the eyes, increased dryness of the skin, redness, flaking and itching of the skin on the skin of the upper extremities (photo 5, 6 and 7). Periodic nasal breathing disorders at night and in the morning. From the anamnesis, it is known that the patient has had skin rashes and itching on the hands for about 4 years, but the skin of the face and upper eyelids was affected for the first time. She used hormone-containing creams and emollients to reduce the redness and itching of the skin on her hands. A few months ago, she changed her place of residence and felt a deterioration in her health

Objectively, swelling of the eyelids and skin around the eyes, rashes on the upper extremities were detected. Nasal breathing was difficult.

ISSN 2307-3373

Photo 4
Redness and swelling of the skin around the eyes (exacerbation)

Photo 4
Redness and swelling of the skin on the right hand (atopic dermatitis)

Photo 5
Redness of the skin on the right hand (atopic dermatitis)

To establish the diagnosis, the patient underwent laboratory (complete blood count, liver and kidney tests, C-reactive protein, total immunoglobulin E, ImmunoCAP Eczema, diamine oxidase) and instrumental (ultrasound of the abdominal cavity and thyroid gland) examinations, and an ophthalmologist consultation. The results of the examinations are presented in Table 2.

Hypersensitivity to allergens of house dust mites and dog hair is the cause of skin lesions and nasal breathing disorders in the patient. To date, the mechanisms of damage to the skin of patients by house dust mite allergens are not known, but many studies have been conducted to prove their relationship.

Contact or inhalation through the respiratory tract and activation of pro-inflammatory cytokines are possible mechanisms of injury [8]. During the period of remission, skin tests with household allergens were performed and allergy to house dust mites was confirmed. For a year, the patient has been receiving allergen-specific immunotherapy with house dust mite allergens with a good clinical effect.

Table 2. Results of the patient's examination O.

Examination	Result
Complete blood count	N
Biochemical blood test	No changes
Kidney tests	No changes
C-reactive protein	8.2 mg/l ↑↑
Total IgE	365 MO ↑↑
ImmunoCAP "Eczema"	Der.p – 79 IU/ml ↑ (house dust mite allergen), Can. f – 53.8 IU/ml ↑ (dog hair allergens)
Diamine oxidase	14.8 U/ml

Conclusions

Blepharitis is a common reason for patients to seek medical care from an ophthalmologist, dermatologist or allergist. Symptoms can occur in patients of any age. Blepharitis does not pose a threat to the patient's life, but it negatively affects the quality of life and can lead to visual impairment. Dermatitis should be treated by a team of doctors consisting of an ophthalmologist, allergist, general practitioner and gastroenterologist. Determining the cause of blepharitis, prescribing treatment and teaching the patient to take care of their eyes, and controlling chronic diseases will help prevent recurrence of inflammation.

ISSN 2307-3373

БЛЕФАРИТ – АЛЕРГІЧНИЙ І НЕ ТІЛЬКИ

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Резюме. Блефарит — поширене захворювання в офтальмології, дерматології та у практиці алерголога. Воно може бути гострим або хронічним. Причиною гострого блефариту найчастіше є віруси (*Herpes simplex* та *Varicella zoster*) та бактерії (рід *Staphylococcus*). Хронічний блефарит є симптомом алергії, метаболічних синдромів, пов'язаних найчастіше із хворобами печінки та цукровим діабетом, автоімунних хвороб, грибкових інфекцій та паразитичних кліщів роду *Demodex*. Печінка є життєво важливим органом, який підтримує імунітет, метаболізм, травлення, зберігає вітаміни та відповідає за детоксикацію. Отже порушення її роботи також може бути причиною ураження шкіри навколо очей. Стрес, через активацію гіпофізарно-гіпоталамус-наднирникової системи, сприяє активації клітин та викиду біологічно активних цитокінів, що в свою чергу є фактором ураження шкіри.
Клінічно блефарит проявляється почервонінням, свербежем та набряком повік, інколи спостерігається утворення лусочок на повіках. Як правило, уражаються обидва ока і хвороба має рецидивний перебіг. У більшості випадків блефарит не несе загрозу для життя пацієнта, однак знижує якість життя, небезпечний розвитком таких ускладнень як ураження кон'юнктиви ока та утворення крайових виразок рогівки.
В статті представлено клінічні випадки пацієнтів із хронічним блефаритом, що клінічно мали подібну симптоматику, однак відрізнялись за етіологією та схемами лікування.

Ключові слова: блефарит, контактний дерматит, токсичний блефарит, атопічний блефарит.

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Цитування: Беш ОМ, Сорокопуд ОО, Гук-Лешневська ЗО, Зенін ВВ. Блефарит — алергічний і не тільки. Астма та алергія. 2024;4:66–72. DOI: 10.31655/2307-3373-2024-4-66-72.

Cited: Besh OM, Sorokopud OO, Guk-Leshnevska ZO, Zenin VV. Blepharitis — allergic and not only. Asthma and allergy (Ukraine). 2024;4:66–72. DOI: 10.31655/2307-3373-2024-4-66-72. Ukrainian.

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Надійшла до редакції / Received: 20.09.2024 р.
Прийнято до друку / Accepted: 21.10.2024 р.

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