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# RECURRENT PTERYGIUM – FEATURES OF SURGICAL TREATMENT

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✧ Pterygium is a fibrovascular degenerative condition of the subconjunctival tissue that proliferates and grows into the cornea in the form of a vascularized fold, destroying the surface layers of the stroma and Bowman's membrane. This disease is common throughout the world. The etiology is not clear, but it is known that the appearance of pterygium is associated with exposure of the eye to ultraviolet rays. The treatment of the de novo occurring pterygium is a relatively simple task and involves surgical removal. But a simple excision is currently unacceptable due to the high recurrence rate. In order to minimize the risk of relapse, numerous adjuvant treatment methods are used, which include anti-metabolites such as Mitomycin C and 5-fluorouracil, amniotic membrane, various types of conjunctival and or limbal grafts; medications such as anti-vascular endothelial growth factor are sometimes used. In the clinical case presented in the article, we successfully used the technique of anterior lamellar keratoplasty and auto-conjunctival transplantation in combination with intra-operative use of anti-metabolite Mitomycin C in a young patient with recurrent stage IV pterygium (degree of activity 3) twice unsuccessfully operated on. As a result of this surgical technique, the transparency of the cornea was restored and high visual acuity was obtained.

✧ ***Keywords:*** pterygium; recurrent pterygium; lamellar keratoplasty; keratoplasty; Mitomycin C; lubricants; antiseptic.

# РЕЦИДИВИРУЮЩИЙ ПТЕРИГИУМ — ОСОБЕННОСТИ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ

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✧ Птеригиум — фиброваскулярное дегенеративное состояние субконъюнктивальной ткани, которая пролиферирует и в виде васкуляризированной складки врастает в роговицу, разрушая поверхностные слои стромы и боуменовой мембраны. Это заболевание распространено во всем мире. Этиология точно не выяснена, но известно, что появление птеригиума связано с воздействием на глаза ультрафиолетовых лучей. Лечение первично возникшего птеригиума является относительно несложной задачей и включает хирургическое удаление. Но простое иссечение в настоящее время неприемлемо из-за высокой частоты рецидивов. Чтобы свести к минимуму риск рецидива, применяются многие вспомогательные методы лечения, включая антиметаболиты, такие как Митомицин-С и 5-фторурацил, амниотическую мембрану, различные вариации конъюнктивальных и/или лимбальных трансплантатов; иногда используются лекарственные препараты, такие как антисосудистый эндотелиальный фактор роста. В клиническом случае, приведённом в статье, мы с успехом использовали технику

передней послойной кератопластики и аутоконъюнктивальной трансплантации в сочетании с интраоперационным применением антиметаболита Митомицина-С у молодого пациента с рецидивирующим птеригиумом IV стадии (3-й степени активности) дважды безуспешно оперированным. В результате данной хирургической методики у больного восстановлена прозрачность роговицы и получена высокая острота зрения.

✧ ***Ключевые слова:*** птеригиум; рецидивирующий птеригиум; послойная кератопластика; кератопластика; Митомицин-С; лубриканты; антисептик.

## INTRODUCTION

Pterygium is a fibrovascular degenerative condition of subconjunctival tissue which proliferates and grows into the cornea as a vascularized fold, destroying surface layers of the stroma and Bowman membrane, while remaining generally covered with conjunctival epithelium. The pterygium is weakly adhered along its entire length to the underlying sclera, while the area of adhesion is always less than its width, such that there are folds on the upper and lower borders. In pterygium, there are several parts: the head (top of a lump), which is attached to the cornea with many vessels; the cervix thinning between the head and body; and the body, which is a "fleshy" thumb [1]. On the cornea with an active growth of subconjunctival tissue, Fuchs' flecks, which are subepithelial grayish calcification nodules around the head of the pterygium can be found. A well-visible brown Stocker's line in the cornea saturated with iron from lactoferrin out of tears appears, as a rule, with a slowly growing pterygium [2, 3].

A global study of pterygium incidence by M.E. Cameron found a link between the level of prevalence and proximity to the equator, the "pterygium belt." In countries located at 120$^{th}$ latitude, this level reaches 22–25% compared to 2% in areas located above the 40$^{th}$ parallel [4]. Pterygium occurs twice as often in men and people whose profession involves a long stay outside such as farmers, rescuers, and sailors. It has been proven that the prevalence of this disease is most predominant in the elderly, but its onsets occur more often at the age of 20 to 40 years [5]. The exact etiology of pterygium has not been clarified; however, it is known that this condition is related to the effect of infrared and ultraviolet rays on the surface of the eyes [6, 7]. This effect can lead to mutations in p53 gene (*TP53*), whose protein normally suppresses cell cycle of epithelium in the limbus. On the other hand, there are evidences that in pterygium progression and recurrence a high level of p53 protein expression (*TP53*) may be found. Apparently, these laboratory findings contradict the presence of a rapidly growing pterygium [8]. Sometimes, degeneration develops with prolonged inflammation of the conjunctiva; however, some researchers range pterygium between elastodisplasias or elastodystrophias [9–11]. Some authors associate the development of pterygium with deficiency of limbal stem cells and their morphological changes [12].

Pterygium can range from small atrophic nonprogressive damages to large "aggressive" and rapidly growing fibrovascular formations that can lead to an expressed change in corneal topography and, in advanced cases, can grow on the optical center of the cornea, leading to significant deterioration in visual functions. An imbalance of matrix metalloproteinases leads to active growth of basal epithelial cells of the limbus, which destroys the Bowman membrane, and consequently tightly adhere to the surface of the cornea [13].

Nowadays, there is no unified classification for this degenerative condition of the conjunctiva. Pterygium is usually evaluated morphologically, that is, by its tendency to progress as well as by the state of the episcleral vessels. The most common international classification is as follows: Grade 1 (no data on progression, pterygium is transparent, atrophic, and vessels of the episclera are clearly visible through it); Grade 2 (progression is possible, pterygium is semi-transparent, protruding, and vessels of the episclera are partially visible); Grade 3 (active progression, pterygium is fleshy, opaque, and episcleral vessels are not visible) [5].

In the Russian Federation, in clinical practice, ophthalmologists most often use a convenient classification proposed by Z.D. Titarenko et al. [14], in which pterygium is divided into five stages, depending on its topography and visual functions [14].

Grade I – when the outgrowth is observed only at the limbus, usually without changes in visual acuity or refraction.

Grade II – when the head of the pterygium is located in the middle of the distance between the

limbus and the projection of the edge of the moderately dilated pupil. This stage is characterized by the appearance of an irregular astigmatism in the area immediately in front of the head of the pterygium and; in the optical area, a low degree regular astigmatism is detected. Visual acuity can be reduced to 0.9–0.7.

Grade III – when the head of the pterygium is located on the cornea at the projection of the margin of the normal diameter pupil. At this grade, due to flattening of the horizontal meridian of the cornea astigmatism reaches 1–3 diopters, and visual acuity can decrease to 0.5.

Grade IV – when the head reaches the center of the cornea (projection of the center of the pupil), significant irregular or regular astigmatism (2.5–7.5 diopters) prevails. Visual acuity is reduced to 0.3–0.2.

Grade V – when the head of the pterygium goes beyond the center of the cornea and can spread further along the cornea. In this case, refraction cannot be determined and visual acuity is below 0.1.

Foreign researchers have recently proposed a classification for assessing the severity of pterygium using corneal topography data [15]. At the onset of the disease, there may be no complaints, or patients are concerned about periodic redness and irritation of the eye. In these cases, as well as in absence of pterygium progression, treatment is conservative. Long-time instillation of lubricants and wearing sunglasses are prescribed. With progression of the disease, deterioration of visual functions, and appearance of astigmatism, especially for young patients, most ophthalmologists currently adhere to surgical treatment option [3, 16–18]. Despite the fact that this disease has been known for thousands of years, no adequate, and unambiguous surgical treatment has been developed. An excellent and comprehensive review of literature by S.V. Trufanov et al. [2], in 2017, demonstrated a wide variety of surgical methods and reported successes of modern pterygium surgery. Simple excision of the pterygium head is currently unacceptable due to high frequency of relapses (up to 89%) [17–19]. It is believed that surgical trauma and subsequent postoperative inflammation activates proliferation of fibroblasts and capillaries in the subconjunctiva, as well as deficiency of limbal stem cells which, in turn, contributes to the recurrence of pterygium [13]. Re-orientation of the pterygium head away from the cornea is not currently used due to high frequency of relapses. After pterygium removal, the conjunctival defect can be left, as in the "naked" sclera method, or a bulbar autoconjunctiva on the pedicle or without it can be used to cover the area of excision of the conjunctival tissue. For the same purpose, amniotic membrane is used; and in the past years, new bioengineering materials have been actively studied in animal models. Biodegradable implants with collagen matrix are porous scaffolds that can stimulate wound healing without regeneration and without use of additional medications, which is promising for the prevention of pterygium relapses [14, 20].

In case of relapse and after several "standard" methods of surgical pterygium treatment, lamellar keratoplasty with corneal periphery involvement is recommended [3]. Given that the main objective in pterygium surgery is to avoid relapse, actively developed auxiliary methods of treatment are very relevant. During and after surgery, nowadays, treatments used include antimetabolites (Mitomycin-C, 5-fluorouracil), antiVEGF drugs, matrix metalloproteinase inhibitors (doxycycline, azithromycin) and beta-radiation [2, 19, 21–24].

## A CLINICAL CASE

In October 2019, a 27-year-old man come to the Ophthalmology clinic of the Academician I.P. Pavlov First St. Petersburg State Medical University with complaints of mild foreign body sensation in both eyes, more in the left eye, as well as a of gradual decrease in visual acuity and periodic redness of the left eye. Case history revealed that, in 2014, he first noticed a "white film" on his right eye. A few months later, similar complaints and symptoms appeared on his left eye. The patient repeatedly consulted an ophthalmologist at his out-patient polyclinic, he was diagnosed with pterygium of both eyes and referred for surgical treatment in one of the medical institutions of Saint Petersburg. On the right eye, in 2014, pterygium excision was performed; in 2016, two surgeries (sequentially after 3–4 months) took place including pterygium removal from nasal and temporal sides and amniotic membrane transplantation. On the left eye, in 2016, pterygium was removed and amniotic membrane transplantation was done; in 2017, pterygium removal was repeated. Therefore, there were three surgeries on the right eye and two on the left eye. At the same time, complaints of redness of the eyes and steady gradual bilateral decrease in visual acuity persisted.

From 2017 to 2019, the patient was not treated anywhere. At the time of contacting our clinic in October 2019, the visual acuity of the right and the left eye was 0.7 and 0.5, respectively, no correction was possible. Following changes were detected at biomicroscopy. Right eye: palpebral fissure of normal width, no restriction of ocular motility; from the nasal side, opaque fleshy tissue with large number of vessels growing on the cornea, which reaches the optical area with limbus involvement from 6 to 11 hours, and from the nasal side, Stocker's line indistinctly visible was detected (Fig. 1). Left eye: palpebral fissure of normal width, no restriction of ocular motility; from nasal and temporal sides, semi-transparent tissue with large number of vessels growing on the cornea from 7 to 11 hours and from 1 to 4 hours, which reaches the projection of the pupillary margin, and Stocker's line indistinctly visible at the pupil margin on the nasal side (Fig. 2). In the other parts of both eyes, conjunctiva is not irritated, lens and vitreous are transparent, and at the fundus, there are no pathological changes. The patient was offered surgical treatment, but was admitted only in January 2020 due to family circumstances. For two months, visual acuity significantly worsened due to the pterygium progression (Fig. 3): visual acuity of the right eye was 0.2, no correction was possible, visual acuity of the left eye was 0.08 with spherical correction 0.1; IOP of the right eye was 14 mm Hg and that of the left one was 12 mm Hg. IOP was measured using iCare device. The established diagnosis was: Both eyes: recurrent pterygium (RE operated three times, LE operated twice) stage IV (according to classification of Z.D. Titarenko et al. [14]) and Grade III (according to the classification of D. Tan) pterygium.

Surgery carried out on the left eye: pterygium excision with anterior lamellar keratoplasty and autoconjunctivoplasty. The course of the surgery was as follows: Standard treatment of the operation area, akinesia with 2% lidocaine solution (4.0 ml), epibulbar anesthesia, and injection of 2% lidocaine solution into the body of the pterygium. Using a circular delaminator, the pterygium tissue was separated from the cornea and episclera throughout. Hemostasis was done using a thermocoagulator. Lamellar keratectomy (depth = 180 microns) was performed using Moria microkeratome oin the optical zone, with a diameter of 8.4 mm. For corneal transplantation, a corneoscleral flap preserved in the Borzenok – Moroz medium (as obtained from the Eye Bank of the Ophthalmology clinic of the Academician I.P. Pavlov First St. Petersburg State Medical University) was used. A lamellar graft was cut from the donor material using Moria microkeratome (cut depth = 160 microns), which allowed to obtain a donor disk of anterior layers of the stroma, with a thickness of 180 microns and diameter of 8.4 mm. A donor corneal graft was fixed in the bed of the recipient with 10/0 interrupted sutures. Mitomycin was applied intraoperatively as an additional therapeutic measure at a concentration of 0.02% for 100 seconds on the exposed sclera from the temporal and nasal sides. From the upper part of the bulbar conjunctiva, a thin flap was cut to the tenon capsule (measuring 10 × 7 mm) and divided into two equal parts. The flap was fixed in the area of the "naked" sclera on the temporal and nasal sides with 8/0 interrupted silk sutures. A soft contact lens was applied (Fig. 4). In the postoperative period, instillation of fluoroquinolone antibiotic Vigamox for 5 days followed by antiseptic Vitabact (1 drop 4 times a day) for 2 weeks and corticosteroids and lubricant Tealoz (1 drop) for 3 months were prescribed. Sutures were removed from the conjunctiva after 2 weeks and those from the cornea 3.5 months after surgery.

A month later, at examination, visual acuity in the left eye was 0.6 with a diaphragm. The patient was under follow-up in our clinic for 6 months (Fig. 5). Visual acuity of the left eye in June 2020 was 0.8 cyl 1.0 D ax 70° = 1.0. He continued the instillation of lubricating drops Tealoz up to 6 times per day. A similar surgical treatment is planned for the right eye.

## DISCUSSION

Surgical treatment of pterygium has been a major challenge to ophthalmologists, as the risk of a relapse is very high with any type of procedure, as well as with the use of additional therapeutic methods. According to literature data, progression and relapse of pterygium depend on many factors and their combination: the history of previous surgical treatment, duration of follow-up period, patient's residence, etc. [25–27]. Although Saint Petersburg is located at latitude 59.9386° North and is therefore not included in the so-called "pterygium belt," patients with progressive forms and relapses of this disease are often found in this region, leading ophthalmologists to a state of dysphoria.

The mechanisms underlying the progression and recurrence of pterygium have not been sufficiently investigated, but it has been proven that intact

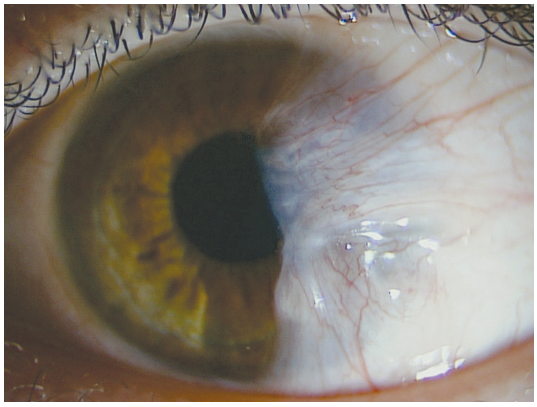

**Fig. 1.** Right eye (October 2019): recurring (operated on three times) stage IV pterygium (according to Z.D. Titarenko), degree of activity 3 (according to the D. Tan classification)

**Рис. 1.** Правый глаз (октябрь 2019 г.): рецидивирующий (трижды оперированный) птеригиум IV стадии (по З.Д. Титаренко), 3-й степени активности (по классификации Д. Тан)

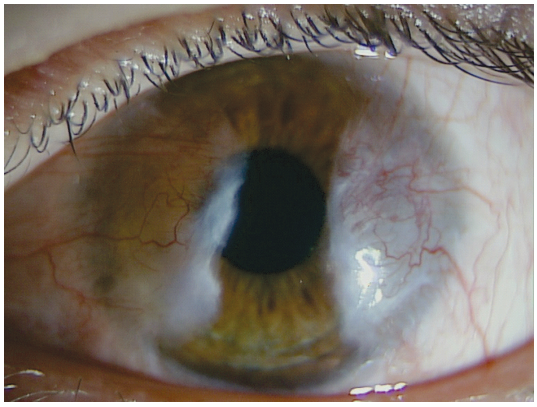

**Fig. 2.** Left eye (October 2019): recurrent (twice operated on) stage IV pterygium (according to Z.D. Titarenko), degree of activity 3 (according to the D. Tan classification)

**Рис. 2.** Левый глаз (октябрь 2019 г.): рецидивирующий (дважды оперированный) птеригиум IV стадии (по З.Д. Титаренко), 3-й степени активности (по классификации Д. Тан)

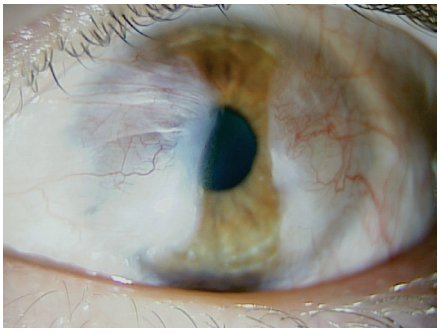

**Fig. 3.** Left eye (January 2020): pterygium progression

**Рис. 3.** Левый глаз (январь 2020 г.): прогрессирование птеригиума

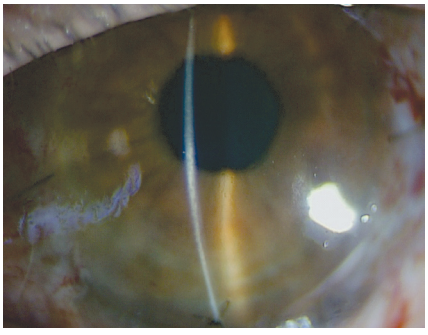

**Fig. 4.** Left eye with soft contact lens, Day 1 after surgery

**Рис. 4.** Левый глаз с мягкой контактной линзой на 1-е сутки после хирургического вмешательства

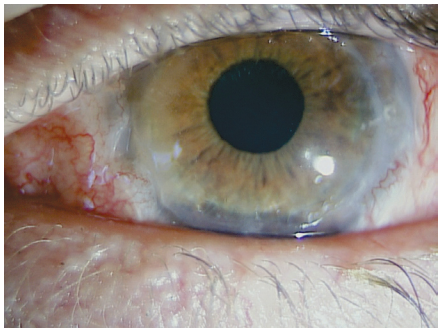

**Fig. 5.** The left eye 5 months after surgery, visual acuity with a correction 1.0

**Рис. 5.** Левый глаз через 5 мес. после хирургического вмешательства, острота зрения с коррекцией 1,0

Bowman membrane is a barrier to the ingrowth of conjunctival tissue [28]. It is logical that a graft containing Bowman membrane is ideal to restore this barrier. Therefore, a lamellar keratoplasty is rationally used as surgical method just for recurrent pterygium, as well as when the cornea becomes thin and cloudy as a result of previous surgeries. Additional medications are used, such as Mitomycins, which inhibit protein synthesis and cell proliferation, thus significantly reducing the rate of recurrence for patients with pterygium [28].

## CONCLUSION

In this clinical case, we successfully applied the technique of anterior lamellar keratoplasty and autoconjunctival transplantation in combination with intraoperative use of antimetabolite Mitomycin C for a young patient with recurrent stage IV pterygium (activity degree 3). In the postoperative period, a prolonged instillation of lubricating drops Tealoz is recommended. As a result of this surgical technique, the patient's corneal transparency was restored and high visual acuity was obtained.

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The authors declare no conflict of interest.

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