FOCAL LASER PHOTOCOAGULATION OF THE OPTIC DISC PERIPAPILLARY NEOVASCULARIZATION IN PATIENT WITH PROLIFERATIVE DIABETIC RETINOPATHY

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Diabetic retinopathy (DR) is one of the most common complications of diabetes mellitus and one of the major causes of blindness in the developed world. Retinal laser photocoagulation is a gold standard for the treatment of DR. Despite its high efficiency, laser therapy has a number of limitations. The emergence of drugs, designed to inhibit the growth of the newly formed blood vessels, in ophthalmic practice made it possible to change treatment strategy in patients with retinal neovascularization. However, this method also has some adverse effects. Given the limitations on the repeated sessions of laser photocoagulation and the risks of ophtalmic complications after the intravitreal injection of the angiogenesis inhibitors, extraordinary situations, when there are negative results of treatment with the use of the described above techniques in one eye and disease progression in the single eye with preserved vision, become a serious problem when performing treatment. The clinical case reported has shown the feasibility of staged laser treatment in patient with the optic disc peripapillary neovascularization. Therapy has resulted in the regression of the newly formed blood vessels and visual function preservation.

Keywords: diabetic retinopathy, focal laser photocoagulation, multispectral imaging, angiogenesis inhibitors, peripapillary neovascularization

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Compliance with ethical standards: the patient submitted the informed consent to laser therapy and personal data processing.

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ФОКАЛЬНАЯ ЛАЗЕРНАЯ КОАГУЛЯЦИЯ ПЕРИПАПИЛЛЯРНОЙ НЕОВАСКУЛЯРИЗАЦИИ ДИСКА ЗРИТЕЛЬНОГО НЕРВА ПРИ ПРОЛИФЕРАТИВНОЙ ДИАБЕТИЧЕСКОЙ РЕТИНОПАТИИ

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Диабетическая ретинопатия (ДР) является одним из наиболее частых осложнений сахарного диабета и одной из ведущих причин развития слепоты в развитых странах. Золотой стандарт лечения ДР — лазерная коагуляция сетчатки. Несмотря на высокую эффективность лазерного лечения, данный метод имеет ограничения в использовании. Появление в клинической практике офтальмолога препаратов, направленных на ингибирование роста новообразованных сосудов, позволило изменить тактику лечения пациентов с неоваскуляризацией сетчатки. Однако и этот метод обладает рядом нежелательных побочных явлений. Учитывая ограничения в проведении повторных этапов лазерной коагуляции, а также рисков офтальмологических осложнений после интравитреального введения ингибиторов ангиогенеза, серьезной проблемой в лечении являются нестандартные ситуации, когда имеется отрицательный результат лечения вышеописанными технологиями на одном глазу и прогрессирование процесса на единственно зрячем другом глазу. Представленный клинический случай продемонстрировал возможность поэтапного лазерного лечения пациента с перипапиллярной неоваскуляризацией ДЗН. Результатом лечения явился регресс новообразованных сосудов с сохранением зрительных функций.

Ключевые слова: диабетическая ретинопатия, фокальная лазерная коагуляция, мультиспектральное исследование, ингибиторы ангиогенеза, перипапиллярная неоваскуляризация

Вклад авторов: Х. П. Тахчиди — концепция и дизайн исследования, редактирование текста; Н. Х. Тахчиди — анализ литературных данных; Е. П. Тебина — сбор и обработка материала, написание текста; Т. А. Касмынина — лазерное лечение пациента.

Соблюдение этических стандартов: от пациента получено добровольное информированное согласие на лазерное лечение и обработку персональных данных.

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Currently, diabetes mellitus (DM) is a global issue. Microvascular complications of DM, such as diabetic retinopathy, nephropathy, neuropathy, are becoming the increasingly important disease manifestations and mortality causes [1].

Diabetic retinopathy (DR) is one of the most common complications of DM and one of the major causes of blindness in the developed world [2]. The prevalence of DR in the developed countries is about 3–4%; the percentage of affected individuals is higher in the older age groups. According to IDF (International Diabetes Federation), in 2017 there were 425 million people with DM all over the world. This indicator is expected to increase to 629 million people by 2040. A total of 3,029,397 patients with DM were registered in Russia in 2019, among them about 294,000 people had type 1 DM (T1D), and 2,736,000 had type 2 DM (T2D) [3, 4].

Regardless of the type of DM, it is an undeniable fact that the longer is the age of DM, the higher is the risk of developing DR. DR is diagnosed in almost all patients with T1D and in more that 60% of patients with T2D within two decades after the disease onset. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), blindness was diagnosed in 3.6% of patients with early-onset T1D and 1.6% of patients with adult-onset T2D. In 86% of cases, blidness in people with early-onset DM resulted from DR [5].

The DR triggers are as follows: chronic hyperglycemia, protein glycation, glucose oxidation through activation of

the polyol pathway, protein kinase activation, elevated levels of free radicals, impaired retinal microcirculation, endothelial dysfunction, hypoxia, increased production of the retinal pro-inflammatory cytokines and production of the vascular endothelial growth factor (VEGF), which result in edema and proliferation [6]. According to foreign and domestic literature, the efficiency of panretinal photocoagulation in patients with DR is assessed based on the degree of the retinal neovascularization suppression, regression of macular edema, visual function improvement or stabilization. According to the listed above criteria, the laser therapy efficacy varies between 60–99% [7, 8]. Despite its high efficiency, laser therapy has a number of limitations: severe diabetic macular edema [9], prominent fibrotic changes in the vitreoretinal interface, restrictions on the repeated sessions of laser photocoagulation.

The emergence of drugs designed to inhibit VEGF in ophthalmic practice made it possible to change the treatment strategy in patients with retinal neovascularization. This treatment type is focused directly on the pathophysiological target in DR. However, despite high efficiency of using the angiogenesis inhibitors, a number of case studies revealed some non-inflammatory adverse events (cataract, elevated intraocular pressure, retinal artery occlusion, vitreous hemorrhage, rhegmatogenous retinal detachment) and inflammatory complications (sterile intravitreal inflammation, brolucizumab-associated retinal vasculitis, post-injection endophthalmitis) [10]. Short duration of therapeutic effect (to an average of three months), the need for repeated injections, and all the listed above risks are considered the disadvantages of this treatment method.

The literature indicates that new foci of neovascularization and proliferation often emerge in various terms after the panretinal laser photocoagulation. Given the limitations on the repeated sessions of laser photocoagulation and the risks of ophtalmic complications after the intravitreal injection of the angiogenesis inhibitors, extraordinary situations, when there are negative results of treatment with the use of the described above technologies in one eye and disease progression in the single eye with preserved vision, become a serious problem when performing treatment. The study was aimed to assess the efficiency and safety of laser photocoagulation of the optic disc peripapillary neovascularization in patient with proliferative diabetic retinopathy.

Clinical case

Patient M. aged 30 contacted the Research Center of Ophthalmology, Pirogov Russian National Research Medical University, in April 2017 for routine funduscopy. It was known from the case history that the patient had type 1 diabeted mellitus since he was nine; no cardiovascular disorder was revealed. In 2007, the patient was diagnosed with bilateral proliferative diabetic retinopathy and therefore subjected to panretinal laser photocoagulation. Intravitreal angiogenesis inhibitor administration was performed in 2008 due to proliferative retinal changes in the right eye, and was complicated by the central retinal artery occlusion with sudden loss of vision.

After admission to the Research Center of Ophthalmology, Pirogov Russian National Research Medical University, the patient underwent a comprehensive ophthalmic examination, which included standard diagnostic tests (visometry for uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA), indirect ophthalmoscopy with the MaxField indirect lens (Ocular Inc.; USA)) and specific assessment methods (multispectral imaging with various filters (Blue-, Green-, Infrared Reflectance, MultiColor) performed with the Spectralis HRA+OCT, OCT2 module at 85,000 Hz (Spectralis HRA+OCT, Heidelberg Engineering, Inc.; Germany). The maximum follow-up period was 4 years.

Laser photocoagulation was performed with the VISULAS Trion ophthalmic laser system, 532 nm (Carl Zeiss; Germany).

During the initial patient assessment the following was revealed: visual acuity of the right eye (OD) — hand motion close to the face (eccentric); UCVA of the left eye (OS) 0.03, BCVA 0.7, incorrigible. Ophthalmoscopy OS revealed pale-pink optic disc with well-defined margins; the lace-like pattern of the newly formed vessels, running from the optic disc to the periphery and spreading in a fan-like manner, was observed predominantly in certain quadrants of the peripapillary region (upper nasal, lower nasal, lower temporal). Retinal vasculature: the artery to vein (A/V) ratio was 2/3, the vessel course remained unchanged, perivascular pigmented coagula were observed along the superior and inferior vascular arcades. Cellophane macular reflex, and weakly pigmented coagula (except for the avascular zone) were revealed. Pigmented coagula, reaching almost the optic disc to a distance of 1800 μm were found in the mid-periphery and far-periphery (Fig. 1A, B).

The following diagnosis was established based on the patient's medical history and the comprehensive ophthalmic examination: proliferative diabetic retinopathy OS, the condition after panretinal laser photocoagulation. Epiretinal fibrosis. Peripapillary neovascularization of the optic disc.

Taking into account the history of complication in the right eye, which developed after the intravitreal injection of the angiogenesis inhibitor and resulted in vision loss (the complication made it impossible to use the anti-VEGF drugs), a decision was made to perform custom laser treatment, which included staged laser photocoagulation: coagulation of the remaining intact peripapillary retinal area between the boundary of the old laser coagula and the zone within 500 μm from the optic disc edge at the beginning, assessing the effect of retinal photocoagulation and the visual function indicators a week later, with subsequent decision on the need for the next stage of focal laser photocoagulation of the newly formed blood vessels.

At the first stage, almost circumferential (except for the zone of papillomacular bundle) focal retinal laser photocoagulation was performed in the peripapillary region between old coagula and the zone within 500 μm from the optic disc edge. The chequerwise laser spots were applied using the following energy parameters: wavelength of 532 nm, power of 60–80 mW (until obtaining the first degree laser burn with the minimum possible parameters), exposure time of 0.08–0.1 s, and spot size of 100 μm. Visual acuity remained stable a week after the first-stage retinal laser photocoagulation. Ophthalmoscopy OS revealed the following: pigmented laser coagula were observed in the peripapillary region (up to 500 μm from the optic disc edge), the lace-like pattern of the newly formed vessels remained active (Fig. 2A, B).

After assessing the left eye (in a week) and detecting the visual function stability, the second-stage focal laser photocoagulation of the newly formed blood vessels (primarily the medium-sized vessels) was performed using the following energy parameters: power of 50–80 mW, exposure time of 0.06–0.1 s, spot size of 100 μm. The second stage was prolonged selectively and involved minimizing bleeding risks and assessing the effectiveness in four sessions performed with an interval of 3–4 weeks.

Examination performed 4 months after the second-stage focal laser photocoagulation of the newly formed blood vessels (four sessions) showed that visual acuity OS was stable: UCVA

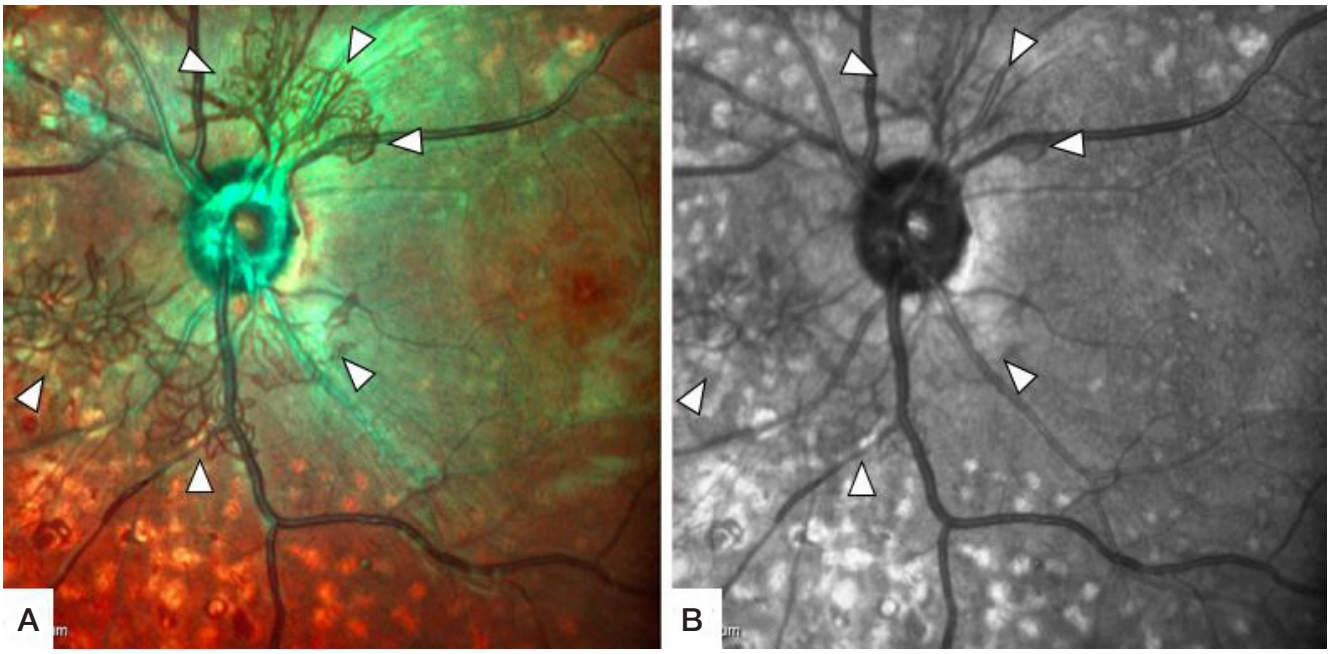

Fig. 1. Prior to laser therapy. **A.** Multispectral image; **B**. Infrared scanning laser ophthalmoscopy: network of the newly formed blood vessels is visible primarily in the upper nasal, lower nasal, and lower temporal sectors of the peripapillary region (*white arrows*)

was 0.03, and BCVA was 0.7. Ophthalmoscopy OS revealed the emptied newly formed vessels in the peripapillary region (Fig. 3A, B).

The follow-up examination performed four years later showed the unchanged visual acuity. Ophthalmoscopy OS revealed a complete regression of the optic disc network of the newly formed vessels in the peripapillary region (Fig. 4A, B).

Clinical case discussion

Diabetic retinopathy remains the leading cause of visual impairment and blindness in the world. More than one third of 285 million people all over the world, who suffer from diabetes mellitus, have DR, and one third of them (approximately 31.7 million) have a vision-threatening proliferative diabetic retinopathy [11]. Currently, the main treatment methods for proliferative diabetic retinopathy are as follows: retinal laser photocoagulation, intravitreal administration of angiogenesis inhibitors, treatment with corticosteroids, and vitreoretinal surgery. All the listed above treatment methods can be used in clinical practice as monotherapy or combination therapy.

The clinical case reported demonstrates the resource capabilities of the proposed peripapillary zone laser photocoagulation technique in the context of inability to use angiogenesis inhibitors due to the complication of the use of those, which have resulted in vision loss in the other eye.

The number of coagula, spot size and energy of the laser beam irradiating the retina should be selected individually

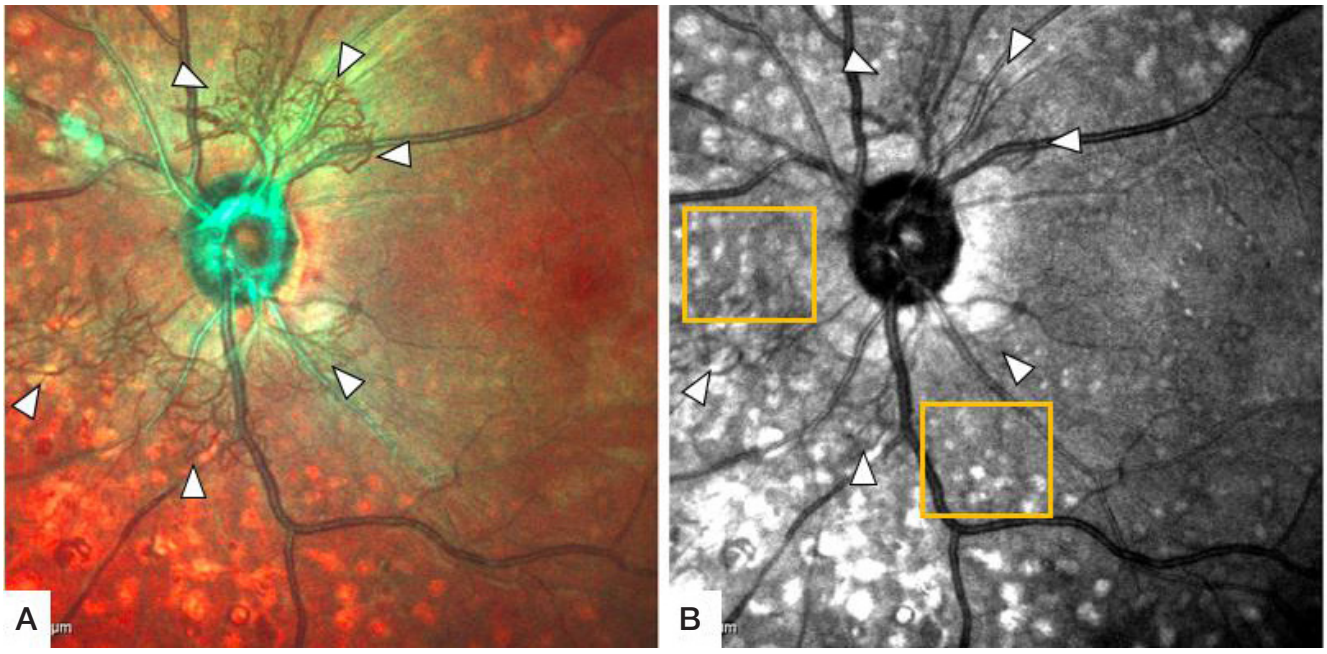

Fig. 2. A week after the first stage of laser photocoagulation. **A.** Multispectral image: network of the newly formed blood vessels in the peripapillary region is still active (*white arrows*). **B**. Infrared scanning laser ophthalmoscopy: network of the newly formed blood vessels in the peripapillary region is still active (*white arrows*), fresh coagula are observed in the peripapillary region (*yellow square*)

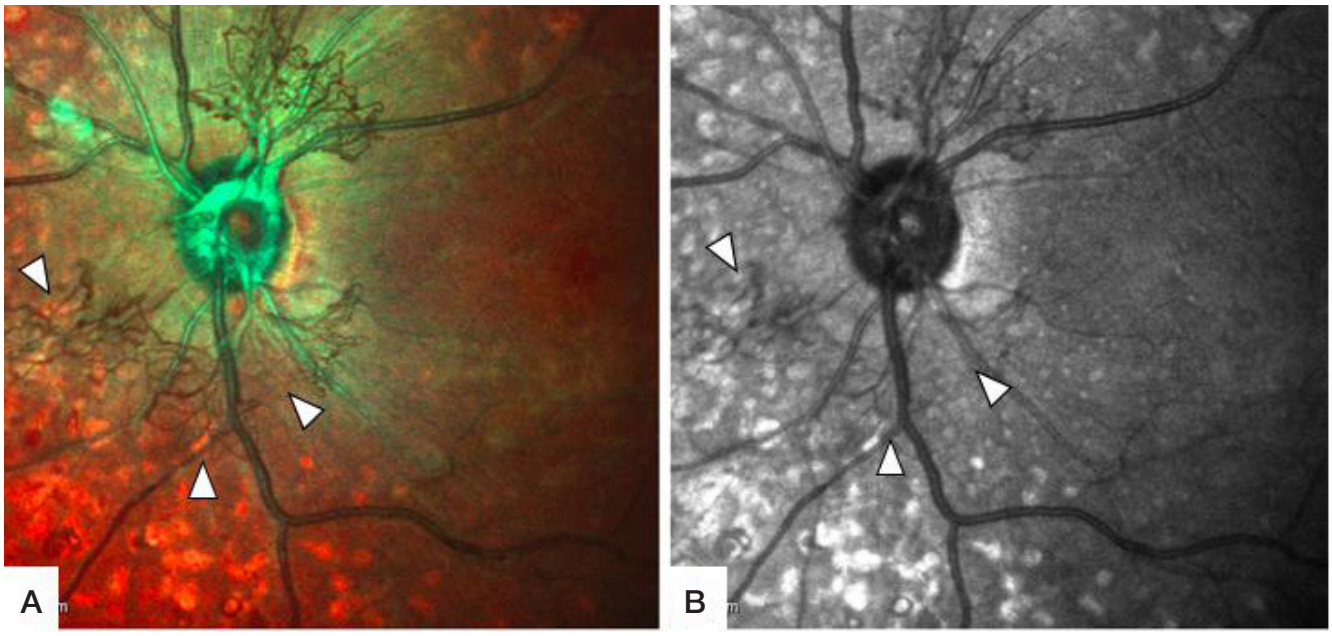

Fig. 3. Four months after the second-stage laser photocoagulation of the newly formed blood vessels. **A**. Multispectral image. **B**. Infrared scanning laser ophthalmoscopy: emptied newly formed vessels are visible in the peripapillary region (*white arrows*)

for a particular patient and oriented towards the lowest possible energy level. Laser exposure of the retinal areas, located most close to the optic disc, reduces "hypoxia" in these zones and, therefore, the new blood vessel formation intensity in the most reactive zone of proliferation, the optic disc. Thus, such preconditioning (performed at the first stage of treatment) of the peripapillary retinal area, with which the lace-like pattern of the new vessels is formed, results in reduced blood flow in these vessels, allowing for the more efficient second-stage treatment, the focal photocoagulation of the newly formed blood vessels. To minimize bleeding risks, one should start with blood vessels not exceeding the medium size, step-by-step in multiple sessions. Such approach allows the older coagula to contribute to blood vessel emptying, reduced blood flow and, therefore, the decreased risk of complications during subsequent photocoagulation.

The proposed laser treatment technique involves the use of the minimum possible energy parameters, allowing for the good morphofunctional outcome that consists in the complete optic disc peripapillary neovascularization regression and baseline visual function preservation.

CONCLUSION

Thus, the findings suggest that the use of the proposed focal laser photocoagulation technique for treatment of the optic disc peripapillary neovascularization ensure the regression of the newly formed blood vessels and preserve the baseline visual functions. The use of focal laser photocoagulation in the proposed peripapillary region expands the possibilities of treating the optic disc neovascularization. The practical effect demonstrates the results of using laser microsurgery in the adjacent areas of the optic disc with visual function preservation.

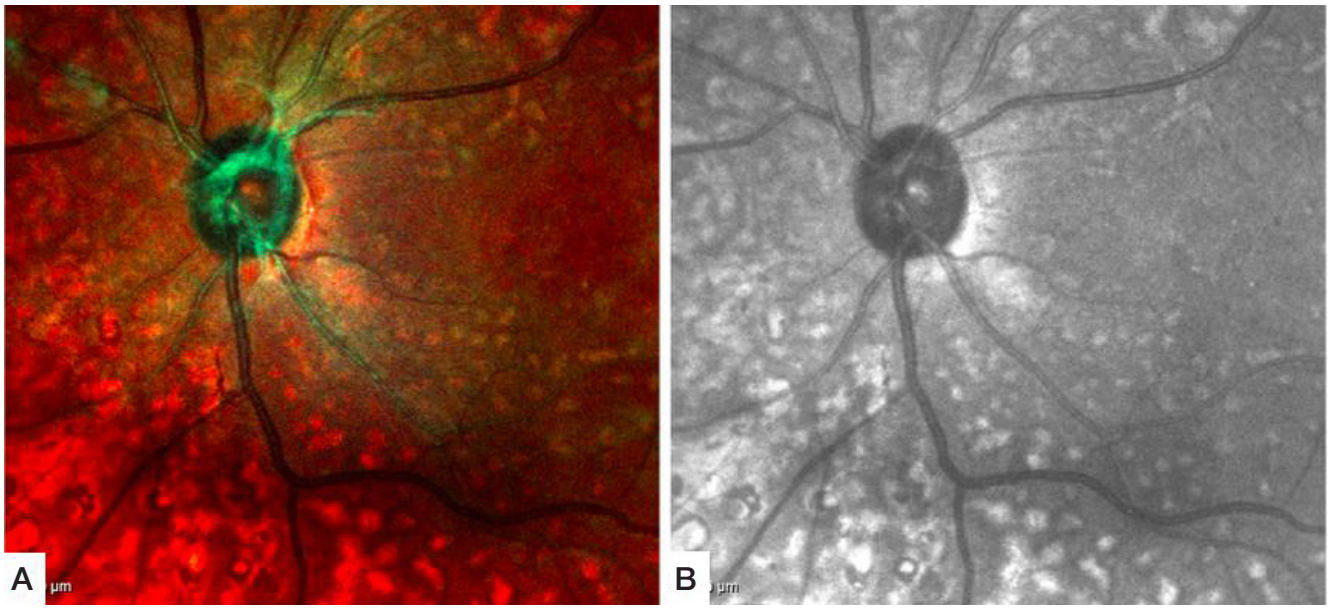

Fig. 4. Four years after the second-stage laser photocoagulation of the newly formed blood vessels. **A**. Multispectral image. **B**. Infrared scanning laser ophthalmoscopy: complete regression of the optic disc network of the newly formed vessels is observed in the peripapillary region

References

1. Stewart MW.Treatment of diabetic retinopathy: Recent advances and unresolved challenges. World J Diabetes. 2016; 7 (16): 333–341.
2. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy XXIII: the twenty-five-year incidence of macular edema in persons with type 1 diabetes. Ophthalmology. 2009; 116 (3): 497–503.
3. Sergushev SG, Homjakova EN. Anti-VEGF preparaty v terapii pacientov s diabeticheskim makuljarnym otekom. Klinicheskaja oftal'mologija. 2019; 25 (4): 238–44. Russian.
4. Federal'nyĭ registr saharnogo diabeta RF, realizuemyĭ FGBU «NMIC jendokrinologii» Minzdrava Rossii. Dostupno po ssylke: https://www. endocrincentr.ru/sites/default/files/all/EVENTS2019/NEWS%20SUM/13.03.19%20Prof.komissia/VIK_Exp_13.03.19.pdf.
5. Smirnova OM. Diabeticheskaja retinopatija. Rezul'taty mezhdunarodnyh mnogocentrovyh issledovanij. Saharnyj diabet. 2010; 13 (1): 80–87. Russian.
6. Bosma EK, van Noorden CJF, Klaassen I, Schlingemann RO. Diabetic Nephropathy. Springer, 2019. DOI: 10.1007/978-3-319-93521-8_19.
7. Burjakov DA, Kachalina GF, Pedanova EK, Kryl LA. Ocenka bezopasnosti povtornyh seansov subporogovogo mikroimpul'snogo lazernogo vozdeĭstvija pri lechenii diabeticheskogo makuljarnogo otёka. Sovremennye tehnologii v oftal'mologii. 2015; 3: 19–21. Russian.
8. Zajka VA, Shhuko AG, Arhipov EV, Bukina VV. Ocenka dolgosrochnoj jeffektivnosti panretinal'noj lazernoj koaguljacii pri saharnom diabete 2-go tipa. Sovremennye tehnologii v oftal'mologii. 2020; (1): 34–36. Russian.
9. Gacu MV, Bajborodov YaV. Kliniko-topograficheskaja klassifikacija diabeticheskih makulopatij. Saharnyj diabet. 2008; 11 (3): 20–22. Russian.
10. Jacob T. Cox, Dean Eliott, and Lucia Sobrin. Inflammatory Complications of Intravitreal Anti-VEGF Injections. J Clin Med. 2021; 10 (5): 981.
11. Yau JW, et al. Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012; (35): 556–64.

Литература

1. Stewart MW.Treatment of diabetic retinopathy: Recent advances and unresolved challenges. World J Diabetes. 2016; 7 (16): 333–341.
2. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy XXIII: the twenty-five-year incidence of macular edema in persons with type 1 diabetes. Ophthalmology. 2009; 116 (3): 497–503.
3. Сергушев С. Г., Хомякова Е. Н. Анти-VEGF препараты в терапии пациентов с диабетическим макулярным отеком. Клиническая офтальмология. 2019; 25 (4): 238–44.
4. Федеральный регистр сахарного диабета РФ, реализуемый ФГБУ «НМИЦ эндокринологии» Минздрава России. Доступно по ссылке: https://www. endocrincentr.ru/sites/default/files/all/EVENTS2019/NEWS%20SUM/13.03.19%20Prof.komissia/VIK_Exp_13.03.19.pdf.
5. Смирнова О. М. Диабетическая ретинопатия. Результаты международных многоцентровых исследований. Сахарный диабет. 2010; 13 (1): 80–87.
6. Bosma EK, van Noorden CJF, Klaassen I, Schlingemann RO. Diabetic Nephropathy. Springer, 2019. DOI: 10.1007/978-3-319-93521-8_19.
7. Буряков Д. А., Качалина Г. Ф., Педанова Е. К., Крыль Л. А. Оценка безопасности повторных сеансов субпорогового микроимпульсного лазерного воздействия при лечении диабетического макулярного отека. Современные технологии в офтальмологии. 2015; 3: 19–21.
8. Зайка В. А., Щуко А. Г, Архипов Е. В., Букина В. В. Оценка долгосрочной эффективности панретинальной лазерной коагуляции при сахарном диабете 2-го типа. Современные технологии в офтальмологии. 2020; (1): 34–36.
9. Гацу М. В., Байбородов Я. В. Клинико-топографическая классификация диабетических макулопатий. Сахарный диабет. 2008; 11 (3): 20–22.
10. Jacob T. Cox, Dean Eliott, and Lucia Sobrin. Inflammatory Complications of Intravitreal Anti-VEGF Injections. J Clin Med. 2021; 10 (5): 981.
11. Yau JW, et al. Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012; (35): 556–64.