DIAGNOSTIC AND TREATMENT METHODS

E.K. Zakharova, I.P. Lutskan, T.R. Poskachina

NEW POSSIBILITIES FOR THE TREATMENT OF NEOVASCULAR AMD. THE REAL CLINICAL PRACTICE

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The results of treatment of patients with neovascular age-related macular degeneration with a modern anti-angiogenic drug registered in Russia in November 2020 were analyzed. After three intravitreal injections in the recommended Treat&Extend regimen, the patients showed positive dynamics in both anatomical and functional parameters during the examination.

Keywords: age-related macular degeneration, retinal pigment epithelium detachment, subretinal fluid, anti-angiogenic therapy, intravitreal injection.

Age-related macular degeneration (AMD) is one of the leading causes of vision loss in people over 50 years of age in the economically developed countries of the world, characterized by irreversible progressive damage to the central zone of the retina. The predicted number of people with age-related macular degeneration in the world by 2040 will increase up to 288 million [20].

In Russia, in 25% of cases, visual disability develops due to diseases of the fundus, AMD being one of the leading causes among them [12] .

In the Republic of Sakha (Yakutia) the incidence of AMD according to 2019 was 195.9 per 100 thousand of the population. Despite the preservation of restrictive measures in connection with the prevention of the spread of a new coronovirus infection, in 2021 the incidence of this pathology increased by 26 %, which is associated with an increase in the availability of a diagnostic option - optical coherence tomography due to an increase in the number of tomographs in the RS (Yakutia) and specialists who own this research technique.

The neovascular form (“wet”) of age-related macular degeneration (nAMD) is characterized by the appearance of pathological choroidal neovascularization caused by the germination of newly formed blood vessels through defects in the Bruch's membrane under the retinal pigment epithelium or neuroepithelium. In the future, it is possible to accumulate intraretinal fluid (IRF), fluid under the retinal pigment epithelium (RPE), subretinal fluid (SRF) - between the neurosensory part of the retina and RPE. This can lead to rapidly progressive significant impairment of central vision and a pronounced decrease in the quality of life in general [5].

Modern advances in the treatment of nAMD are due to the active use of drugs that suppress neoangiogenesis [7, 10, 13, 17]. Antiangiogenic therapy can significantly improve the anatomical and functional parameters of patients with nAMD. Since this disease is chronic and requires long-term treatment, which creates a burden for the patient and for medical institutions, the selection of the optimal dosing regimen, which would reduce the number of necessary injections without loss of therapeutic effect, remains relevant [1, 4, 8], as well as the introduction of new modern drugs with these functions [2, 3].

In RS(Ya), angiogenesis inhibitors for the treatment of nAMD have been introduced since 2012. In dynamics over the past three years, the number of intravitreal injections of angiogenesis inhibitors (IVIs) has almost doubled by 49.3%, from 659 in 2019 to up to 1300 in 2021, of which about 50% were performed in patients with nAMD.

In 2021 Brolucizumab (Vizkyu), a new molecule registered by Novartis in Russia in November 2020, was introduced to treat patients with nAMD at the State Autonomous Institution of the Yakut Republican Ophthalmological Clinic (SAI RS (Ya) YROC). This is the next generation of anti - VEGF drugs , the variable domain of a monoclonal antibody. Its effect is based on the unique properties of the molecule: low molecular weight and high molar concentration contribute to the achievement of a therapeutic effect expressed in terms of speed and duration. Currently, the drug has been approved for use in more than 60 countries around the world [6,11,15,16,19].

Aim: to analyze the results of nAMD treatment in 17 patients of YROC RS(Y) who received three loading IVIs with Brolucizumab in real clinical practice in 2021.

Material and methods: In 2021 190 intravitreal injections of Brolucizumab were performed in 129 patients in the hospital of the State Agrarian University of the Republic of Sakha (Yakutia) of the Yaroslavl Regional Clinic. Of these: 20% of patients previously not treated with angiogenesis inhibitors and 80% switched from another previously performed angiogenic drug. During the study period, out of 129 patients: 17 received three injections, 27 - two injections, 85 - one injection.

In the group of patients who received three injections, 41% were already treated with other angiogenesis inhibitors and intravitreal administration of Brolucizumab was carried out in the Treat & Extend “treat and extend the interval” mode after 3-4 months [9,14].

The functional response to the treatment was assessed by the change in the maximum correctable visual acuity (MCVA), the anatomical response according to the dynamics of the pathological fluid in the retina: intraretinal fluid (IRF), subretinal fluid (SFR) and detachment of the retinal pigment epithelium (RPE) [5,18].

The results of treatment on the example of two of our own clinical observations are presented:

Case report No.1. The patient M., 72 years old, in February 2019 addressed to the YROC with complaints of decreased

ZAKHAROVA Ekaterina Kimovna – Candidate of Medical Sciences, Head of the Department of the Yakut Republican Ophthalmologic Clinic RS(Ya), Associate Professor of the Basic Department of Ophthalmology of the Medical Institute, M.K. Ammosov Yakutsk State Medical University, katya1961@mail.ru; **LUTSKAN Ivan Petrovich** – Candidate of Medical Sciences, Chief Physician of the Yakut Republican Ophthalmologic Clinic RS(Ya), Associate Professor of the Department of Public Health and Public Health, General Hygiene and Bioethics of the Medical Institute, M.K. Ammosov Yakutsk State Pedagogical University, lutskan@mail.ru; **POSKACHINA Tamara Romanovna** – Candidate of Medical Sciences, Associate Professor, Head of the Basic Department of Ophthalmology of the Medical Institute, M.K. Ammosov Yakutsk State Medical University, doka14@list.ru

vision, the appearance of a dark "spot" in front of the left eye.

Visit No.1 (02/23/2019) OS: BCVA OS = 0.06 n/c; IOP OS - 29 mm Hg. Art. according to Maklakov.

Fig. 1 a) OCT of the macular area of the left eye of the patient M.

b) OCT-angiography at the level of the outer retina; c) OCTA at the level of choriocapillaries (Fig. 1a) revealed: SRF, intraretinal inclusions, subretinal neovascular membrane (SNM), in the OCT angiography mode (Fig. 1b, 1c) - an extensive loop-like vasculature in a coral-like shape in the outer retina.

Diagnosis: OS - AMD, type I choroidal neovascularization; OUG III "c", incomplete complicated cataract.

Since 2019 the patient underwent 11 IVI Aflibercept in the left eye, then operations: phacoemulsification (PE) with implantation of an intraocular lens (IOL) and non-penetrating deep sclerectomy (NPDS).

Visit No. 11 (24.07.2020) OS: BCVA OS = 0.3 n/c; IOP - 18 mm Hg. Art.

Fig. 2 a) OCT of the macular area of the left eye of the patient M.

b) OCTA at the level of the outer retina; c) OCTA at the level of choriocapillaries

As a result of the treatment, according to OCT data (Fig. 2a), the following was observed: a decrease in the height of the neuroepithelium (NE), a decrease in intraretinal inclusions, a decrease in the height of the SNM , however, a thin layer of SRF ≤200 μm of subfoveal localization was preserved , according to OCT angiography (Fig. 2b, 2c) "mature vessels" were traced in the outer retina and the layer of choriocapillaries. The patient constantly saw a translucent "spot" in front of the left eye.

From April 2021 the patient received 3 IVI Brolucizumab in the Treat & Extend mode once every three months. A month after the third injection at the control examination, a positive trend was revealed.

Visit No.15 (11/14/2021) OS: BCVA OS = 0.5 n/c; IOP - 17 mm Hg. Art.

Fig. 3 OCT of the macular area of the left eye of the patient M.

No SRF was detected on OCT (Fig. 3). The patient noted an improvement in vision, increased clarity, and the absence of a translucent “spot” in front of the left eye.

Case report No. 2. Patient K., 67 years old. Complaints about the deformation of the lines, a reading disability

Visit No.1 (26.07.2021) OS: BCVA OS = 0.3 n/c.

Fig. 4. OCT of the macular area of the left eye of the patient K.

OCT (Fig. 4): The foveolar profile is

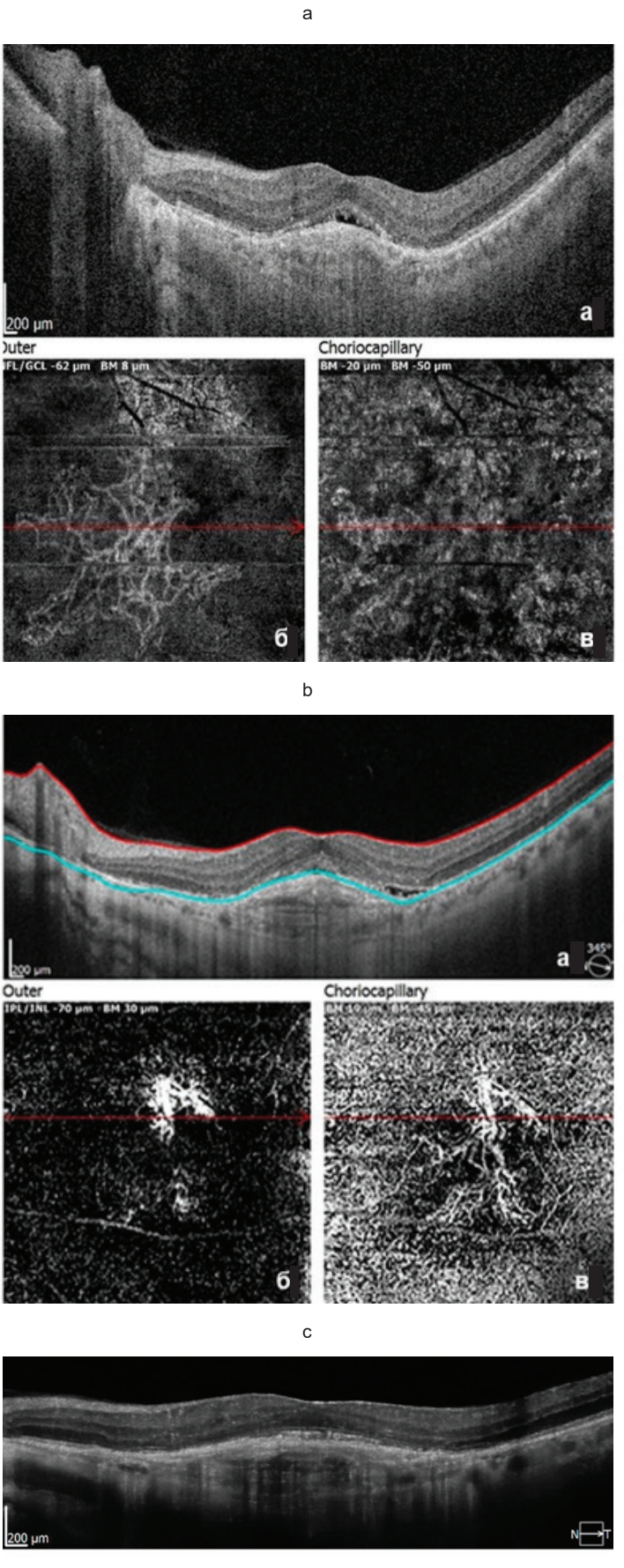


Fig 1. Patient M., A - 23.02.2019, B - 24.07.2020, C - 14.11.2021. a - OCT of the left eye macular area, b - OCTA at the outer retina level, c - OCTA at the level of choriocapillaries

deformed. The thickness of the retina is increased, NE detachment, detachment of the retinal pigment epithelium (RPE) with mixed reflectivity content, SNM is determined subfoveolarly, the RPE contour is heterogeneous, intermittent.

Diagnosis: OS AMD, type I choroidal neovascularization.

3 bootstrap IVI Brolucezumab were conducted. At the control examination 1 month after the third injection, a positive trend was revealed.

Visit No. 3 (24.09.2021) OS: BCVA OS = 0.5n/c.

Fig. 5 OCT of the macular area of the left eye of patient K.

On OCT (Fig. 5), the deformation of the foveolar profile is significantly less, a flat detachment of the RPE with medium reflectivity content is preserved, the contour of the RPE is inhomogeneous, and a discontinuous layer of photoreceptor articulation is traced.

Results and discussion: After 3 IVI Brolucizumab, all 17 patients noted a subjective improvement in vision: a decrease in line distortion, the disappearance of the “spot” in front of the eye, or the “spot” became more transparent.

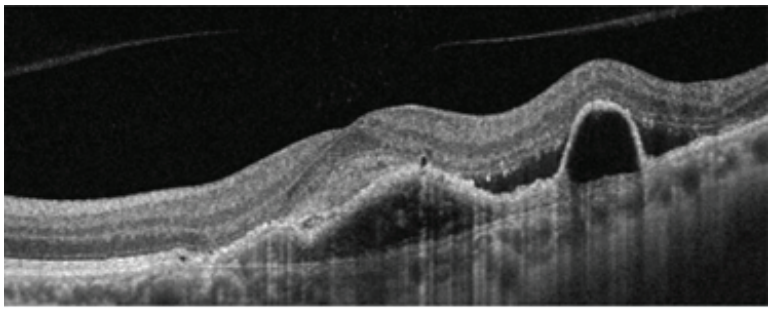
1. Improvement of the best correctable visual acuity (BCVA) by 1-2 lines, in 75% of cases.
2. According to OCT data, 100% showed positive dynamics: the absence or a significant decrease in pathological fluid in the retina: IRF, SRF, and OPES.
3. When switching patients from injections of other angiogenic drugs, loading doses were not required, therapy was continued in the "treat and increase the interval" mode.
4. Of the 96 patients who received from 1 to 2 IVI Brolucizumab, according to the results of the diagnostic study after 1 month, conducted in 62 patients, 64% showed a positive trend according to OCT.
5. During the therapy of 190 IVI Brolucizumab, 129 patients did not experience any manifestations of local adverse events in any case.

Conclusion: In all 17 patients who received 3 IVI Brolucezumab, there was a positive trend in anatomical and functional parameters.

Taking into account the peculiarities of the region of the RS (Y): a vast territory, with an area of 3.1 million square km., low population density of 0.3 people per 1 sq. km, which leads to non-compliance with the dosing regimen due to the large distance of patients from the clinic, the therapy with Brolucizumab allows switching to regimens with fewer visits, which will increase patient adherence to treatment and preserve the visual functions of patients.

In the ongoing conditions of restrictive measures in connection with the prevention of the spread of the new coronovirus infection COVID -19, the treatment of patients with Brolucizumab can reduce the burden on the patient and the healthcare system.

a



b

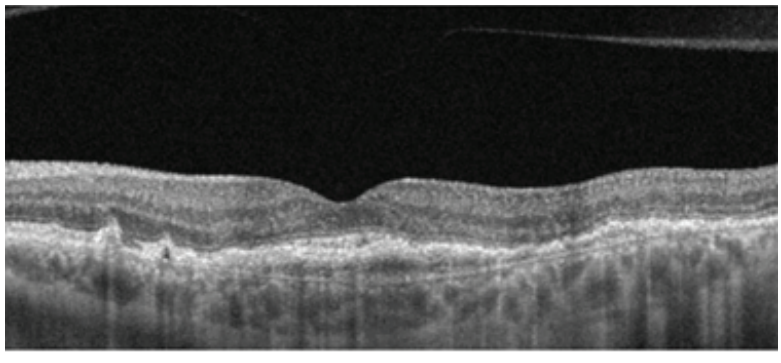


Fig. 2. Patient K. OCT of macular area of the left eye: a - 26.07.2021, b - 24.09.2021

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