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Comparative analysis of treatment of patients with toxoplasma retinochoroiditis

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***Aim**: to compare the effectiveness of complex drug treatment of patients with toxoplasma retinochoroiditis.*

***Methods**: A total of 33 patients (45 eyes) diagnosed with toxoplasma retinochoroiditis were examined at the Republican Specialized Scientific and Practical Medical Center of Eye Microsurgery (RSSPMCEM). Among them were 13 men (39.3%) and 20 women (60.7%). The patients' age ranged from 19 to 56 years. Depending on the proposed treatment, the patients were divided into 2 groups. I – the main group. All patients in the main group were recommended to use Spiramycin 3,000,000 IU orally, 1 tablet once a day for 14 days, intramuscular injections of Immunomodulin 0.01% – 1 ml – 1 time per day – 10 days, parabulbar injections of Dexamethasone 0.5 ml 1 time per day for 5 days in the affected eye, as well as instillation of drops of Bromfenac 0.09% 1 drop 2 times a day – a month.*

II. Control group. All patients in the control group were recommended to use Spiramycin 3 000 000 IU orally, 1 tablet once a day for 14 days, parabulbar injections of Dexamethasone 0.5 ml once a day for 5 days in the affected eye, as well as instillation of Bromfenac 0.09% drops, 1 drop 2 times a day – a month.

***Results:** Our study revealed that a pronounced functional result was achieved after 3 months of treatment, and positive dynamics were observed throughout the entire observation period.*

***Conclusion:** The additional use of immunomodulatory therapy demonstrated greater efficacy in the treatment of toxoplasma retinochoroiditis over six months. The main group showed greater statistically significant improvements in BCVA (0.41±0.05 to 0.68±0.05) compared to the control (0.43±0.05 to 0.58±0.05), RNFL thickness increased to 82 ±1.5 µm from 78±1.6 µm, and macular edema decreased to 278±3.8 µm from 312±4.2 µm. Despite structural disorganization persisting, immunomodulatory therapy demonstrated a significant advantage in improving functional and anatomical outcomes.*

Key words:

toxoplasma retinochoroiditis, optical coherence tomography, computed perimetry, spiramycin, immunomodulin

Introduction. Toxoplasma gondii is an obligate intracellular parasite and is one of the most common parasitic zoonoses worldwide [1,3,11]. More than 100 years have passed since T. gondii was first described by Charles Nicolle and Louis Manceau in 1908 during their studies of Leishmania at the Pasteur Institute in Tunis [5,9,12]. The name of the parasite is associated with its morphology (toxo - arch or bow; plasma - life) and the animal in which it was found (gundi). Eye damage in this infection often occurs with the involvement of the retina and choroid in the pathological process [4,8]. The inflammatory process is often present in the anterior segment of the eye [7,14]. Toxoplasma retinochoroiditis is a common cause of posterior uveitis and can lead to blindness if not treated in a timely manner [2,6,10,13]. The lack of uniform treatment standards for this nosology emphasizes the relevance of this problem.s for this nosology emphasizes the relevance of this problem.

Aim. To compare the effectiveness of complex drug treatment in patients with toxoplasma retinochoroiditis.

Material and methods

33 patients (45 eyes) diagnosed with toxoplasma retinochoroiditis were examined at the Republican Specialized Scientific and Practical Medical Center of Eye Microsurgery (RSSPMCEM). Among them were 13 men (39.3%) and 20 women (60.7%). The patients' age ranged from 19 to 56 years. The average age was 34.5±2.3 years. For the conduct of scientific research, in accordance with the Helsinki Declaration, the Ethics Committee for Medical Research of the Ethics and Professional Development Institute of the Republic of Uzbekistan was approved, and voluntary informed consent was obtained from all patients. The criterion for inclusion of patients in the study was the presence of toxoplasma retinochoroiditis in one

or both eyes. The exclusion criteria from this study were: retinochoroiditis of other etiology (cytomegalovirus, tuberculosis), vasculitis of the optic nerve, inflammatory and degenerative diseases of the organ of vision, traumatic injuries of the eyeball, autoimmune and syndromic diseases of the eye, congenital anomalies of the organ of vision, hypersensitivity to spiramycin and immunomodulin or any other component of the drug. All patients underwent visometry, autorefractometry, non-contact tonometry, biomicroophthalmoscopy, computer perimetry (CP), B-scanning, optical coherence tomography (OCT), optical coherence tomography with angio-mode (OCTA), as well as enzyme-linked immunosorbent assay (ELISA) for IgM and IgG. The observation period was 6 months.

To analyze the morphometric parameters of the retina, an optical coherence tomograph (OCT) with angiography DRI OCT TOPCON Triton plus (Ver. 10.13) was used. OCT included obtaining a macular map with subsequent extraction of central retinal thickness (CRT) parameters from it. In addition, OCT was used to assess the thickness of the retinal nerve fiber layer (RNFL), verify the alteration and dystrophy of the retinal pigment epithelium, and also determine the presence of any type of fluid: fluid under the retinal pigment epithelium (RPE) or intraretinal fluid (IRF) by reviewing all structural scans of the macular map. OCT angiography determined the density of macular blood flow in the central zone in %, as well as the presence or absence of newly formed vessels starting from the Superficial layer ending before the Choriocapillaris layer.

Depending on the treatment, the patients were divided into 2 groups.

I – the main group consisted of 18 patients (25 eyes) with toxoplasma retinochoroiditis. All patients in the main group were recommended to use Spiramycin 3,000,000 IU orally, 1 tablet once a day for 14 days, intramuscular injections of Immunomodulin 0.01% – 1 ml – 1 time per day – 10 days, parabulbar injections of Dexamethasone 0.5 ml 1 time per day for 5 days in the affected eye, as well as instillation of drops of Bromfenac 0.09% 1 drop 2 times a day – a month.

II – control group consisted of 15 patients (20 eyes) with toxoplasma retinochoroiditis. All patients in the control group were recommended to use Spiramycin 3,000,000 IU orally, 1 tablet once a day for 14 days, parabulbar injections of Dexamethasone 0.5 ml once a day for 5 days in the affected eye, as well as instillation of Bromfenac 0.09% drops, 1 drop 2 times a day – a month.

The MedCalc 18.4.1 software package (MedCalc Software, Belgium) was used for statistical data processing. Data are presented as mean ± standard deviation. One-way analysis of variance with repetitions was used to assess the statistical significance of differences in functional data before and after drug treatment. The difference was considered statistically significant at $p<0.05$.

Results

The best corrected visual acuity (BCVA) of patients in the control group before treatment averaged 0.43±0.05, and 0.41±0.05 in main group. Intraocular pressure (IOP) according to pneumotonometry was within 14.1±2.1 mm Hg in the control group before treatment and 13.8±1.7 mm Hg in the main group. According to biomicroophthalmoscopy, the inflammatory focus was in the central zone in 16 cases (35.5%), in the paracentral zone in 18 cases (40.0%), and in the equatorial zone in 11 cases (24.5%). The volume of the lesion was conditionally estimated by the diameter of the optic nerve disk (PD- Papilla Diameter) and averaged 4 PD in both groups. According to computer perimetry, the average photosensitivity was 18.2±1.5 dB and 17.9±1.4 dB in the control and main group, respectively. The deviation of the average photosensitivity (MD – Mean Deviation) averaged -10.15 dB in control group and -10.18 dB in main group, the deviation of the average photosensitivity from the age norm (PD – Pattern Deviation) was -8.37 dB in control group and -8.38 dB in main group. On OCT, the average retinal thickness in the macular zone was 370 μm (microns) in control group and 374 μm in main group with the presence of intraretinal cysts in the outer plexiform and inner nuclear layers of the retina. Analysis of the retinal nerve fiber layer verified thinning and averaged 73 μm in control group and 72 μm in main group. OCTA revealed the absence of newly formed vessels from the Superficial layer ending up to the Choriocapillaris layer. The average blood flow density in the macula was 35.2±1.2 in control group and 34.9±1.3 in main group. The IgM and IgG titers on average before treatment for control group were 1.34 U/ml and 1.72 U/ml, for main group it was 1.37 U/ml and 1.75 U/ml. As can be seen from the functional data, there was no statistical difference between the groups before treatment. After completion of the treatment course, the average BCVA in the main group averaged 0.58±0.05 in the 1st month of observation, 0.72±0.05 in the 3rd month of examination and 0.68±0.05 in the 6th month of observation. In the control group, after the 1st month, the average BCVA was 0.52±0.05, in the 3rd month 0.64±0.05 and in the 6th month 0.58±0.05 (table 1). We revealed no statisti-

Table 1. Visual acuity indicators of patients in the study groups after treatment

	Before treatment	1st month	3rd month	6 months
Main group	0.41±0.05	0.58±0.05	0.72±0.05	0.68±0.05*
Control group	0.43±0.05	0.52±0.05	0.64±0.05	0.58±0.05

* – statistical significance was $p<0.05$ between main and control group after 6-month period.

Table 2. Intraocular pressure indicators of patients (in mmHg) in the study groups after treatment

	Before treatment	1st month	3rd month	6 months
Main group	13.8±1.7	14.8±2.2	14.6±2.1	14.4±2.1
Control group	14.1±2.1	14.7±2.2	14.7±2.1	14.2±2.2

Table 3. Mean deviation (MD) in DB (Decibel) in the study groups after treatment

	Before treatment	1st month	3rd month	6 months
Main group	-10.18± 0.64	- 8.98± 0.58	- 8.12± 0.45	-7.34± 0.42*
Control group	-10.15± 0.62	- 9.21± 0.59	- 8.43± 0.46	- 8.22± 0.44

* – statistical significance was p <0.05 between main and control group after 6-month period.

Table 4. Indicators of deviation of average photosensitivity from the age norm (PD – Pattern Deviation) in DB(Decibel) in the study groups after treatment

	Before treatment	1st month	3rd month	6 months
Main group	-8.38± 0.43	-7.52± 0.31	-7.01± 0.26	-6.47± 0.25*
Control group	-8.37± 0.42	-7.86± 0.33	-7.49± 0.28	-7.23± 0.26

* – statistical significance was p <0.05 between main and control group after 6-month period

Table 5. Retinal nerve fiber layer indices in μm in the study groups after treatment

	Before treatment	1st month	3rd month	6 months
Main group	72± 1.4	75± 1.3	79± 1.6	82± 1.5*
Control group	73± 1.4	75± 1.4	77± 1.6	78± 1.6

* – statistical significance was p <0.05 between main and control group after 6-month period

cal significance between two groups for all studied indicators before treatment.

Intraocular pressure data did not change significantly over the entire observation period in patients in both groups (Table 2).

The volume of the inflammatory locus in biomicroophthalmoscopy decreased and was equal to an average of 2 PD after 6 months of observation. The data of static perimetry of patients in the main group showed an increase in average photosensitivity to 19.6±1.4 dB for 1 month of observation, 21.4±1.6 dB for the 3rd month of observation and 21.8±1.6 dB for the 6th month of the study. In the control group, after the 1st month of observation, the average photosensitivity was 17.8±1.5 dB, on the 3rd month 18.6±1.4 (Table 3, 4).

The average retinal thickness in the macular zone according to OCT data decreased to 278 μm (microns) compared to the control 312 μm (-microns) over the entire observation period, but disorganization in the outer plexiform and inner nuclear layers with the presence of intraretinal cysts remained.

The blood flow density in the macular zone according to OCTA data did not change significantly in both groups and was equal to 36.3±1.1% in the main group and 36.18±1.1% in the control group, respectively, at the 6th month of observation.

Analysis of the retinal nerve fiber layer did not reveal significant changes during the 1st month of observation, but significantly increased during the 3rd and 6th months of observation in the main group (Table 5).

We can notice that RNFL in main group was moderately higher than its in control group 82 and 78 after 6-month period in respective order (Fig. 3).

IgM titers on average after treatment at the 6th month in the main group were 0.76 U/ml, and in the control group 0.86 U/ml (Fig. 4).

IgG titers on average after treatment at the 6th month in the main group were 1.12 U/ml, and in the control group 1.21 U/ml (Fig. 5).

Discussion

A study was conducted in patients with toxoplasma retinochoroiditis using modern diagnostic and treatment methods. The etiology of uveitis was confirmed by the ELISA method. Comparative results of the treatment indicate that the inclusion of an immunomodulator in complex therapy contributed to a significant improvement in clinical and functional indicators, as well as morphometric

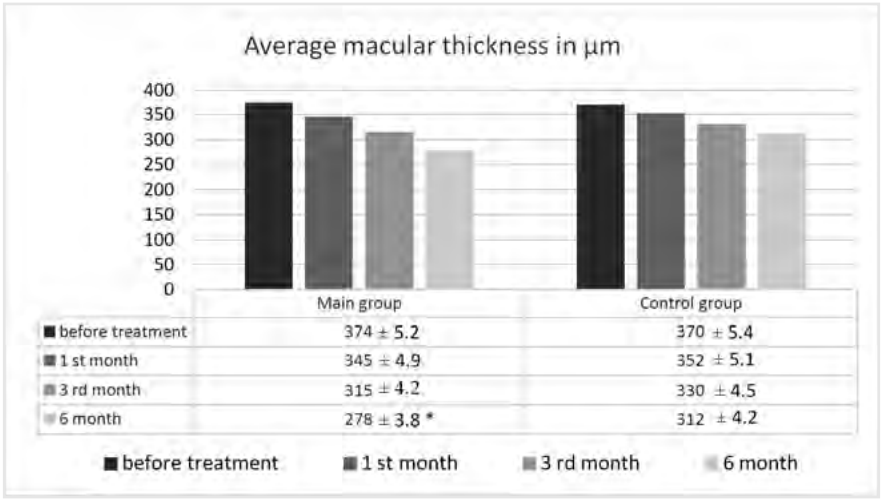

Fig. 3. Average thickness of the macular zone in µm in the study groups after treatment.

Note. * – statistical significance was p<0.05 between main and control group after 6-month period

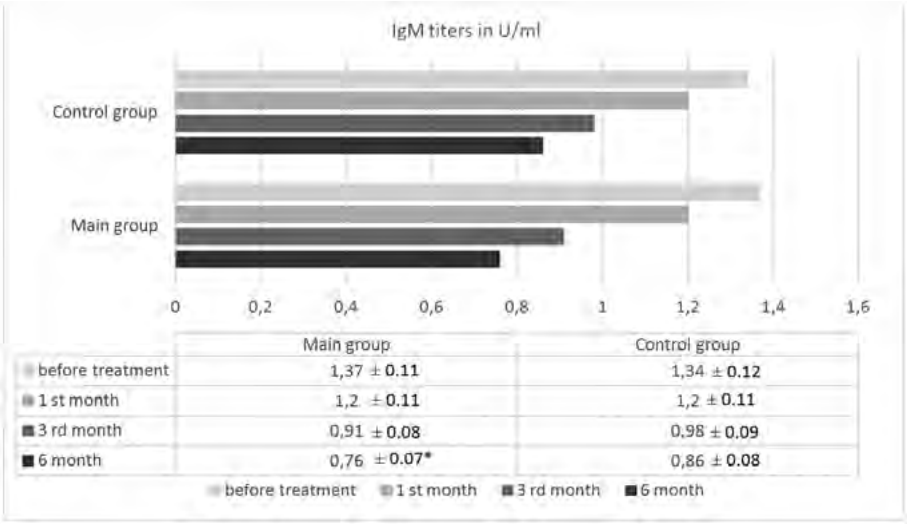

Fig. 4. IgM levels in U/ml in the study groups after treatment

Note. * – statistical significance was p<0.05 between main and control group after 6-month period

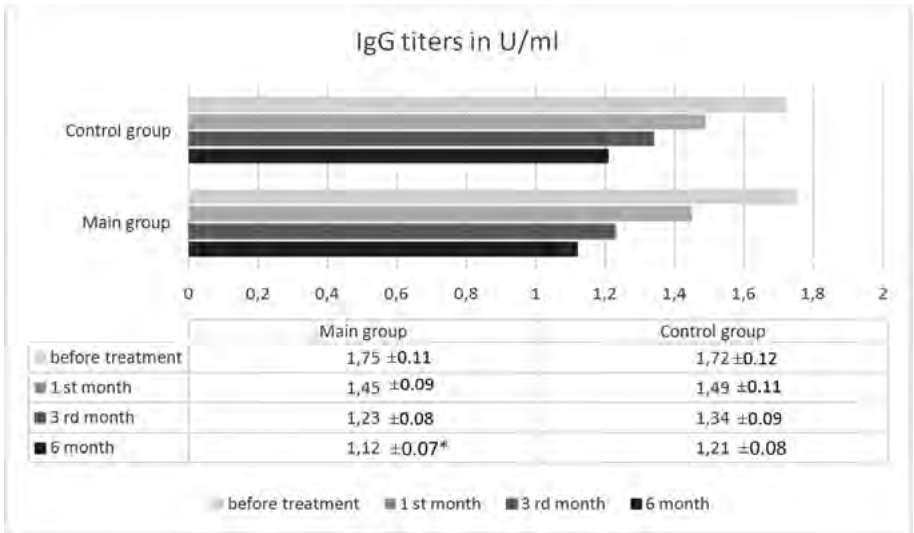

Fig. 5. IgG levels in U/ml in the study groups after treatment.

Note. * – statistical significance was p <0.05 between main and control group after 6-month period

characteristics of the fundus, which correlates with an increase in BCVA and visual fields, as well as the leveling of immunological parameters in patients with toxoplasma retinochoroiditis. Complex treatment of patients with this disease is prescribed jointly with infectious disease doctors. For a very long time in our country, the combination drug (Sulfadoxine+ Pyrimethamine 500 mg/25 mg) was used to treat systemic toxoplasmosis, which for some reason is currently not available. Based on our study, the use of the drug Spiramycin from the Macrolide group is due to the fact that it is a bacteriostatic drug that blocks the synthesis of folic acid, which in turn is a substrate for

the dissemination of toxoplasmosis. In addition, Spiramycin can be successfully used in pregnant women with toxoplasmosis. According to the research by Holland G.N. et al., 85% of patients with toxoplasma retinochoroiditis have a successful outcome. As in our studies, Holland et al. considered the criteria for success to be an increase in patients' visual acuity, a decrease in the size of the inflammatory locus, and a decrease in the thickness of the macular zone after active inflammation [12,13]. Based on world literature, there are many scientific works devoted to the complex treatment of toxoplasma retinochoroiditis, but there are no studies on the use of an immunomodulator in the treatment of these patients [2,10]. The use of an immunomodulator along with antibiotics and anti-inflammatory drugs significantly increases functional data over a long period of observation and is a safe and affordable treatment regimen for this nosology.

Based on our research, we can conclude that both groups after treatment showed positive dynamics in terms of functional results. Moreover, the functional data of the main group prevailed over similar data of the control group. According to our data, we can confirm that complex treatment of patients with toxoplasma retinochoroiditis with the use of an immunomodulator significantly improves the functional results of patients, as well as the morphological state of the retina in this pathology, which allows not only to preserve but also to improve visual acuity and prevent visual blindness in these patients. Obviously, a multimodal approach is necessary in order to verify the correct diagnosis and localization of the inflammatory process. In addition to modern instrumental examination methods, specific laboratory tests are used to confirm the diagnosis. Treatment should be comprehensive, timely, and safe with mandatory supervision by an infectious disease specialist.

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Information about authors and disclosure of information

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Author's contribution. *SMU – data collection and analysis, writing – original draft; ZAR – data collection and analysis, formal analysis, writing – review and editing; AON – data collection and analysis, writing – original draft; MMU – conceptualization, analysis, project administration, writing – review and editing. All authors read and approved the final version of the manuscript. All authors analysed the results and approved the final version of the manuscript to publication.*

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Disclaimer. *The opinions expressed in this article are those of the authors and do not reflect the official position of the institution.*

Abbreviation. *RSSPMCEM – Republican Specialized Scientific and Practical Medical Center of Eye Microsurgery; BCVA – Best Corrected Visual Acuity; OCT – Optical Coherence Tomography; CP – Computer Perimetry; RPE – Retinal Pigment Epithelium; RNFL – Retinal Nerve Fiber Layer; IRF – Intraretinal Fluid; CRT – Central Retinal Thickness, MD – Mean Deviation; PD – Papilla Diameter.*

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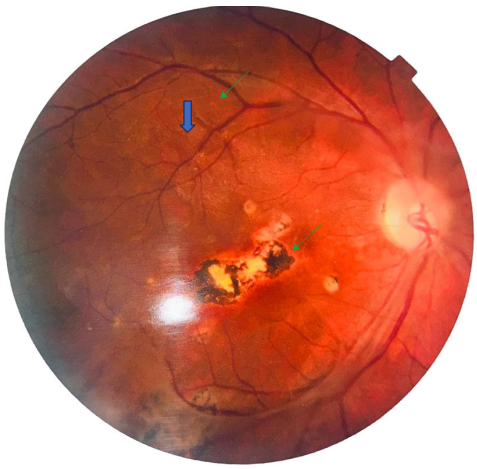

Fig. 1. Fundus of the right eye of a patient toxoplasma retinochoroiditis with multifocal recurrent lesions (blue arrow – recent formed scar, green arrows – old scars).

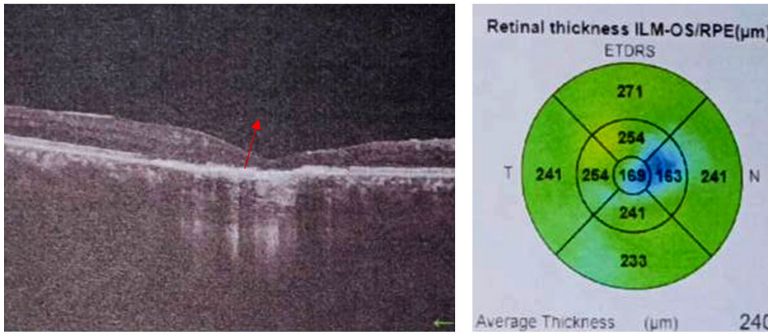

Fig. 2. Macular area of a same patient in fig.1 with toxoplasma retinochoroiditis with chronic central lesion of the right eye with the presence of subretinal fibrosis and its thickness analysis in microns (red arrow – subretinal fibrosis)

Фото до статті «Сафроненкової І.О., Буйко О.С., Єлагіної В.А. «Ультразвукові особливості злоякісних епібульбарних новоутворень різного гістогенезу (меланома і карцинома)»

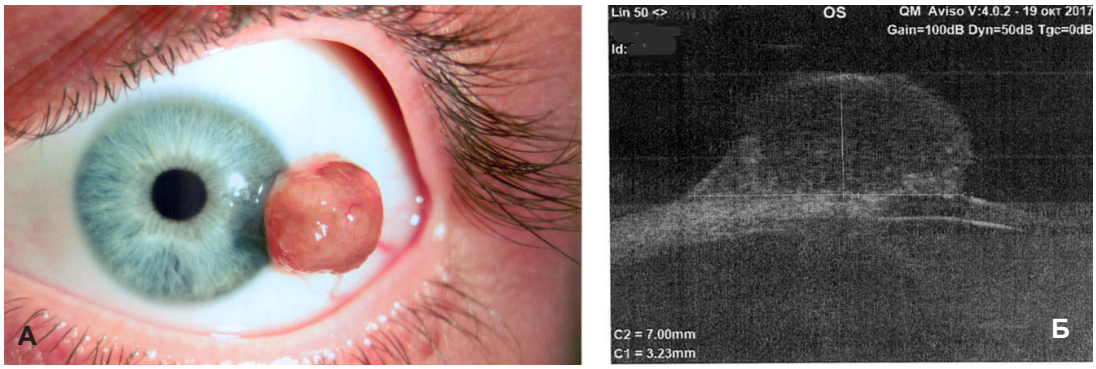

Рис. 1. А – меланома кон'юнктиви склери і рогівки; Б – сонограма меланоми кон'юнктиви склери і рогівки.

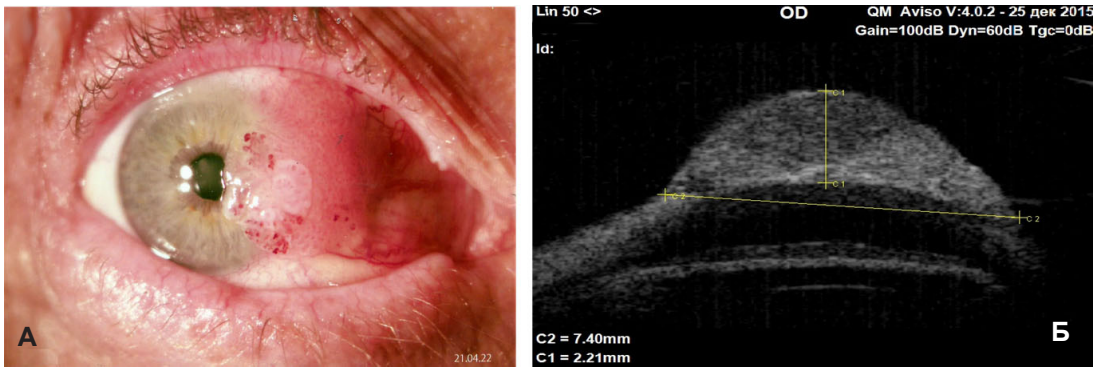

Рис. 2. А – карцинома кон'юнктиви склери і рогівки; Б – сонограма карциноми кон'юнктиви склери і рогівки.

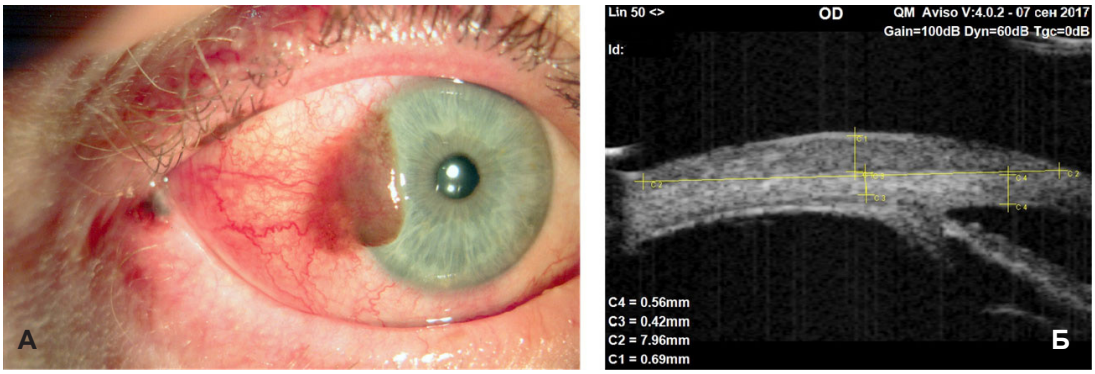

Рис. 3. А – Меланома кон'юнктиви склери і рогівки; Б – сонограма меланоми кон'юнктиви склери і рогівки.