Original Research Paper

Volume - 12 | Issue - 04 | April - 2022 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Ophthalmology

UVEITIC GLAUCOMA: RESULTS OF A RETROSPECTİVE CLİNİCAL, EPİDEMİOLOGİCAL AND ETİOPATHOGENETİC ANALYSİS

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ABSTRACT

Purpose - to evaluate the results of a comparative retrospective analysis of the clinical material of patients with uveal glaucoma (UG) based on the materials of the National Centre of Ophthalmology named after acad. Zarifa Aliyeva and branches of the Centre.

Material And Methods- A retrospective analysis of the clinical material was 1172 patients over the age of 18 years with uveitis and UG according to the five-year data of the National Centre of Ophthalmology named after acad. Zarifa Aliyeva, Masalli, Ganja branches and the data of the Sheki branch for two years of its functioning. Research methods: ophthalmic, laboratory, general clinical, statistical.

Results- The absolute number of patients with uveal pathology was 1172 (47.9% in the acute stage, 52.1% in the chronic stage). Out of all 1172 patients diagnosed with Uveitis, 581 (49.6%) were diagnosed with uveal ocular hypertension (UOH). There was no statistical difference when comparing the frequency of detection of UOH depending on the stage of the inflammatory process. Basically, out of 581 patients UOH was found with anterior uveitis (78.7%). Due to the use of special research methods (gonioscopy, tonometry, perimetry, optical coherence tomography, Heidelberg retinotomography), when changes in the optic nerve disc and the visual field were detected, uveal glaucoma has been diagnosed. UG out of all 1172 patients was found in 134 patients (11.4%), mainly in the chronic stage of the uveal process (67.2%). Despite persistent recommendations to patients at risk of developing UG about the need for re-treatment, in the overwhelming majority cases of late visits of patients in the stage of already advanced glaucoma were recorded - 40.3%, requiring radical surgical treatment to eliminate late organic secondary complications of uveitis.

Conclusion- In order to detect and treat UG in a timely manner, regular dynamic monitoring of patients with UOH is required both in the acute and in the chronic stages of the inflammatory process of the vascular tract.

KEYWORDS : uveitis, uveal glaucoma, uveal ophthalmic hypertension

INTRODUCTION

Uveitis with its secondary complications, being a polyetiological inflammatory disease of the vascular tract of the eye, is one of the common causes of low vision and blindness [1-3]. Uveal glaucoma (UG) – is one of the severe complications of uveitis, leading to the development of primary disability among the population of young, working age people [4,5]. The frequency of development of UG ranges from 10 to 60% in various etiopathogenetic groups of uveitis. At the same time, according to various data of modern literature, the proportion of UG among all nosological forms of glaucoma is 24-40%. An increase in intraocular pressure (IOP) in uveitis is due to the influence of various etiological factors and pathogenetic mechanisms and can be both a manifestation of uveal ophthalmic hypertension (UOH) and UG. Main differences between UG and UOH consist in the presence of glaucoma-specific changes in the optic nerve head (ONH) and visual field. Some authors also focus on the so-called uveal preglaucoma, in which there are scotomas in the field of view during stress tests and an increase in the blind spot during stress campimetric tests [6].

There are 3 main clinical forms of UG: closed-angle, open-angle, mixed. The stages of UG, the state of IOP and the stabilization of the process are classified in the same way as in primary glaucoma. The main problem of timely detection of hypertension in uveitis is associated with the focus of the ophthalmologist on the elimination of the inflammatory process. UG can occur both at the acute stage of the activity of the inflammatory process of the vascular tract, and in the late period of chronic uveitis, when signs of active inflammation are stopped. This necessitates long-term follow-up of patients after uveitis [7].

In connection with the foregoing, the study of the problem of detection, differential diagnostic examination, timely preventive, etiotropic, symptomatic treatment and dispensary observation of patients with UG is very relevant and has important social significance.

Purpose

To evaluate the results of comparative clinical, epidemiological and etiopathogenetic monitoring of uveal glaucoma based on the materials of the National Centre of Ophthalmology (NCO) named after acad. Zarifa Aliyeva and branches of the Center.

MATERIAL AND METHODS

To achieve the goal of the study, a retrospective analysis of the clinical material of patients over the age of 18 with uveitis and HS was carried out according to five-year data from the NCO named after academician Zarifa Aliyeva, Masally, Ganja branches and data from the Sheki branch for two years of its operation. The main database for the analysis was the 1C-EMS electronic patient registration system, which operates at the Center and corresponds to the clinical algorithm for outpatient admission and inpatient treatment of patients who apply.

Diagnostic research methods: ophthalmological, laboratory, general clinical, consultations of specialists (cardiologist, endocrinologist, rheumatologist, pulmonologist, dermatovenereologist, otolaryngologist, etc.).

Ophthalmological methods: biomicroscopy, fundus ophthalmoscopy, visometry, autorefractometry, tonometry (non-contact, Goldmann's, Maklakov's), gonioscopy, perimetry, optical coherence tomography (OCT), retinotomography according to Heidelberg, ultrasound A/B-scanning, photography of the fundus, electroretinography (ERG) and registration of visual evoked potentials (VEP), fluorescein angiography (FAG).

Laboratory methods: a general blood test with a detailed hemogram, a blood test for sugar and glycosylated hemoglobin, a coagulogram, a lipid and mineral spectrum, liver and kidney tests, rheumatic tests, serological reactions to detect possible infection with hepatitis B and C, syphilis, HIV infection, herpes, cytomegalovirus, toxoplasmosis, etc.

When classifying uveitis, data from the SUN project (Standartisation of Uveitis Nomenclature Project) were used. Statistical processing of data was carried out using the Excel program and the results were processed by methods of variation statistics.

RESULTS AND DISCUSSION

Table 1 presents the results of a summary assessment of the applying of patients with uveal pathology in the NCO named after academician Zarifa Aliyeva and the branches of the Centre in the acute and chronic stages. According to the analysis of the presented data, over the past five years, mainly patients with uveitis applied to the Center in Baku (794 patients – 67.8%), 19% (223 patients) – to the Masally branch, 9.5% (112) – to the Ganja branch. Over the past two years of functioning, 43 patients who were diagnosed with uveitis turned to the Sheki branch. When comparing the frequency of treatment of patients depending on the stage of the inflammatory process, it was found that the treatment of patients in the acute stage with a slight exaggeration was noted only in the Centre (in the acute stage - 50.6%, in the chronic – 49.4%). In all branches, the frequency of patient referrals in the chronic stage of the inflammatory process of the vascular tract

prevailed (Masally branch – 56.1%, Ganja – 60.7%, Sheki – 60.5%). On average out of 1172 patients with uveal pathology more than half (611 – 52.1%) referred for the first time to the Center and branches at the stage of chronic inflammation of the uveal tract. This is mainly due to patients coming to us after a certain course of symptomatic treatment in other medical institutions. When contacting the Centre and branches, the basis of the algorithm of our diagnostic study of patients with uveal pathology was to identify the main source that causes inflammation of the choroid, in order to carry out not only symptomatic, but also specific etiotropic treatment. However, during the initial treatment in the chronic stage, the elimination of the organic consequences of secondary complications of uveitis presents significant difficulties.

Table 1. Patients With Uveal Pathology In The Acute And Chronic Stages At The NCO Named After Acad. Zarifa Aliyeva And The Branches Of The Center (n, %)

	Number of patients diagnosed with Uveitis (n, %)	In the acute stage (n,%)	In the chronic stage (n,%)
NCO named after acad. Zarifa Aliyeva	794 (67,8)	402 (50,6)	392 (49,4)
Masally branch	223 (19,0)	98 (43,9)	125 (56,1)
Ganja branch	112 (9,5)	44 (39,3)	68 (60,7)
Sheki branch	43 (3,7)	17 (39,5)	26 (60,5)
Total	1172 (100)	561 (47,9)	611 (52,1)

Table 2 presents the comparative results of assessing the frequency of detection of UOH in patients with uveitis in the acute and chronic stages in absolute and relative proportions. On average, out of all 1172 patients who came to the Centre and branches with a diagnosis of uveitis, 581 (49.6%) had cases of increased intraocular pressure (IOP). The ratio of the frequency of detection of UOH cases depending on the stage of the inflammatory process of the vascular tract, on average, does not have a statistical difference: 50.1% – in the acute stage, 49.9% – in the chronic stage of uveitis.

Table 2. The Results Of The Assessment Of The Frequency Of Registration Of Uveal Ophthalmic Hypertension In Patients With Uveitis In The Acute And Chronic Stages (n, %)

	Number of patients with UOH (n, %)	In the acute stage (n,%)	In the chronic stage (n,%)
NCO named after acad. Zarifa Aliyeva	441 (55,5)	250 (56,7)	191 (43,3)
Masally branch	91 (40,8)	27 (29,7)	64 (70,3)
Ganja branch	37 (33)	10 (27)	27 (73)
Sheki branch	12 (27,9)	4 (33,3)	8 (66,7)
Total	581 (49,6)	291 (50,1)	290 (49,9)

The release of prostaglandins, expansion and increase in vascular permeability in uveitis leads to a violation of the hemato-ophthalmic barrier (HOB), which, in turn, leads to the penetration of blood cells and proteins into the chamber moisture and the vitreous body and, subsequently, to the formation of prerequisites for the development of UOH. The main pathogenetic causes of UOH are inflammatory edema of the drainage apparatus, excessive pigmentation of the Schlemm's canal zone, deposition of gelatinous exudate on the trabeculae, hypersecretion and changes in the composition of the intraocular fluid produced, organization of exudate in the anterior chamber angle, posterior and anterior synechiae, goniosinechia. However, it is not always possible to decide in each specific case what exactly led to the development of UOH – synechia, inflammatory damage to the drainage apparatus, hypersecretion of aqueous humor or organic changes in the iridocorneal angle. Very often we are faced with a combination of various factors listed above. UOH often develops in anterior uveitis. In our study, out of 581 patients with increased IOP, 457 UOH were diagnosed with anterior uveitis (78.7%), 85 with panuveitis (14.6%), 39 with intermediary uveitis (6,7%). UOH can be transient, non-permanent, amenable to antihypertensive treatment and does not affect the state of the ONH. In the case of persistent UOH, leading to a violation of the ONH and visual field, various forms of UG develop. The following table (Table 3) shows the results of registering the incidence of UG in patients after UG against the background of persistent UOH.

The first column shows, in absolute and relative proportions, the rates of detection of cases of UG among all patients with identified uveal pathology. The second and third columns show the indicators of detection of UG depending on the stage of activity of the inflammatory process of the choroid. Of all 1172 patients who referred to the Centre and branches with a diagnosis of uveitis, UG was diagnosed in 134, which is an average of 11.4%. Comparing the data in the second and third columns, it should be noted that both in the Centre and in the branches, UG developed mainly in the chronic stage of the uveal process (67.2%). Cases of registration of UG in the acute stage were noted during relapses of chronic uveitis, against the background of already existing glaucoma-specific organic changes in the drainage system, which impede the outflow of intraocular moisture.

Table 3. The Results Of Assessing The Frequency Of Registration Of Uveal Glaucoma (UG) In Patients With Uveitis In The Acute And Chronic Stages (n, %)

	Number of patients with UG (n, %)	In the acute stage (n,%)	In the chronic stage (n,%)
NCO named after acad. Zarifa Aliyeva	97 (12,2)	34 (35,1)	63 (64,9)
Masally branch	22 (9,9)	6 (27,3)	16 (72,7)
Ganja branch	10 (8,9)	2 (20)	8 (80)
Sheki branch	5 (11,6)	2 (40)	3 (60)
Total	134 (11,4)	44 (32,8)	90 (67,2)

Of the 134 patients with UG, 76 (56.7%) were female, 58 (43.3%) were male. Of these, born in 2003-1990 – 22 (16.4%), 1989-1970 – 52 (38.8%), 1969-1940 – 60 patients (44.8%).

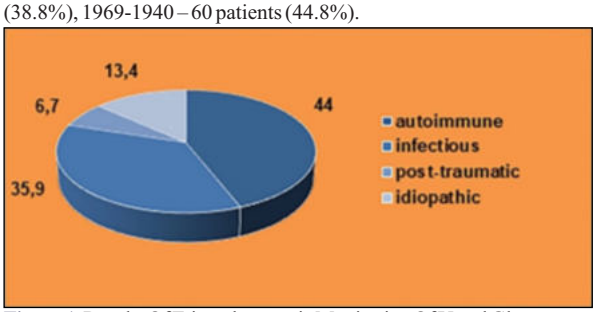

Figure 1. Results Of Etiopathogenetic Monitoring Of Uveal Glaucoma

Figure 1 presents the results of the etiopathogenetic analysis of uveitis, the secondary complication of which was UG in this study. The main cause of uveitis was systemic autoimmune diseases (59 patients, 44%): rheumatoid arthritis, Behcet's disease, reactive arthritis, ankylosing spondylitis, Harada's uveitis, sarcoidosis, autoimmune thyroiditis. Uveitis of infectious origin (herpesvirus infection, tuberculosis, HIV), complicated by secondary UG, was diagnosed in 48 patients (35.9%). UG as an outcome of post-traumatic uveitis was found in 9 (6.7%) patients. In the remaining 18 patients (13.4%), the etiology of uveitis could not be determined – idiopathic uveitis.

Figure 2 presents the results of a comparative assessment of patients with UG depending on the state of the iriocorneal angle. Of the 97 patients with UG in Baku, 53 (54.6%) patients had closed-angle glaucoma (CAG), 44 (45.4%) had open-angle glaucoma (OAG). In the Masally branch: out of 22 patients - 14 (63.6%) with CAG, 8 (36.4%) – with OAG; in Ganja, out of 10 – 4 (40%) with CAG, 6 (60%) – with OAG; in Sheki, out of 5 – 3 (60%) with CAG, 2 (40%) – with OAG. Overall, of the 134 patients with UG, 74 (55.2%) had CAG, and 60 (44.8%) had – OAG.

Table 4 presents the results of assessing the distribution of patients by stages of glaucoma detected in them. As it can be seen from the table, both in the group of patients with CAG and in the group with OAG, the prevailing majority were cases of treatment of patients in moderate (II) – 29.9% and advanced (III) stages of glaucoma – 40.3%. The initial stage of glaucoma was registered in 11.9%, the terminal stage – in 17.9% of cases of detection of UG. The results obtained allow us to conclude that the late treatment of patients in the stage of already developed or advanced glaucoma prevails. Patients with UOH upon discharge from inpatient treatment received recommendations on the use of appropriate antihypertensive treatment and the need for re-treatment to monitor the possible risk of transition from UOH to UG. Unfortunately, not all patients strictly follow these recommendations, which complicates the further treatment of UG.

UG was treated with conservative medical, laser and surgical methods. Medical treatment was carried out with antihypertensive drops (beta-blockers, carbonic anhydrase inhibitors). The effectiveness of drops in UG was noted mainly in the initial stages of UG at an IOP level not higher than 30-32 mm Hg, with the possibility of constant dynamic monitoring of patients.

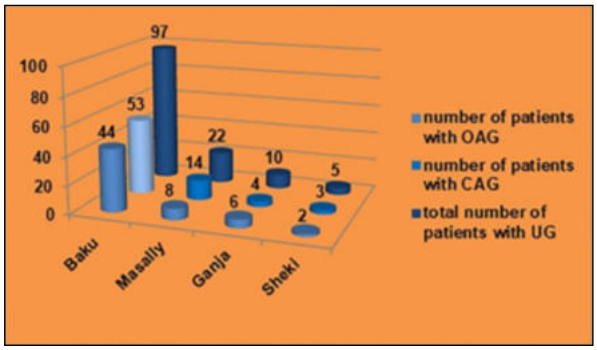

Figure 2. Distribution Of Patients With UG Depending On The State Of The Anterior Chamber Angle

With the ineffectiveness of conservative treatment, laser iridectomy was used (32 patients, 23.9%). Given the possibility of exacerbation of the uveal process after abdominal surgery, surgical methods of treatment (sinus trabeculoectomy (21 patients (15.7%), insertion of a drainage implant (27 patients (20.1%)) were resorted with the failure of laser therapy, as with organic lesions of the drainage apparatus in UG, surgical intervention was a pathogenetic resolution of this pathology.

Table 4. The Results Of Assessing The Distribution Of Patients By Stages Of UG (n, %)

	Patients with CAG (n, %)	Patients with OAG (n, %)	Total
Initial stage, I	9 (12,1)	7 (11,7)	16 (11,9)
Moderate stage, II	23 (31,1)	17 (28,3)	40 (29,9)
Advanced stage, III	31 (41,9)	23 (38,3)	54 (40,3)
Terminal stage, IV	11 (14,9)	13 (21,7)	24 (17,9)
Total	74 (55,2)	60 (44,8)	134 (100)

Below is an example of a clinical case of one of these patients treated at the Centre.

Patient S.Z., born in 1990, referred to the Centre for the first time in December 2020. Complaints of decreased vision, pain, lacrimation and photophobia of the left eye. From the anamnesis: he has been suffering since 2017, he is treated irregularly, over the past year he has noted an exacerbation for the second time. In March 2020, he referred for treatment at the polyclinic at the place of residence, received outpatient treatment, applied antihypertensive drops from a number of prostaglandins. This exacerbation of the disease is associated with a two-week acute respiratory disease with a rash of blisters on the upper lip. Suffering from rheumatoid arthritis, treated by a rheumatologist irregularly. At the initial contact with us, the visual acuity of the right eye was 0.2 with a correction of 1.0, the visual acuity of the left eye was 0.02 with a correction of 0.09. IOP according to Goldmann on the right eye 15 mm Hg, on the left 38 mm Hg. Ophthalmological status of the right eye: the adnexa is normal, the cornea is transparent, the anterior chamber is of normal depth, the moisture of the anterior chamber is clean, the pupil is round, it reacts vividly to light, the passing media are transparent, the fundus is without pathology. Ophthalmological status of the left eye: slightly edematous eyelids, corneal edema, small precipitates on the corneal endothelium, deep anterior chamber, turbid moisture in the anterior chamber, irregularly shaped pupil, poorly responsive to light, exudative film in the pupil area, underlying departments are not visualized. Ultrasound B-scan of the left eye: the membranes are adjacent, floating opacities in the vitreous body, excavation is traced in the region of the optic nerve head.

Electrophysiological study, registration of visual evoked potentials (pattern): the right eye is normal, the left eye - the latency of the P100 component is at the upper limit of the norm, the amplitude is reduced, the number of functional fibers is reduced. General examinations were carried out (general blood test with a detailed hemogram, blood test for sugar and glycosylated hemoglobin, coagulogram, lipid and mineral spectrum, liver and kidney tests, rheumatic tests, serological reactions to detect possible infection with hepatitis B and C, syphilis, HIV-infection, herpes, cytomegalovirus, toxoplasmosis, chest x-ray, ultrasound of internal organs, ECG). Abnormalities were found in the laboratory parameters of rheumatic tests and serological results of studies of antibodies of herpes virus infection: (C-reactive protein - 96 mq / l (N - 0-6 mq / l), rheumatoid factor 24 BV / ml (N - 0-12 BV / ml), antistreptolysin - 400 (N - 0-200 BV/ml), IgG Herpes 1+2 - 32.1 NV (N - ≤ 9 NV), CMV IgG - 19.8 BV/ml (N - ≤ 9 BV /ml).

Diagnosis: Mild myopia in both eyes. Acute uveitis of the left eye of rheumatic origin with associated herpes virus infection.

To clarify the diagnosis of the presence of uveal glaucoma in the left eye, it is recommended to conduct an examination of the fundus during its visualization, gonioscopy, perimetry, OCT, or Heidelberg retinotomography.

The patient was consulted by a rheumatologist, an infectious disease specialist. Appropriate general and local anti-inflammatory treatment with the use of antihypertensive drops was prescribed. Two weeks later, the ophthalmological status of the left eye: visual acuity – 0.05 with a correction of 0.3, IOP according to Goldmann on the right eye 12 mm Hg, on the left 36 mm Hg. The adnexa is normal, slight corneal edema, the precipitates have resolved, the anterior chamber is deep, the moisture of the anterior chamber is clean, the pupil is irregular in shape, the light reacts poorly, the exudative film in the pupil area has resolved, there are slight opacities in the vitreous body, the optic disc is pale, the boundaries are clear, CDR - 0.8, the macular reflex is erased, the arteries are narrowed. Goniscopy revealed synechia in the iridocorneal angle (Figure 3). Ultrasound B-scan of the left eye: the membranes are adjacent, slight opacities in the vitreous body, extended excavation in the region of the optic nerve head.

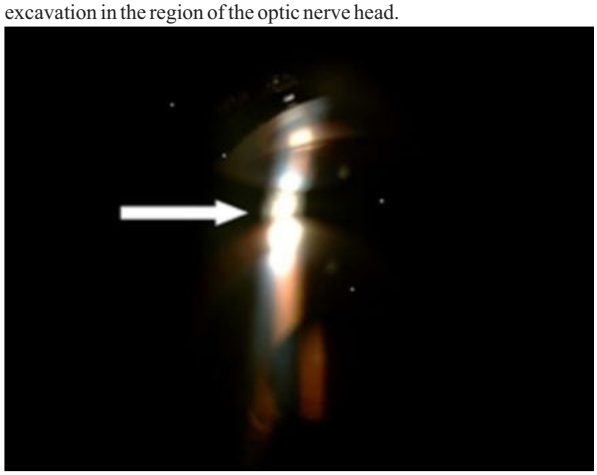

Figure 3. Photo Registration Of Gonioscopy Of The Patient S.Z. (synechia are indicated by an arrow)

OCT of the left eye showed a sharp decrease in the thickness of the retinal nerve fiber layer and the ganglion cell layer in the macula region (Figure 4), as well as a moderate thinning of the peripapillary layer of retinal nerve fibers. It is necessary to note changes in the parameters of the optic nerve head on OCT, namely, a decrease in the area of the rim (Rim Area = 0.63), an increase in the linear and vertical E/D ratios (cup/disc) (Linear CDR = 0.82, Vertical CDR = 0, 75) and, accordingly, an increase in the value of the excavation volume (Cup Volume = 0.27) (Figure 5).

These changes indicate glaucomatous atrophy of the optic nerve head. In the right eye, the OCT parameters were within the normal range. According to the perimetry data, a concentric narrowing of the field of view within 10-15 degrees was observed in the left eye.

These changes indicate glaucomatous atrophy of the optic disc. In the right eye, the OCT parameters were within the normal range. According to the perimetry data, a concentric narrowing of the field of view within 10-15 degrees was observed in the left eye.

Final clinical diagnosis: Mild myopia in both eyes. Uveitis of the left eye. Uveal glaucoma of the left eye of the III degree.

Surgery with a drainage implant was recommended. Given the recent acute nature of the inflammatory process, YAG laser iridectomy was

performed prior to intraocular surgery to possibly achieve a temporary reduction in IOP. However, it was not possible to achieve a stable decrease in IOP. Two weeks later, antiglaucoma surgery was performed on the left eye with the introduction of a drainage valve. After 3 months, during the patient's repeated visit, IOP in the left eye was 17 mm Hg, visual acuity was 0.2 with correction, the eye was calm. The patient was taken to the dispensary.

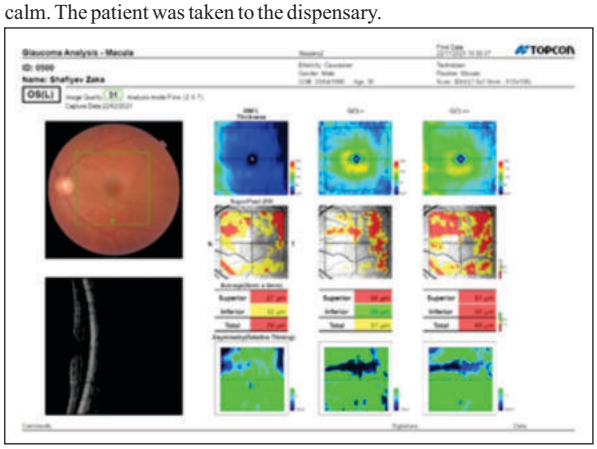

Figure 4. OCT left eye (macula)

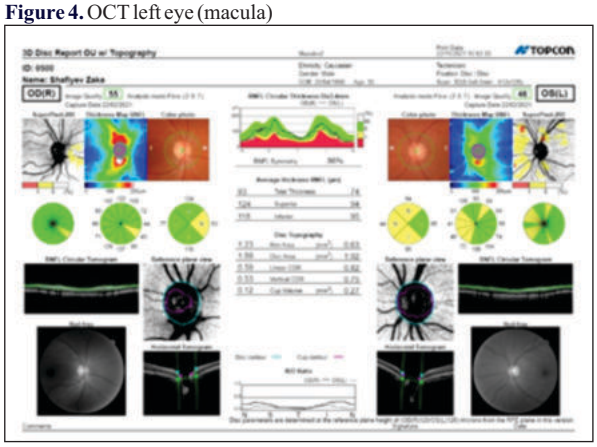

Figure 5. OCT (Disc report OU topography)

CONCLUSIONS

1. Uveal glaucoma of all 1172 patients with uveitis was found in 134 patients (11.4%), mainly in the chronic stage of the uveal process (67.2%).

2. In the prevailing majority, there were cases of late visits of patients in the stage of already advanced glaucoma – 40.3% ($p \leq 0.05$), requiring radical surgical methods of treatment to eliminate late organic secondary complications of uveitis.

3. For the purpose of timely detection and treatment of uveal glaucoma, constant dynamic monitoring of patients with uveal ophthalmic hypertension, both in the acute and chronic stages of the activity of the inflammatory process of the vascular tract, is necessary.

Conflict of Interest

The authors declare no conflict of interest.

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