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The uveitis–glaucoma–hyphema syndrome. Part 1. Pathogenesis, clinical features, diagnosis

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ABSTRACT

BACKGROUND: The uveitis–glaucoma–hyphema (UGH) syndrome was first described in 1978 as a complication of anterior chamber polymethyl methacrylate intraocular lenses implantation. Introduction into practice of foldable intraocular lenses with intracapsular fixation has reduced the incidence of UGH. However, this complication still occurs today, especially with extracapsular intraocular lens fixation.

AIM: The aim of this study is to describe "uveitis–glaucoma–hyphema" syndrome pathogenesis, clinical features, and diagnosis.

MATERIAL AND METHODS: A retrospective analysis of medical data for 2017–2021 identified 100 patients (101 eyes) diagnosed with UGH syndrome, they made up the study group. Complaints, medical history, biomicroscopy, visual acuity and intraocular pressure were assessed. 37 patients underwent anterior segment ultrasound biomicroscopy using the Accutome UBM Plus (USA).

RESULTS: The occurrence of UGH syndrome is at least 0.19%. The leading UGH syndrome risk factor was intraocular lens material. In 49% of cases these were AcrySof hydrophobic intraocular lenses. The second UGH risk factor was extracapsular (mixed and sulcus) intraocular lens fixation, occurring, according to ultrasound biomicroscopy, in 54 and 19% of cases, respectively. The most significant diagnostic UGH sign was hyphema (93%). Ocular hypertension was detected in 66%, and uveitis in 57% of cases.

CONCLUSIONS: The main UGH syndrome manifestations are hyphema and iris transillumination after phacoemulsification complicated by posterior capsule rupture with extracapsular hydrophobic intraocular lens fixation. The most informative instrumental method to assess intraocular lens position is ultrasound biomicroscopy.

Keywords: phacoemulsification; intraocular lens; complication; Ellingson syndrome; uveitis–glaucoma–hyphema syndrome; glaucoma; vitreous hemorrhage; ultrasound biomicroscopy.

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Синдром «увеит – глаукома – гифема». Часть 1. Патогенез, клиника, диагностика

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АННОТАЦИЯ

Актуальность. Синдром «увеит – глаукома – гифема» (УГГ) впервые описан в 1978 г. как осложнение имплантации переднекамерных полиметилметакрилатных интраокулярных линз. Внедрение в практику гибких интраокулярных линз с внутрикапсульной фиксацией снизило частоту возникновения УГГ. Однако это осложнение встречается и сегодня, особенно при внекапсульной фиксации.

Цель — описание патогенеза, клинической картины и диагностики синдрома «увеит – глаукома – гифема».

Материалы и методы. Ретроспективный анализ данных историй болезни за 2017–2021 гг. выявил 100 пациентов (101 глаз) с диагнозом УГГ, которые составили исследуемую группу. Оценивались жалобы, анамнез, результаты биомикроскопии, а также острота зрения и внутриглазное давление, 37 пациентам выполнялась ультразвуковая биомикроскопия переднего отрезка на приборе Accutome UBM Plus (США).

Результаты. Встречаемость УГГ составляет не менее 0,19 %. Ведущим фактором риска УГГ оказался материал интраокулярных линз. В 49 % случаев это были гидрофобные линзы на платформе AcrySof. Вторым по значимости фактором риска УГГ стала внекапсульная (смешанная и сулькусная) фиксация интраокулярной линзы, встречающаяся, по данным ультразвуковой биомикроскопии, в 54 и 19 % случаев соответственно. Наиболее значимым диагностическим признаком УГГ оказалось наличие гифемы (93 % случаев). Офтальмогипертензия определялась у 66 %, а увеит — у 57 % пациентов.

Заключение. Основные проявления УГГ — гифема и трансиллюминация радужки у пациента после осложнённой разрывом задней капсулы факоэмульсификации с внекапсульной фиксацией гидрофобной интраокулярной линзы. Наиболее информативным инструментальным методом оценки положения интраокулярной линзы является ультразвуковая биомикроскопия.

Ключевые слова: факоэмульсификация; интраокулярная линза; осложнение; синдром Эллингсона; синдром «увеит – глаукома – гифема»; глаукома; кровоизлияние в стекловидное тело; ультразвуковая биомикроскопия.

Как цитировать

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BACKGROUND

The uveitis–glaucoma–hyphema (UGH) syndrome was first described in 1978 as a complication of anterior chamber polymethyl methacrylate intraocular lens (IOL) implantation occuring due to traumatization of the iris by them [1]. The introduction into everyday clinical practice of foldable IOLs with intracapsular fixation significantly decreased the prevalence of the UGH syndrome [2, 3], which reached about 2% during the 1980s [4]. However, this complication is still encountered by today, first of all, by compromised capsular support driving to implant the IOL into the ciliary sulcus [5].

The generally accepted main UGH manifestations are the opalescence and cells in the anterior chamber fluid, ocular hypertension, hyphema, iris transillumination, vitreous hemorrhage, macular edema [6–8]. Such combination of manifestations is often interpreted as idiopathic anterior uveitis leading to the prescription of only medical anti-inflammatory and hypotensive treatment not influencing the cause of the disease, and having a temporary effect [9, 10]. The unintentional abandonment from appropriate surgical treatment focused on elimination of mechanical iris and ciliary body traumatization by the intraocular lens is fraught with secondary glaucoma development due to recurrent hemorrhages [11].

Based on the above, *the aim of the present study* is in description of the algorithm of the UGH diagnosis, based upon the characteristic combination of symptoms and clinical signs as well as upon the most informative complementary examination methods.

MATERIALS AND METHODS

The study was carried out in the Ophthalmology centre of the Saint Petersburg City Budget Healthcare Institution "City multifield hospital No. 2", where during 2017–2021, within the obligatory medical insurance, 52,443 patients were operated with following diagnoses according to the ICD-10: H25.0 (Incipient age-related cataract), H26.2 (Complicated cataract), H27.0 (Aphakia), as well as T85.2 (Complication of mechanical nature related to the intraocular lens).

From 1101 patients, treated for conditions coded as T85.2, in 100 people (38 of them being women) aged 74.37 ± 9.95 years, the UGH syndrome was revealed, being bilateral in one patient.

Analyzing case histories, complaints were evaluated (visual acuity loss, pain, photophobia, ocular redness, floaters in the visual field), ophthalmological history (presence of glaucoma, pseudoexfoliative syndrome, cataract extraction on the background of capsular support weakness, ocular injuries preceding crystalline lens surgery, implanted IOL's model, intraoperative complications, time from the cataract extraction until the first UGH symptoms), biomicroscopy results (presence of hyphema, opalescence and cells in the anterior chamber fluid, vitreous hemorrhage, IOL position), data of objective examination (visual acuity testing, Maklakov applanation tonometry). Best corrected visual acuity (BCVA) and intraocular pressure (IOP) were taken into consideration at the first hospital admission and at the concluding control examination.

Instrumental examinations were performed if indicated: biometrey for the IOL calculation (n = 53) using IOL–Master 500 (Carl Zeiss, Germany) and Biometer Al100 (Tomey, Japan), sonography of the vitreal cavity (n = 81) in the B-scan regimen (Ultrasonic B scanner UD8000, Tomey, Japan) and ultrasound biomicroscopy (UBM) of the anterior segment (n = 37) using the Accutome UBM Plus (USA).

Non-inclusion criterion was a traumatic or dystrophic IOL dislocation, which did not cause the UGH development.

Statistical analysis

Based on the case history analysis of patients with the UGH syndrome, a database in Microsoft® Excel (Version 16.72) was created. Statistical analysis was performed using the Jamovi program (Version 2.2). Methodsof descriptive statistics were applied using mean value (*M*), median (*Me*), and standard deviation (*SD*). Since the number of patients in the study group was 100 (101 eyes), in translation of numerical parameters (n) into ratio of a part to the whole (%), there was a quite predictable practically near-complete agreement between them (n ≈%). In comparison of normally distributed samples, the t-criterion for paired samples was used. In comparison of rated values, a binominal logistic regression was used (McFadden determination factor). At $p \leqslant 0.05$, the differences were estimated as significant ones.

At statistical data analysis, visual acuity equal to light perception (both with correct and with incorrect light projection) was considered equivalent to 0.0001 in decimal values, and blindness — to 0.

RESULTS

The UGH prevalence was 0.19% among all patients treated for cataract during the five-year period — from 2017 through 2021.

In the table 1, main clinical manifestations of the UGH in patients of the study group are shown.

On the Figure 1, the fractions of various IOL models leading to the UGH syndrome development are demonstrated. Conspicuous is the fact that most often (49%) the UGH syndrome was associated to hydrophobic IOLs on the AcrySof platform.

In the table 2, the results are shown of the UBM of the anterior segment performed in 37 patients of the

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Table 1. Subjective symptoms and clinical features of patients with uveitis–glaucoma–hyphema syndrome (*n* ≈ %)

Таблица 1. Субъективные симптомы и клинические признаки синдрома «увеит – глаукома – гифема» у пациентов исследуемой группы (*n* ≈ %)

Parameter	Value, *n*
Visual acuity decrease	101
"Fogging" of vision	96
Pain in the eye	43
Photophobia	46
Ocular redness	65
Floaters in the visual field	52
Cellular suspension and opalescence of the anterior chamber fluid	57
Ocular hypertension	66
Hyphema	93
Vitreous hemorrhage	52
Presence of glaucoma	57
Presence of pseudoexfoliative syndrome	37
Zonular weakness before surgery	20
Injury preceding cataract extraction	10
Intraocular lens position (according to biomicroscopy data):	
• In the capsular bag	63
• In the ciliary sulcus	16
• Mixt fixation	13
• Pupillary fixation	9
Intraoperative complications:	
• Absence	82
• Rupture of the posterior capsule	18
• Zonulodialysis	1
Vitreous status:	
• Preserved	97
• Avitria	4
Intraocular lens model:	
• AcrySof	49
• Not established	41
• T-19	3
• Akreos Adapt AO	3
• Leuco sapphire S-7	2
• RSP-3	1
• T-26	1
• Zeiss Asphina 404	1
Time to uveitis-glaucoma-hyphema syndrome development, years, *M* + *SD* (*Me*)	7.72 ± 5.77 (7.00)
Axial length of the eyeball, mm, *M* ± *SD* (*Me*)	24.09 ± 1.20 (24.00)
Best corrected visual acuity, *M* ± *SD* (*Me*):	
• Upon admission	0.25 ± 0.29 (0.10)*
• At the final control examination	0.43 ± 0.31 (0.40)*
Intraocular pressure, mm Hg, *M* ± *SD* (*Me*):	
• Upon admission	25.30 ± 5.10 (26.00)*
• At the final control examination	18.38 ± 2.86 (18.00)*

* $p < 0.001$

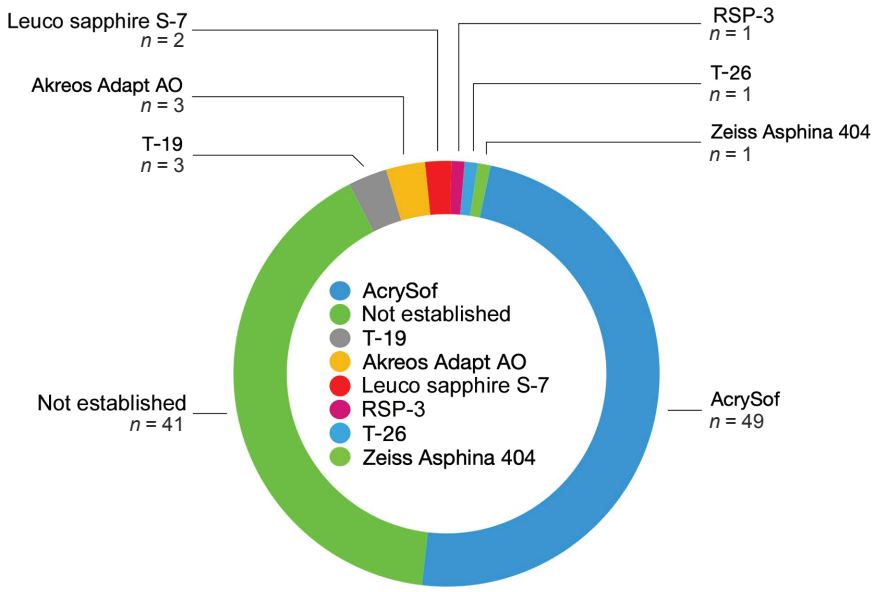

Fig. 1. Models of intraocular lenses which caused uveitis–glaucoma–hyphema syndrome in patients of the study group
Рис. 1. Модели интраокулярных линз, вызвавших развитие синдрома «увеит – глаукома – гифема» у пациентов исследуемой группы

Table 2. Anterior segment ultrasound biomicroscopy data of 37 patients of the study group
Таблица 2. Данные ультразвуковой биомикроскопии переднего отрезка 37 пациентов исследуемой группы

Parameter	*n*, (amount, %)
Fibrosis of the capsular bag	27 (73)
Soemmering's ring	9 (24)
Tilt of the intraocular lens	22 (59)
Intraocular lens position:	
• In the capsular bag	10 (27)
• In the ciliary sulcus	7 (19)
• Mixt fixation	20 (54)

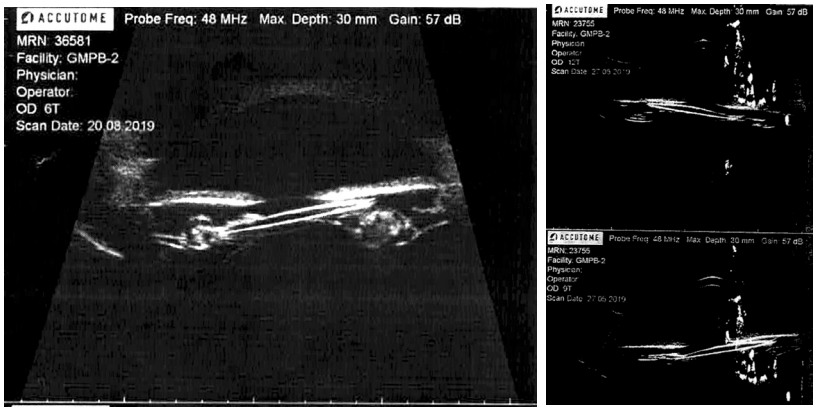

Fig. 2. Typical S-shaped single piece IOL position leading to uveitis–glaucoma–hyphema syndrome development. Tilt of optical part with haptic element displacement into the ciliary sulcus
Рис. 2. Типичное положение S-образной интраокулярной линзы, приводящее к развитию синдрома «увеит – глаукома – гифема». Наклон оптической части со смещением гаптического элемента в борозду цилиарного тела

study group. The Figure 2 demonstrates a typical position of the S-shaped IOL leading to the UGH syndrome development.

In the table 3, the differential diagnosis of various diseases with the UGH syndrome is presented.

DISCUSSION

The prevalence of the UGH syndrome among patients operated at the Saint Petersburg City Budget Healthcare Institution "City multifield hospital No. 2" is no less

Table 3. Differential diagnosis of uveitis–glaucoma–hyphema syndrome with other diseases
Таблица 3. Дифференциальная диагностика синдрома «увеит – глаукома – гифема» с другими заболеваниями

Parameter	Uveitis–glaucoma–hyphema syndrome	Herpetic uveitis	Neovascular glaucoma	Dystrophic intraocular lens dislocation
Hyphema	+++	+/–	++	–
Ocular hypertension	++	++	+++	–
Uveitis	++	+++	–	–
Iris transillumination	+++	++	–	–
Vitreous hemorrhage	++	–	+	–
Intraocular lens malposition	++	–	–	+++

Note. Prevalence of signs: (–) — absence, (+/–) — possibly, (+) — rare (++) — often, (+++) — very often.

than 0.19%. Thus, this disease is registered much more rarely than a dystrophic or traumatic dislocation of the "IOL-capsular bag" complex (0.5–3.0%, according to literature data [12]).

The median of the time of the UGH syndrome development after cataract extraction is 7 years (variation limits — from 8 months to 28 years), this coincides with the results of other authors [10].

Evaluating the ophthalmologic history, the attention is driven to the presence of glaucoma in 57% of patients, what is significantly higher than its prevalence among people of 40–80 years equal to 3.54% [13, 14]. The pseudoexfoliative syndrome, to the contrary, is found only in 37% of study participants, whereas its prevalence in our region reaches 57% [15]. Preoperative zonular weakness manifesting itself by iridophakodonesis, was revealed in 20% of cases. It is also worth noting a sufficiently high amount (10%) of traumatic cataracts.

The leading factors associated to the development of the UGH syndrome appeared to be the material from which the IOL is produced and the design of its rim. In the half of cases, it were hydrophobic lenses on the AcrySof platform, what aligns with literature data [16]. The iris traumatization is quite likely conditioned by the friction of the square edge of the optic and the haptic parts of given IOL models [17]. Much more rarely (4% of observations), the cause of the UGH syndrome was a fixation of the hydrophilic IOL Akreos Adapt AO in the ciliary body sulcus. Finally, in single cases, the UGH syndrome was associated with domestic IOLs (polymethyl methacrylate T-19, T-26, RSP-3, leuco sapphire S-7), which predominated in the time of intra- and extracapsular cataract extraction.

As the second significant major risk factor for the UGH syndrome development appeared the extracapsular (mixt and sulcus) IOL fixation encountered, according to UBM data, in 54 and 19% of cases, correspondingly. A not rare cause for alternative intracapsular IOL fixation methods is the rupture of the posterior capsule, the prevalence of which (18%) in the study group, by an order of magnitude exceeded its mean prevalence in cataract surgery — 1.8% [18].

The mechanism of iris traumatization in extracapsular IOL position is obvious, as opposed to UGH syndrome development in endocapsular IOL position established in 27% of patients. The UBM data analysis allowed revealing a typical for S-shaped IOLs angulation of the haptic element leading to the slope of the artificial lens (59%) and to the subsequent migration its haptic element into the ciliary body sulcus which is conditioned by the capsular bag fibrosis and Soemmering's ring formation (Figure 3). In some cases, an extruding of the IOL's optic from the capsular bag occurred with preservation of it's the position of haptic elements in the crystalline lens bag.

Most common complaints of patients were visual acuity decrease (100%) and "fogging" of vision (96%). In most patients (65%), there was ocular redness, 52% mentioned floaters, having a significant relation to vitreous hemorrhage (R^2 = 0.675, p < 0.001). Somewhat more rarely, patients presented complaints on photophobia (46%) and pain in the eye (43%). Altogether, the described subjective symptoms of the UGH syndrome corresponds to literature data [10].

At examination, in the overwhelming majority of patients hyphema was revealed (93%), in 2/3 — ocular hypertension (66%), in a half (52%), there was a vitreous hemorrhage. Uveitis was revealed in 57% of cases. Unfortunately, in none of the case histories iris transillumination was mentioned, in spite of the fact that this sign is encountered in the UGH syndrome extremely frequently — up to 90% [10] (Figure 3).

Thus, the UGH syndrome by no means obligatory suggests the presence of a classic triad "uveitis–glaucoma–hyphema". The most significant diagnostic sign of this disease appeared to be the presence of blood in the anterior chamber fluid. No less important criterion is the iris transillumination. It could also be a sign of herpetic uveitis, but develops by this condition significantly more rarely than in the UGH syndrome (40 and 90%, correspondingly) [10]. Moreover, the combination of

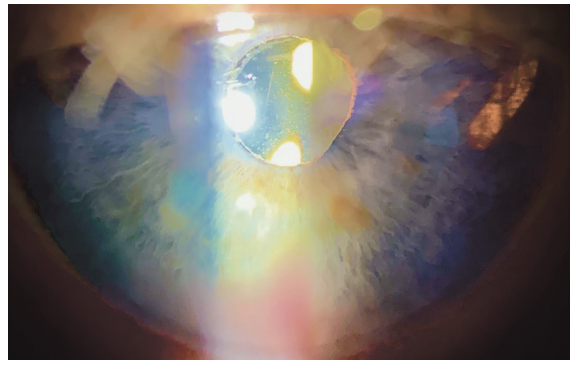

Fig. 3. Iris transillumination in haptic-iridal contact zone, microhyphema
Рис. 3. Трансиллюминация радужки в зоне её контакта с гаптическим элементом интраокулярной линзы, микрогифема

iris transillumination and hyphema in a pseudophakic eye makes the differential diagnosis of these two conditions substantially more easy.

Encountered in the UGH syndrome cellular suspension in the anterior chamber fluid may consist both from leucocytes, which left the circulatory bed due to increased permeability of the blood-aqueous barrier caused by the mechanical action of the IOL on the iris and/or ciliary body, and from lysed red blood cells, practically undistinguishable from leucocytes at biomicroscopy. For this reason, the biomicroscopic signs of anterior uveitis (fluorescence of the anterior chamber fluid and suspension of cells) are not to be considered as key-signs of the UGH syndrome.

The increase of intraocular pressure also cannot pretend to play a role of a leading criterion for the UGH syndrome diagnosis, and only complements the above mentioned signs.

CONCLUSIONS

Thus, the main manifestations of the uveitis–glaucoma–hyphema syndrome are hyphema and iris transilluminations in a patient after a phacoemulsification complicated by the posterior capsule rupture, with hydrophobic IOL extracapsular fixation. In 66 and 57% of cases, the clinical picture is complemented by ocular hypertension and anterior uveitis. Most informative imaging method for IOL position evaluation is the ultrasound biomicroscopy [19].

ADDITIONAL INFORMATION

Authors' contribution. All authors have made a significant contribution to the development of the concept, research, and preparation of the article, as well as read and approved the final version before its publication. Personal contribution of the authors: D.F. Belov — study concept and design, writing, statistical data processing, literature review; V.P. Nikolaenko — writing, literature review; D.A. Shuvaev — data collection and processing, literature review; V.V. Potemkin — study concept and design, writing, literature review, surgical interventions; K.V. Khripun — text writing, surgical interventions; I.V. Terekhova — text writing, diagnostic studies.

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Competing interests. The authors declare that they have no competing interests.

ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Вклад каждого автора: Д.Ф. Белов — концепция и дизайн исследования, написание текста, статистическая обработка данных, обзор литературы; В.П. Николаенко — написание текста, обзор литературы; Д.А. Шуваев — сбор и обработка данных, обзор литературы; В.В. Потемкин — концепция и дизайн исследования, написание текста, обзор литературы, проведение хирургических вмешательств; К.В. Хрипун — написание текста, проведение хирургических вмешательств; И.В. Терехова — написание текста, диагностические исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

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