• Clinical Research •

Surgical management of uveitis-glaucoma-hyphema syndrome

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Abstract

● **AIM:** To report outcomes of patients after intraocular lens (IOL) repositioning or exchange for the version of the uveitis-glaucoma-hyphema (UGH) syndrome that does not include closed loop anterior chamber IOL (nUGH).

● **METHODS:** Chart review of patients with nUGH who underwent IOL repositioning or exchange by one surgeon were reviewed. The main outcome measures were best corrected visual acuity (BCVA) as a decimal fraction preoperatively and postoperatively after IOL repositioning or exchange. Clinical findings evaluated included the presence of uveitis, hyphema, elevated intraocular pressure (IOP), and other complications such as pigment dispersion or vitreous hemorrhage. The number of anti-inflammatory and glaucoma medications were assessed before and after IOL repositioning or exchange.

● **RESULTS:** The study included 14 pseudophakic eyes. The median time at the onset of contemporary UGH after cataract extraction and IOL implantation (CE/IOL) was 7.5y. IOL repositioning or exchange was performed at a mean duration of 8.1±4.7mo (median: 4mo) after onset of UGH. The mean BCVA was improved from 0.45±0.26 preoperatively after onset of UGH syndrome to 0.76±0.22 (*P*=0.016) after IOL repositioning or exchange. Among the 14 eyes, uveitis, elevated IOP, and hyphema were present preoperatively in 13, 13, and 6 eyes, respectively. Uveitis and hyphema resolved in all cases after IOL surgery. The mean IOP was reduced from 26.4±4.5 mm Hg preoperatively to 14.7±4.9 postoperatively (*P*=0.01). The mean number of glaucoma medications used was reduced from 1.7±1.1 medications preoperatively to 0.8±1.08 (*P*=0.04) postoperatively.

● **CONCLUSION:** IOL repositioning or exchange is an effective treatment in many cases for medically resistant contemporary UGH syndrome.

● **KEYWORDS:** intraocular lens complications; secondary glaucoma; vitrectomy

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INTRODUCTION

Uveitis-glaucoma-hyphema (UGH) syndrome, in its initial description, was the now rare tripartite postoperative complication. Its name describes that occurred after cataract extraction and rigid anterior chamber intraocular lens implantation (CE/IOL)[1-2]. Ellingson[1] first described this syndrome in 1978 as a complication of the rigid, closed loop anterior chamber (AC) intraocular lens (IOL) haptics applying mechanical trauma to the adjacent uveal tissue, resulting in iris erosion with subsequent intraocular inflammation, hyphema, and elevated intraocular pressure (IOP). This phenomenon, if untreated, progressed to glaucomatous optic neuropathy[1-2]. AC IOL explantation was recommended in these cases. Redesigned AC IOLs and the overwhelming prevalence of posterior chamber (PC) IOLs have greatly decreased its incidence. However, a newer form of UGH (nUGH), sharing many of the same clinical signs and pathophysiology, can occur with AC and PC IOLs now in use; while this seems to be well recognized, anecdotally, the literature is sparse in its description and treatment. This was first reported for 3-piece sulcus placed IOLs as the "pseudophakic posterior iris chafing syndrome"[3]. Most commonly this is encountered in the context of a secondary glaucoma in an eye that evidences iris chafing by the IOL; the particulate matter may be inflammatory cells, red blood cells, or iris pigment. Clear distinction of the nature of the particles is not always possible but their role as an impediment to aqueous outflow is the common glaucoma mechanism. Frank hyphema is not as

common as in the originally described UGH. nUGH may be also be associated with cystoid macular edema (CME; uveitis spectrum)[4-5], vitreous hemorrhage without hyphema[6-7] and secondary corneal decompensation[8]. This has subsequently been seen with virtually all types of AC IOLs and PC IOLs (implanted in the sulcus or in the capsular bag)[9-11]. While PC IOLs have been designed for capsular fixation, and it is well reported that sulcus fixation is to be avoided when possible due to its association with more adverse side effects such as the nUGH syndrome[12]. However, there are cases in which sulcus placement was either unintentional, or chosen due to inadequate capsular support. A similar problem has been reported with cosmetic iris implants[8]. Although, what we are referring to as the nUGH syndrome is not rigidly defined, we perceive there is a descriptive consensus is as just described. This condition is diagnosed mainly on the basis of clinical findings but ultrasound (US) and ultrasound biomicroscopy (UBM) are valuable diagnostic tools for determining the orientation and position of the IOL and haptics in suspected cases[13].

Management may differ in accordance to the presentation. The majority of cases cause minimal symptoms (and might even go undiagnosed) and are transient or will resolve with topical steroids and anti-glaucoma medications, the first line of treatment[14]. We suggest that IOL repositioning or exchange may be considered for medically-refractory (*e.g.* corticosteroids) UGH to reduce or eliminate the direct contact between the IOL and uveal tissue.

The purpose of the current study was to characterize the features of medically refractory cases of nUGH syndrome, and to evaluate the best corrected visual acuity (BCVA) outcomes of IOL repositioning or exchange for patients.

SUBJECTS AND METHODS

Ethical Approval The study protocol was approved by Institutional Review Board (IRB) of the University of Miami, Miller School of Medicine. The study and data collection conformed with the principles of the Declaration of Helsinki. Surgical consent was obtained in all patients, but informed consent for inclusion in the current study was waived by our institution's IRB.

A retrospective chart review of all patients who underwent IOL repositioning or exchange for postoperative UGH by one surgeon (Smiddy WE) at the Bascom Palmer Eye Institute from May 2014 through May 2019. The primary outcome measures were BCVA, IOP, number of bottles of glaucoma medicine used, and resolution of the signs and symptoms.

Only patients with IOL-related UGH syndrome with at least 3mo follow-up information after IOL repositioning or exchange were included in the study. Excluded patients were those with UGH syndrome not related to IOL, those with follow-up data less than 3mo and those with incomplete preoperative and/or postoperative data. Fourteen eyes with nUGH criteria were identified. These were referred to the retinal surgeon by a glaucoma specialist. Medical treatment (at least one IOP-lowering bottle and topical corticosteroids) had been tried and determined to be insufficient before concluding surgery was indicated, but there was no standardized protocol or duration of medical treatment trial. Iris chafing was deduced from corresponding iris depigmentation. The indications for surgery were not strictly objective; the decision for surgery reflected a conclusion that the IOP and media opacities were excessive or too frequent for long-term safety. Data collected from the charts included preoperative BCVA before and after IOL repositioning or exchange, age, gender, past ocular history, time of onset of UGH, gonioscopy findings, type and position of implanted IOL causing UGH, evidence of iris chafing, type and position of newly implanted IOL, type and number of glaucoma medications used before and after surgery, and imaging results (if performed). BCVA was recorded on a standard Snellen's chart and reported as the decimal fraction of Snellen measurements. IOP was measured using Goldmann applanation tonometer. Anterior segment was examined using slit lamp biomicroscopy and detailed fundus examination was done using 90 and 20 D lenses. Findings of imaging studies such as UBM and spectral domain optical coherence tomography (SD-OCT; Cirrus, Carl Zeiss Meditec, Inc., Dublin, CA, USA) were collected when available.

Standard surgical techniques involved IOL exchange or repositioning, depending upon the individual clinical circumstances. Pars plana vitrectomy was performed in all eyes using 23 g pars plana instrumentation. IOL repositioning usually involved scleral suturing using 9-0 polypropylene sutures (to loop the haptics and attach to the scleral under diametrically placed scleral flaps), but if a sufficient anterior capsular rim was present, sutures were unnecessary. The frequencies of the specific management choices are enumerated in the results. The primary plan was always to relieve IOL-medicated iris chafing by repositioning an existing PC IOL and exchanging an existing AC IOL for a PC IOL. However, if the PC IOL could not be repositioned, it was exchanged. The surgeon made a judgement as to whether a new IOL was placed in the AC, the sulcus, or sewn into the sclera based on the individual situation of the eye and patient.

Statistical Analysis Data were entered and encoded using the statistical package SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 24. All BCVA values were recorded in decimals fraction. Numerical data were expressed as mean±standard deviation and compared using a paired 2-sample *t*-test. Categorical data were expressed in percentages and compared by the Fisher's exact test. All tests were considered statistically significant at $P<0.05$.

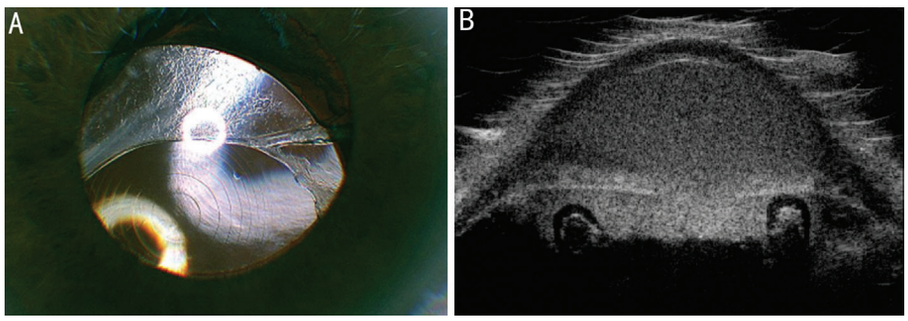

Figure 1 A 89-year-old female A: Preoperative color slit lamp photograph showing multifocal IOL inferiorly dislocated and somewhat tilted such that the superior optic was rubbing on the posterior iris surface. A Baerveldt tube is apparent superonasally in this right eye. BCVA was 0.33 (20/60) and the IOP was 31 mm Hg on 2 medications. B: A week later, a total hyphema occurred and was washed out by the glaucoma surgeon. The UBM demonstrates this as well as the IOL haptic (lucent horseshoe shaped areas behind the iris) in contact with the temporal iris. Vitrectomy with repositioning of the IOL using scleral sutures was performed to position the IOL in a more level, centered location, more posterior to the iris, with return of BCVA of 1.0 (20/20) off all drops, 1y after surgery.

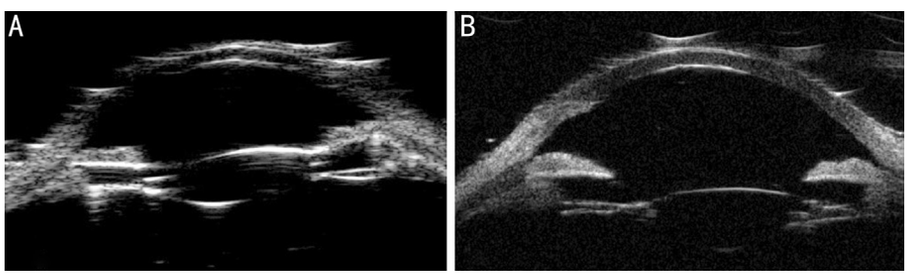

Figure 2 A 59-year-old male Vision of left eye is 0.33 (20/60) and IOP of 31 mm Hg despite 2 glaucoma medications and frequent topical corticosteroid treatment. The BCVA in the right eye was 0.005 (1/200) with a dense cataract. A: UBM shows tilted IOL with contact to the iris. B: UBM appearance after IOL vitrectomy with IOL repositioning that included capturing the optic behind the residual peripheral capsule, showing the IOL positioned well posterior to the iris in a more level orientation. The visual acuity returned to 20/30, but 2 medications were still necessary to control the IOP, and one drop of steroid daily was still being used, 2mo after surgery.

RESULTS

The study cohort included 14 eyes of 14 patients with a mean age of 71.5±13 (range: 46-89)y at the time of onset of UGH. Eight (57%) right eyes were included and 8 (57%) patients were male. Twelve PC IOLs (one which had been iris fixated) and 2 AC IOLs were included in the study. The haptics in the PC IOLs were both in the capsular bag in 2 eyes, one in the bag and one in the sulcus in 2 eyes, or both in the sulcus (6 eyes), sewn to the iris (1 eye) or previously scleral sutured (1 eye). The PC IOLs were one-piece type (6 eyes) or 3-piece (6 eyes, including one multifocal IOL) types. The median time from CE/IOL to onset of UGH was 7.5y (mean: 11.4±8.4y, range: 2mo-30y).

The mean preoperative BCVA was 0.45±0.26 (range: 0.13-1). The mean preoperative IOP was 26.7±6.1 mm Hg (range: 16-36 mm Hg) using a mean of 1.7±0.88 glaucoma medications (range: 0-3). Four eyes had a pre-existing history of glaucoma with tube shunts implanted in 2 of these eyes (Figure 1).

The clinical features included 13 eyes (93%) with uveitis, 13 eyes (93%) with elevated IOP (defined as IOP above 22 mm Hg without glaucoma medications), and 6 eyes (43%) with hyphema. Only one patient did not have uveitis, however he developed recurrent hyphema for which he underwent IOL exchange. All patients had evidence of iris chafing; in the 12 eyes with PC IOL (7 in sulcus, 5 in bag) this was due to the haptic (9 eyes), the optic (2 eye), and affected by both for the iris-sutured IOL. One eye had a concurrent vitreous hemorrhage. CME was not documented preoperatively in any eye; it was looked for by clinical examination, but not systematically imaged. Two patients had pseudoexfoliation, which may have contributed to IOL displacement and iris chafing, possibly in association with zonular dehiscence typical of pseudoexfoliation.

IOL repositioning or exchange was performed at a mean duration of 8.1±4.7mo (median: 4mo) after diagnosis of UGH. Seven eyes underwent repositioning with scleral suturing and in one eye the IOL was repositioned without sutures, but with capture of the apparently offending optic behind residual capsular rim (Figure 2). Six eyes underwent IOL exchange-for an AC IOL (2 eyes), scleral-sutured IOL (3 eyes, including both initially AC IOLs and a one plate haptic IOL), sulcus-implanted IOL (one eye due to good anterior capsular support).

The mean postoperative follow-up examination duration was 17.6±13.4mo (median: 15mo, range: 3-46mo). Uveitis and hyphema resolved in all cases after IOL surgery but recurrent vitreous hemorrhage in the perioperative period necessitated vitreous lavage in one patient. The mean BCVA improved from 0.45±0.26 (range: 0.13-1) to 0.76±0.22 (range: 0.005-1; P=0.016) after IOL repositioning or exchange. Eight eyes had improved BCVA, 4 eyes maintained the same preoperative BCVA, one eye had a worse BCVA (0.005) after 3y of follow-up, and one was limited to follow-up information of only 2mo. Nine patients achieved BCVA of 0.5 or better, and only 1 patient had BCVA below 0.1, an eye that had advanced glaucoma that likely was the cause of severe vision loss 3y postoperatively. No differences in final BCVA analysis between the IOL exchange versus IOL reposition subgroups were observed (P=0.55).

The mean IOP was reduced from 26.7±6.1 mm Hg preoperatively to 14.8±4.6 at the final follow-up examination (P=0.01). The mean number of glaucoma medications was reduced from 1.7±0.88 medications preoperatively to 0.8±0.74 (P=0.04) postoperatively. In one eye, elevated IOP (26 mm Hg) persisted after IOL exchange and was refractory to medical treatment so a tube shunt was placed with reduction of the IOP to 17 mm Hg, which was achieved 1mo after tube shunt implantation. One patient with vitreous hemorrhage after IOL repositioning with scleral sutures resolved after 3wk but another (one eye) required vitreous lavage a month later. A third patient, possibly influenced by concurrent anticoagulant therapy, developed recurrent hyphema postoperatively which resolved with AC washout. No cases of clinical CME were identified. Postoperative OCT was obtained in only 4 eyes in which there was any clinical suspicion of this (Table 1).

Table 1 Clinical features of study cohort

Patient	Age at secondary IOL surgery	Eye	Gender	Inciting IOL	Secondary IOL surgery	Preexisting glaucoma	Preop. IOP	Postop. IOP	Preop. glaucoma medications	Postop. glaucoma medications	Target of intervention
1	62y	OD	M	PC IOL (3-piece)	Scleral-sutured IOL	No	36	19	1	0	IOP control
2	80y	OD	M	PC IOL (3-piece)	Scleral-sutured IOL	Yes	16	9	2	2	Glare and blurred vision
3	59y	OS	M	PC IOL (single-piece)	IOL exchange (AC IOL)	No	32	21	3	1	IOP control, elimination of iris chafing.
4	63y	OD	F	PC IOL (single piece)	Scleral-sutured IOL	Yes	27	8	1	0	IOP control and elimination of iris chafing.
5	72y	OD	M	PC IOL (iris 3-piece fixated)	Scleral-sutured IOL	No	20	17	2	0	Recurrent uveitis and hyphema
6	89y	OD	F	AC IOL	IOL exchange (sulcus-placed, sutureless)	No	16	22	2	2	Recurrent uveitis
7	89y	OD	F	PC IOL (3-piece)	Scleral-sutured IOL	Yes	27	6	3	1	Recurrent hyphema and IOP control
8	62y	OS	M	PC IOL (3-piece)	Scleral-sutured IOL	No	24	17	3	2	Vitreous hemorrhage
9	60y	OS	F	PC- IOL (single piece)	IOL repositioning	No	31	11	1	1	IOP control
10	46y	OD	M	PC IOL (single piece)	IOL exchange (AC IOL)	No	34	15	2	1	IOP control
11	78y	OS	F	PC IOL (single-piece)	IOL exchange (scleral-sutured)	Yes	22	13	0	0	Recurrent uveitis and IOP control
12	89y	OD	F	PC IOL (3-piece)	Scleral-sutured IOL	No	32	15	1	1	IOP control
13	72y	OS	M	AC IOL	IOL exchange (scleral-sutured)	No	27	17	2	0	IOP control
14	81y	OS	M	PC- IOL (single piece)	IOL exchange (scleral-sutured)	No	30	18	1	1	Recurrent hyphema and IOP control

IOL: Intraocular lens; PC: Posterior chamber; AC: Anterior chamber; IOP: Intraocular pressure.

DISCUSSION

The current study demonstrates that surgically eliminating (or at least mitigating) the IOL-iris contact in medically refractory cases improved the symptoms of nUGH, providing circumstantial evidence for the hypothesized etiologic mechanism. The method of accomplishing that goal was tailored each case and included IOL exchange or repositioning, with scleral suture fixation.

The current study also attempts to characterize the features of an nUGH syndrome, finding that they are somewhat more variable compared to the classic counterpart condition, with hyphema being a less frequent component (although hyphema and vitreous hemorrhage certainly may occur). The principal, unifying element, however, remains chronic IOL-induced trauma and inflammation from the IOL–although prominent chafing by the haptic or optic seemed to be more common than frank erosion. The pathophysiology in these cases likely involves a mixed mechanism–primary inflammation from the

iris trauma, but also frictional release of cellular particles that impede aqueous outflow. Asaria *et al*[15] reported presence of melanosomes on the haptic arms in patients presenting with UGH syndrome, derived from damaged pigment epithelial cells or iris stroma as a result of recurrent chafing. Cases manifesting milder degrees of these processes may respond to medical treatment with anti-inflammatory medications and IOP-lowering medications rather than needing surgery.

Sulcus implantation of certain IOLs with sharper, square-shaped optic edges may be more likely to cause nUGH especially if there is IOL decentration[16].

Several hypotheses have been suggested as a cause of nUGH syndrome in case of in-the bag IOLs[9]. Zonular laxity as a result of pseudoexfoliation syndrome may have potentiated some of the nUGH features by allowing excessive IOL mobility due to zonular loss in 2 eyes in the current study. Early diagnosis and management of nUGH might be particularly important in such cases that might already have glaucomatous optic atrophy. Combined glaucoma surgery (tube shunt) with IOL exchange has been recommended in some such cases[17].

Another hypothesis for pathophysiologic mechanism is plateau-iris like configuration with anteriorly rotated ciliary processes and extensive capsular fibrosis causing chafing against the posterior iris surface[9]. This might explain why there appears to be substantial variation in IOL-iris positioning even when the IOL seems appropriately placed in some eyes. A postmortem study by Apple *et al*[18] showed that 47% of patients with in-the bag implanted IOL had one haptic slipped out to the sulcus, especially in eyes with a large capsulorrhexis. This conclusion malpositioned haptics might be more common than the surgeon suspected might still be the case in some eyes. It has been recommended to place single piece IOLs in the bag, not sulcus, with circumferential overlapping of the appropriately-sized anterior capsule over the optic edges to prevent the consequences seen by eyes in the current series[16].

Limitations of this study are principally rooted in its retrospective design, as standardized testing and examination schedules were not pursued. The follow-up interval is fairly short in some cases, but the generally rapid and positive results are encouraging findings indicating expectation for long term benefit. Long-term visual field testing would be confirmatory.

The features of nUGH syndrome mimic its classic counterpart with a few differences, including the possibility of a mixed mechanism. Inflammation and iris pigment load might be overlooked by the clinician, Thus, even minorly malpositioned IOLs may play an important pathologic role in chronic iris chafing-related consequences[17]. Surgical management of the IOL position has a high rate of successful resolution of IOL induced, nUGH.

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