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Inter-Eye Differences in Patients with Pseudoexfoliation Syndrome Presenting with Intraocular Lens Dislocation

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Purpose: To analyze differences in glaucoma diagnosis and glaucoma severity between fellow eyes in patients with pseudoexfoliation syndrome (PXF) who present with intraocular lens (IOL) dislocation.

Design: Retrospective matched case-control study. Eyes presenting with IOL dislocation (case group) were compared with fellow eyes (control group).

Participants: Patients from a tertiary referral practice in Mississauga, Ontario, Canada.

Methods: Consecutive patients with PXF and prior bilateral uneventful cataract surgeries with in-the-bag IOLs who presented with IOL dislocation between 2008 and 2013 were identified (n = 71). Indicators of glaucoma severity were compared between fellow eyes using McNemar's test and Wilcoxon signed-rank tests. Indicators of glaucoma severity were also compared pre- and post-IOL exchange/repositioning in the eye with IOL dislocation.

Main Outcome Measures: Glaucoma diagnosis, corrected distance visual acuity (CDVA), intraocular pressure (IOP), optic nerve cup-to-disc (C/D) ratio, mean deviation (MD) on visual field, retinal nerve fiber layer (RNFL) thickness, and glaucoma medication requirements (GMRs).

Results: Seventy-one participants were included. The affected eye was more likely to have glaucoma ($P < 0.0001$) and have more severe glaucoma ($P = 0.0001$). In addition, the affected eye had worse mean CDVA (1.14±0.79 logarithm of the minimum angle of resolution [logMAR] vs. 0.35±0.46 logMAR, $P < 0.0005$), higher mean IOP (19.2±7.2 vs. 14.7±3.6, $P < 0.0005$), higher C/D ratio (0.54±0.22 vs. 0.51±0.20, $P = 0.006$), greater mean number of glaucoma medication classes (1.4±1.4 vs. 0.5±1.1, $P < 0.0005$), worse MD (−13.83±6.89 decibels [dB] vs. −6.59±6.63 dB, $P < 0.0005$), and worse mean RNFL thickness (69.2±26.3 vs. 82.4±13.7, $P = 0.001$). In the affected eye, there were early postoperative improvements in mean CDVA, IOP, and GMRs.

Conclusions: In patients with PXF, the eye presenting with IOL dislocation was more likely than its fellow eye to have a diagnosis of glaucoma and to have glaucoma of greater severity. *Ophthalmology 2015;122:480-485 © 2015 by the American Academy of Ophthalmology.*

Pseudoexfoliation syndrome (PXF) is an age-related systemic disorder of extracellular matrix with prominent manifestations in the eye.[1,2] Genetic risk factors for PXF have been identified, including single nucleotide polymorphisms in the lysyl-oxidase-like 1 gene that codes for lysyl-oxidase-like 1, an enzymatic protein important in extracellular matrix metabolism and turnover.[1,2] Overproduction, over-aggregation, and inadequate breakdown of extracellular fibrillin are all thought to be implicated in the deposition of pseudoexfoliative material (PXM) on anterior segment structures in eyes with PXF.[1] Classic intraocular findings in PXF include "dandruff-like" material in the anterior chamber, deposits in a concentric bulls-eye pattern on the anterior lens capsule, and visualization of PXM at the pupillary margin, on the lens zonules, or on the trabecular meshwork.[2] Other ocular manifestations of PXF include iris depigmentation resulting in peripupillary transillumination defects, trabecular meshwork hyperpigmentation, phacodonesis, and lens subluxation associated with zonular weakness.[2]

Although PXF is a systemic disorder with PXM present throughout the body, only the eye is known to have associated disease.[3] Pseudoexfoliation syndrome is the most common identifiable cause of open-angle glaucoma.[3] The Early Manifest Glaucoma Trial found 55% of individuals with PXF develop glaucoma (i.e., pseudoexfoliative glaucoma [PXG]) within an average of 9 years.[4] Pseudoexfoliation syndrome initially may appear as a unilateral disease with asymmetric PXM deposition and glaucomatous changes. However, 15% to 40% of individuals go on to have bilateral involvement within 5 to 10 years.[5–7] Cataract formation is another pathologic process that occurs with increased incidence in patients with PXF, constituting the most common cause for surgical intervention.[8] Weakened zonules and poor mydriasis in PXF eyes increase the risk of complications of cataract surgery, including capsular phimosis, inflammation, intraocular pressure (IOP) spikes, and intraocular lens (IOL) dislocation.[9]

Abnormal PXM deposition, increased oxidative stress, and depressed antioxidant protection all may contribute to the pathogenesis of PXF.[1] Heightened activity of pathologic mechanisms of PXF may manifest in both glaucomatous disease progression and increased postoperative complications,

http://dx.doi.org/10.1016/j.ophtha.2014.09.003
ISSN 0161-6420/14

such as IOL dislocation. The purpose of this study was to assess the differences in glaucoma severity between fellow eyes in patients with PXF presenting with late spontaneous IOL dislocations. We hypothesized that eyes with IOL dislocation were associated with greater glaucoma severity than their fellow eyes.

Methods

This was a noninterventional retrospective matched case-control study; eyes presenting with IOL dislocation (case group) were compared with fellow eyes (control group). This study was conducted at a single center, in accordance with the Tri-Council Policy Statement for Ethical Conduct of Research Involving Humans and the Declaration of Helsinki. Ethics approval was obtained from Institutional Review Board Services, Ltd, in Aurora, Ontario, Canada. Institutional Review Board Services, Ltd, is Canada's largest central institutional review board, with boards in both Canada and the United States, accredited by the Association for the Accreditation of Human Research Protection Programs, Inc.

Ontario Health Insurance Plan billing codes for IOL exchange and repositioning were used to identify patients with dislocated IOLs presenting between January 2008 and May 2013 (n = 463). This timeframe was chosen for logistic purposes; the clinic's electronic health records dated back to 2008. Of the individuals presenting with IOL dislocation between 2008 and 2013, those with PXF and previous cataract extraction using the same technique in both eyes with bilateral posterior chamber IOL implants in the bag presenting with spontaneous IOL dislocation were included in this study (n = 79). Patients with asymmetric use of capsular bag stabilizers from the initial cataract surgery (n = 7) or missing data from the preoperative assessment for IOL exchange or repositioning (n = 1) were excluded. All corrective IOL exchange and repositioning surgeries were performed by the same surgeon.

The preoperative visit before IOL exchange or repositioning surgery was considered the baseline visit. Preoperative parameters were recorded, including demographic information (age, gender, race), medical history, ocular history, glaucoma diagnosis, glaucoma medications, presenting symptoms, direction of IOL dislocation, time elapsed between initial cataract surgery and presentation of IOL dislocation, and ocular examination findings: corrected distance visual acuity (CDVA) converted to logarithm of the minimum angle of resolution (logMAR) equivalents, IOP, optic nerve cup-to-disc (C/D) ratio, mean deviation (MD) on visual field, and retinal nerve fiber layer (RNFL) thickness. Intraoperative parameters also were recorded, including date of surgery, surgical technique (IOL exchange or repositioning alone, or IOL exchange or repositioning combined with IOP-reducing glaucoma surgery), and type of new lens implant in IOL exchange. Combining lens correction with glaucoma surgery was up to the surgeon's discretion and generally done in cases of high IOP (i.e., >20 mmHg). Postoperative data (glaucoma medications, CDVA, IOP, C/D ratio, MD, and RNFL thickness) were obtained from visits 3 to 6 months after IOL exchange or repositioning, depending on the time of discharge from the surgical team.

Statistical analyses were performed using SPSS software (version 17, International Business Machines Corp, Armonk, NY). McNemar's test and Wilcoxon signed-rank tests were used to compare affected eyes, defined as the eye presenting with IOL dislocation or the eye with more severe dislocation in the case of bilateral dislocations, and their fellow eyes on the basis of the following baseline parameters: glaucoma diagnosis, glaucoma medication classes, CDVA, IOP, C/D ratio, MD, and RNFL thickness. Wilcoxon signed-rank tests were also used to compare glaucoma medication classes, CDVA, IOP, C/D ratio, MD, and RNFL thickness pre- and post-IOL exchange or repositioning in the affected eye.

Table 1. Patient Demographics

No. of Participants	71
Male (%)	29 (41)
Female (%)	42 (59)
Caucasian (%)	64 (94)
Mean age (yrs)	80.0±6.3

Results

A total of 71 fellow eyes (142 eyes) were included in the analysis, each undergoing cataract extraction and posterior chamber IOL implantation between 1990 and 2011. Table 1 summarizes the demographic characteristics of study participants. The median age was 80 years, with a minimum age of 64 years and a maximum age of 93 years. Female patients constituted 59% of the study population; 94% (64/68) of study participants were white.

A diagnosis of PXF was found in both eyes in 72% (n = 51) of fellow eyes, but presented asymmetrically in the remaining 28% (n = 20), with pseudoexfoliative findings only in the eye with IOL dislocation. Of the asymmetric cases, 7 (35%) later developed signs of PXF bilaterally.

Glaucoma was the most common ocular comorbidity, affecting 56% (n = 40) of study participants. All patients with glaucoma (n = 40, 100%) had the disease diagnosed in the eye with IOL dislocation; 68% (n = 27) had a concomitant glaucoma diagnosis in the eye without IOL dislocation; no individuals had a diagnosis of glaucoma solely in the eye without IOL dislocation.

Table 2 summarizes the characteristics of the original cataract surgery, original type of IOL implant, and IOL dislocation. Original cataract surgery was performed by phacoemulsification in 96% (68/71) of fellow eye pairs. One-piece acrylic lenses (n = 32) and 3-piece acrylic lenses (n = 22) made up the majority of original IOL implants that dislocated. The most common direction of dislocation was in the inferior quadrants (n = 66). Bilateral IOL dislocation was present in 3% (4/71) of fellow eye pairs.

The mean duration of time between the initial cataract surgery and the IOL exchange or repositioning surgery was 7.7±4.8 years (minimum = 1 year; maximum = 20 years). A total of 73 corrective surgeries were performed, including bilateral IOL exchange in 2 of 4 cases with bilateral IOL dislocation. Intraocular lens exchange was preferred over repositioning in 93% (68/73) of corrective surgeries. Of these cases, all but 1 used an iris enclavated lens for exchange (Table 3). Of the IOL exchange surgeries, 30 were combined with IOP-reducing glaucoma surgery, including the use of trabecular microstents (n = 13), tube shunt drainage devices (n = 12), or trabeculectomy (n = 5) (Table 3). Of the IOL repositioning surgeries, 1 was combined with IOP-reducing glaucoma surgery using a tube shunt drainage device (Table 3). Complications in eyes post-IOL exchange or repositioning included transient early hypotony (n = 7) requiring ophthalmic viscosurgical device refill of the anterior chamber (n = 6), transient IOP spike (n = 2), and a dislocated nasal haptic requiring IOL repositioning (n = 1).

Table 4 summarizes the comparison of glaucoma severity between fellow eyes. Within each fellow eye pair, a glaucoma diagnosis was ascertained in the eye presenting with IOL dislocation or in both eyes, but never isolated to the eye without IOL dislocation. Given this finding, an odds ratio is inestimable. The affected eye with IOL dislocation was more statistically