Pseudoexfoliation syndrome and secondary cataract

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Abstract

Pseudoexfoliation (PEX) syndrome is frequently associated with impairment of the blood-aqueous barrier. This study analysed if this might stimulate secondary cataract following cataract extraction.

Methods—This historical cohort study included 197 eyes of 197 patients (99 with and 98 without PEX) that underwent extracapsular cataract extraction with posterior chamber lens implantation (PMMA optic) between 1985 and 1991. Secondary cataract was defined as opacification of the axial posterior capsule and decrease of visual acuity by two or more lines. Mean follow up was 23.8 months. For statistical analysis, the Kaplan–Meier method and multivariate Cox regression analysis were used.

Results—Secondary cataract was observed within 24 months in 35% (SD 7%) of all eyes, and was significantly more frequent in eyes with PEX (45 (11)% than in eyes without PEX (24 (9%)%, p<0.03). Eyes with diabetes mellitus (n=32) showed a significantly lower frequency of secondary cataract (11 (11)% than eyes without diabetes mellitus (39 (8)%, p<0.01). The influences of sex, open angle glaucoma, type of cataract, surgeon, positioning of IOL, and phacoemulsification versus nuclear expression on secondary cataract did not reach statistical significance.

Conclusion—The higher frequency of secondary cataract could be considered as another potential complication of cataract surgery in eyes with PEX.

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Pseudoexfoliation (PEX) syndrome is diagnosed by slit-lamp detection of deposits of a fibrillogranular material on the anterior lens capsule and at the pupillary margin.1 2 It is frequently associated with open angle glaucoma,3 melanin dispersion,4 poor pupillary dilatation,5 and may present with a specific type of PEX keratopathy.6 These features in combination and may present with a specific type of PEX melanindispersion,4 poorpupillarydilatation,5 capsuleandatthepupillarymargin.12 Itisfre- fribillogranular material on the anterior lens nosed by slit-lamp detection of deposits of a Pseudoexfoliation (PEX) syndrome is diag- nosis of dysfunction of the blood-aqueous barrier in PEX15–18 with consecutive increase of aqueous flare9 and aqueous protein concentration.10 There is also an increasing number of reports on inflammatory reactions and fibrin formation in eyes with PEX following cataract extraction19–22 or trabeculectomy.23 Based on these observations, we hypothesised that increased and prolonged breakdown of the blood-aqueous barrier may also lead to a higher rate of secondary cataract in eyes with PEX. We performed a historical cohort study to analyse the frequency of secondary cataract in eyes with and without PEX following extracapsular cataract extraction and posterior chamber lens implantation.

Methods

From the clinical documentation data base of all patients who underwent extracapsular cataract extraction (ECCE) with implantation of a posterior chamber intraocular lens (PC-IOL) at our institution between 1985 and 1991, a sample of 99 patients with PEX and a sample of 98 patients without PEX was extracted. The control group of patients without PEX was matched for age, sex, and presence of diabetes mellitus (group matching). For those patients in whom PEX was manifest in both eyes and cataract extraction had been performed in both eyes, one eye was chosen at random. In the control group, only patients without PEX in either eye were included and one eye was chosen at random if both eyes had undergone cataract surgery. Exclusion criteria were traumatic cataract following penetrating ocular injury, history of uveitis, history of previous intraocular surgery, and intraoperative rupture of the posterior capsule and/or vitreous loss. Surgery was performed by a total of 10 surgeons, with three very experienced surgeons operating on 80% of all patients. Either nuclear expression or phacoemulsification were used. Plano convex non-heparin coated IOLs with 6.5 to 7.0 mm optics in the remainder of the eyes. All data were collected by reviewing the standardised patient charts and the standardised computerised surgical report. Factors analysed included presence of PEX, preoperative visual acuity, presence of open angle glucoma, surgeon, nuclear expression or phacoemulsification, intended localisation of IOL (ciliary sulcus or capsular bag), intraoperative use of viscoelastics, intraoperative complications (rupture of posterior capsule, vitreous loss), postoperative visual acuity, development of secondary cataract, and Nd:YAG capsulotomy. The exact type of
opening of the anterior lens capsule (can
openertechnique, letterbox technique, or con-
tinuous circular capsulorhexis) was not re-
corded. Secondary cataract was defined as
opacification of the axial posterior capsule vis-
able at slit-lamp examination associated with a
decrease of best corrected visual acuity by two
ormorelines. It was not differentia
ted between proliferative pearl-type and fibrotic secondary
cataract. For patients who were not followed in
our hospital, a standardised questionnaire was
sent to their ophthalmologists to gain infor-
mation on postoperative visual acuity and
development of secondary cataract, using the
above mentioned criteria.

Influence of patient age, sex, and diabetes
mellitus was analysed within the PEX and
non-PEX group.

For statistical analysis of secondary cataract,
the Kaplan–Meier estimate for the probability
of secondary cataract after 24 months was
determined in the different patient groups. For
all patients and separately for patients with and
without PEX, additional probabilities for
secondary cataract after 6, 12, and 18 months
are presented. All other rates of secondary
(cataract are 24 month Kaplan–Meier esti-
mates. For the main results 95% confidence
intervals (rate plus or minus 2 SE) are given.
Significance testing was performed using the
Cox regression model with inclusion of the
matching criteria.

Results
Mean patient age at surgery was 76.5 (SD 6.6)
years (range 57–90 years), and there were 64
males and 133 females. Mean follow up was
23.8 (15.4) months (range 3–84 months).
Diabetes mellitus was present in 32 of the 197
patients. The demographic distribution was
very similar in eyes with and without PEX
(Table 1).

For all eyes the secondary cataract rate was
4% (SD 3%) after 6 months, 19 (6) % after 12
months, 26 (6) % after 18 months and 35 (7) %
after 24 months.

For patients without PEX the rates were 6
(5)%, 14 (7)%, 16 (7)%, and 24 (9)%, whereas
2 (3)%, 25 (9)%, 36 (10)%, and 45 (11)% of
the patients with PEX developed secondary
cataract after 6, 12, 18, and 24 months
(p<0.03, Cox regression analysis) (Table 2),
with the Kaplan–Meier curve indicating that
the difference between eyes with and without PEX at
about 1 year after surgery (Fig 1). Eyes of
patients with diabetes mellitus developed
secondary cataract far less frequently (11
(11)%) than eyes of patients without diabetes
mellitus (39 (8)%, p<0.01, Cox regression
analysis) (Table 2), with the Kaplan–Meier
curve indicating that the difference between
eyes with and without diabetes mellitus started
early in the postoperative period (Fig 2). Con-
sidering both PEX and diabetes, eyes with
PEX without diabetes had the highest occur-
rence of secondary cataract (52%), followed by
eyes without diabetes without PEX (26%), and
by eyes with diabetes with PEX (13%) (Table
2). The lowest occurrence of secondary
(cataract was observed in the group of eyes with
diabetes without PEX (8%).

The proportion of secondary cataract was
higher for eyes with open angle glaucoma (33
(10)%) versus 27 (12)% in eyes without open
angle glaucoma, nuclear cataract versus corti-
cal cataract (41 (12)% in eyes with nuclear
cataract versus 30 (9)% in eyes with cortical
(cataract), IOL placement into the ciliary sulcus
(38 (12)%) versus placement into the capsular
bag (33 (10)%), and phacoemulsification (46
(16)% versus nuclear expression (31 (8)%).

![Figure 1 Kaplan–Meier survival curve of secondary cataract following extracapsular
cataract extraction and posterior chamber lens implantation in eyes with or without
pseudoexfoliation (PEX).](image-url)

<p>| Table 2 Secondary cataract according to pseudoexfoliation (PEX) and diabetes mellitus (DM) |</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>No</th>
<th>Secondary cataract rate after 24 months* (SD)</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All eyes</td>
<td>197</td>
<td>35 (7)%</td>
<td>&lt;0.03</td>
</tr>
<tr>
<td>Eyes with PEX</td>
<td>99</td>
<td>45 (11)%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Eyes without PEX</td>
<td>98</td>
<td>24 (9)%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Eyes with DM</td>
<td>32</td>
<td>11 (11)%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Eyes without DM</td>
<td>165</td>
<td>39 (8)%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Eyes with PEX and with DM</td>
<td>17</td>
<td>13%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Eyes with PEX without DM</td>
<td>82</td>
<td>52%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Eyes without PEX with DM</td>
<td>15</td>
<td>8%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Eyes without PEX without DM</td>
<td>83</td>
<td>26%</td>
<td>&gt;0.3</td>
</tr>
</tbody>
</table>

*Kaplan–Meier estimate.
†Cox regression analysis with diabetes mellitus, PEX, patient age (p>0.9) and sex.
(p>0.3) included.
However, none of these differences reached statistical significance (Table 3).

The influence of patient age at surgery on development of secondary cataract seemed to be different for eyes with and without PEX. Whereas the frequency of secondary cataract decreased with increasing patient age in PEX (from 55% in patients younger than 71 years to 34% in patients older than 80 years), it apparently increased with increasing patient age in patients without PEX (from 7% in patients younger than 71 years to 36% in patients older than 80 years) (Table 4).

### Discussion

Opacification of the posterior lens capsule after cataract surgery is a major medical and socioeconomic problem. Formation of secondary cataract may result from two mechanisms, with many pathogenetic factors still poorly understood. Migration of lens epithelial cells onto the posterior lens capsule leads to the proliferative variant with formation of Elschnig pearls, or metaplasia of lens epithelial cells into myofibroblasts is followed by fibrosis and contracture of the posterior capsule. The reported incidence of secondary cataract after extracapsular cataract surgery varies widely, ranging between 14% and 53% without PC-IOL implantation and between 7% and 50% with PC-IOL implantation. It is difficult to compare the rates of secondary cataract formation in various studies because of high variations in follow up time, definition of secondary cataract, patient age, surgical techniques, and type of intraocular lenses.

Many factors have been reported to influence development of secondary cataract, most notably patient age, type of cataract, intraocular lens design including presence of laser ridges, intraocular lens placement, phacoemulsification, and intraocular lens material.

Clinical reports on inflammatory reactions and fibrin formation in eyes with PEX following cataract extraction appear to be related to ultrastructural changes of the morphological correlates of the blood-aqueous barrier. Accordingly, electron microscopy and tracer studies have demonstrated alterations of the endothelial cells and basement membrane of the iris vessels and the non-pigmented ciliary epithelial cells with formation of secondary cataract, as blood-ocular barrier breakdown is directly correlated with defects of the blood-aqueous barrier and formation of secondary cataracts in our study rather speaks against a direct correlation between defects of the blood-aqueous barrier and formation of secondary cataract, as blood-ocular barrier breakdown is frequently seen in diabetic patients. Thirdly, weakened zonular support may lead to focal areas of zonulolysis with increased capsular folds.

### Table 3 Secondary cataract according to ocular and surgical factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>All eyes</th>
<th>PEX</th>
<th>No PEX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of eyes</td>
<td>Secondary cataract (SD)</td>
<td>No of eyes</td>
</tr>
<tr>
<td>Nuclear cataract†</td>
<td>78</td>
<td>41 (12)%</td>
<td></td>
</tr>
<tr>
<td>Cortical cataract†</td>
<td>89</td>
<td>30 (9)%</td>
<td></td>
</tr>
<tr>
<td>Presence of glaucoma</td>
<td>81</td>
<td>33 (10)%</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Absence of glaucoma</td>
<td>116</td>
<td>27 (12)%</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Most experienced surgeon</td>
<td>104</td>
<td>38 (10)%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Less experienced surgeons</td>
<td>93</td>
<td>31 (10)%</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>Phacoemulsification†</td>
<td>49</td>
<td>46 (16)%</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Nuclear expression†</td>
<td>146</td>
<td>31 (8)%</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>IOL implantation 'in the sulcus'†</td>
<td>73</td>
<td>38 (12)%</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>IOL implantation 'in the bag'†</td>
<td>124</td>
<td>33 (10)%</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>Intraoperative use of hyaluronic acid†</td>
<td>95</td>
<td>39 (11)%</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td>Intraoperative use of heparin†</td>
<td>75</td>
<td>27 (10)%</td>
<td>&gt;0.9</td>
</tr>
</tbody>
</table>

*Univariate Cox regression analysis, similar results after inclusion of PEX, sex, diabetes mellitus, and age.
†Factors not present or not documented in all eyes.

### Table 4 Secondary cataract according to age and pseudoexfoliation (PEX)

<table>
<thead>
<tr>
<th>Age group</th>
<th>PEX</th>
<th>No PEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>57–70</td>
<td>32</td>
<td>32%</td>
</tr>
<tr>
<td>71–80</td>
<td>102</td>
<td>36%</td>
</tr>
<tr>
<td>81–90</td>
<td>63</td>
<td>34%</td>
</tr>
<tr>
<td>All ages</td>
<td>197</td>
<td>35 (7)%</td>
</tr>
</tbody>
</table>

\*No of eyes with secondary cataract (SD) \( p \) Value*
and subsequent facilitated migration of lens epithelium or fibrotic changes. Finally, it has been demonstrated that intracocular hypoxia exerts a strong stimulatory effect on proliferation of intraocular cells.28 As anterior chamber hypoxia has been demonstrated in eyes with PEX,29 this may induce proliferation of lens epithelium and cause secondary cataract.

An unexpected and surprising finding of the present study was the reduced incidence of secondary cataract in eyes of patients with diabetes mellitus, as we had rather expected secondary cataract to be more frequent in diabetic eyes as a result of the impairment of the blood-ocular barriers. However, our data have to be cautiously interpreted with regard to diabetes mellitus and secondary cataract, as this study was not designed to evaluate the effect of diabetes mellitus on the frequency of secondary cataract; the number of eyes with diabetes was small (n=32); and we did not analyse the diabetic population in our study in detail with regard to stage of diabetic retinopathy and other factors. Therefore, we cannot exclude the possibility that our sampling scheme may have induced an overestimation of the role of diabetes mellitus. Knorz et al20 and Tetz and Petz27 observed similar findings of decreased incidence of secondary cataract in diabetics independently, whereas the contrary has also been reported.21

The influence of other factors—intended location of IOL, phacoemulsification, surgeon, and type of cataract—did not reach statistical significance in our study with regard to the occurrence of secondary cataract. However, these results must also be seen in light of the fact that this study was not designed specifically to evaluate the effect of these factors on secondary cataract.

PEX may be associated with potential serious ocular complications including rapidly progressive open angle glaucoma,19 corneal decompensation secondary to PEX keratopathy,17 spontaneous subluxation or luxation of the lens,19 cilio-lenticular angle closure glaucoma,50 and complications during cataract surgery. From the results of our study, it appears that secondary cataract should be added to the already long list of complications of cataract surgery in PEX (Table 5). Thus, in eyes with PEX, surgeons should probably try to take intraoperative measures to reduce remaining lens epithelium and minimise the chance of secondary cataract formation, and patients with PEX should probably be informed of their increased risk of developing secondary cataract.

Table 5  Pseudoexfoliation as a potential risk factor in cataract surgery

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudoexfoliation</td>
<td>1.5 (1.1-2.1)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.7 (0.4-1.2)</td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>2.0 (1.5-2.6)</td>
</tr>
</tbody>
</table>