Pseudoexfoliation and its degenerative process

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Abstract
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PSEUDOEXFOLIATION AND ITS DEGENERATIVE PROCESS

BY

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Pseudoexfoliation syndrome is defined as a deposition of light gray to white dandruff-like material on the anterior lens surface, pupillary margin, trabecular meshwork and ciliary processes. Clinically, what is seen is a central area of exfoliative material on the lens capsule upon dilation of the pupil. The formation of the substance and its composition is still not fully determined. It has been speculated that PXF is due to abnormal basement membrane cell synthesis brought on by old age, or that it is due to changes in the neuroectodermal uveal tract. Others suggest a relationship of PXF fibers to elastosis. Pseudoexfoliation syndrome occurs more frequently within the elderly population usually between the ages of 60-80. PXF is very frequently associated with glaucoma therefore understanding its degenerative process can be of great help for developing improved treatment methods and protocol.

Prevalence of PXF and PXF Glaucoma

The prevalence rate of pseudoexfoliation was found to be 0.6 percent for ages 52-64 years with an increase to 2.5 percent for ages 65-74 years and up again to 5.0 percent for those aged 75-85 years according to the Framingham Eye Study. Furthermore, the general population had a prevalence rate of only 1.8 percent. 24.3 percent of the subjects aged 50 years or older from a region in Greece were found to have PXF and among them 39.5 percent had elevated IOP's of >22mmHg. The Eskimos of Greenland had a much lower incidence of PXF at 4.5 percent in individuals 70 years or
greater although until recently, there had never been any
demonstration of PXF within the population.9

Moreno-Montanes' study examined 546 eyes with open angle
glaucoma and found 243 of them to have PXF glaucoma.
Pseudoexfoliative glaucoma resided at 6 percent for patients under
60 years old, but rose dramatically to 74.2 percent in patients 80
years or older.10

Patients with unilateral glaucoma and PXF in the fellow eye
will develop ocular hypertension at a 75 percent rate during a 6-
year follow up according to Brooks and Gillies. After ocular
hypertension develops, there will be a one in four chance that
glaucoma will be diagnosed during another 6-year period.11 A
study done earlier by Hansen and Sellevold agrees, having
determined that 21-26 percent will have glaucoma over a 5-year
duration.7 A Finnish study cites that among patients who have PXF
of the lens capsule 50 percent to 61 percent will also have

glaucoma.12

A 1990 article by Teikari, Kaprio and Koskenvuo looked at 6
pairs of twins with pseudoexfoliation of the lens capsule. All but one
of the pair were identical twins. It was found that only two sets of
twins, both identical, matched for pseudoexfoliation while the rest of
the twins did not match. While a family history of pseudoexfoliation
reported suggests a genetic basis, the lack of concordance in a
significant number of twins also suggests environmental factors may
play a part in the development of PXF.12

Tarkkanen reported that patients with pseudoexfoliative
glaucoma in general had higher IOP's, more rapid loss of V.F. and
poorer treatment response than compared to chronic open angle glaucoma. Another study by Moreno-Montanes and Paredes also noted Higher IOP's and increased visual field defect. It was further found that PXF glaucoma developed earlier in men and with higher mean IOP and increased campimetric defects compared to women. Henry's research concluded that PXF incidence was greater in females by 2 to 3 times while Layden determined the rate of prevalence to be equal.

Degenerative Changes of the Eye

It is known that many differing degenerative changes occur within the PXF eye. Some changes when seen may be important for earlier detection of PXF. Studying much of these processes should help to better understand this disease. A study by Brooks and Gilles noted that microneovascularization and hypoperfusion (ischemia of arteries) was found in all but 2 out of 25 subjects with unilateral PXF. (Microneovascularization and hypoperfusion were undetermined in the 2 subjects due to unsatisfactory photos taken during iris angiography.) Although the control patients did show some microneovascularization and hypoperfusion changes, it was only a small percentage and most all were mild cases. It was determined that hypoperfusion results directly from PXF and in turn leads to
neovascularization. Histologic changes of vessel lining have been observed which most possibly are a part of the exfoliative process.14

The study by Carpel determined that pupil dilation was significantly less (1 mm or greater) in PXF eyes than compared to its normal fellow eye or an age and sex-matched normal population. This is presumed to be due to iris infiltration and fibrosis from pseudoexfoliation. This reduced dilation along with weakened zonules will produce an increased risk factor for vitreous loss during cataract surgery.15 Raitta also concluded that inadequate mydriasis, weak zonules and peripheral iridocapsular adhesions due to PXF were important clinically when evaluating extracapsular cataract extraction.16

Zonular fragility is another significant degenerative change commonly observed in pseudoexfoliation syndrome. Chijiwa et al., found that zonular fibers began to degenerate by first losing its regularity. Fine granules would later deposit onto the fibers and increase its deposition until a dense aggregate of exfoliative material is formed. From this study Chijiwa determined that the zonular fibrils were one source of pseudoexfoliative material and that the alteration of zonular fibers is the source of lens dislocation.6 There is also a higher incidence of zonular rupture in cataract surgery.15

Miyake studied the corneal endothelium of subjects with and without pseudoexfoliation syndrome. The corneal endothelium was evaluated based on cell density, coefficient of variation in cell size and the percentage of hexagonal cells. The affected eye definitely showed increased variability in endothelial cell size and shape while the eyes of those without pseudoexfoliation syndrome showed few
such abnormalities. The endothelium of the normal fellow eye of PXF patients contained pleomorphism and polymegathism of similar magnitude as the exfoliative eye. Brooks also noted decreased endothelial cell count in the PXF eye along with pleomorphism and polymegathism. A possible explanation for Miyake's results in the study could be due to an abnormal metabolic process but this is not proven.

A study by Mizuno was undertaken to look for any significant correlation of pseudoxfoliation syndrome to acid phosphatase which is a marker enzyme of the lysosomal enzymes. Mizuno had noticed from his previous study on pseudoexfoliation syndrome that there appeared to be an abnormal increase in lysosomes in the iris and ciliary body so therefore believed PXF to be due to a consequent increase in acid phosphatase. Examination of the anterior lens surface, iris and aqueous humor of PXF subjects found flecks of lead phosphate which was defined to mean a strong or moderate activity of acid phosphatase. Although acid phosphatase activity is normally found in the lens and iris, its detection is usually barely detectable even with cataractous eyes. Mizuno concluded that lysosomal enzymes were either directly or indirectly involved in the manifestation of pseudoexfoliation.

PXF has been associated with increased anterior chamber angle pigmentation. All patients of Rouhianen's study diagnosed with PXF were positive for pigmentation while non-pigmentation of the anterior chamber angle was the common finding in normal eyes. The most heavily pigmented trabecular meshwork belonged to patients with pseudoexfoliative glaucoma. It appeared according to the
analysis of variance that iris color did not have an input on trabecular meshwork pigmentation. From this conclusion, it is suggested that light pigmented eyes (blue to gray-green) with positive pigmentation in the anterior chamber angle always be considered a sign of pathological change.3

Pseudoexfoliative material within the conjunctiva of patients has frequently been found by researchers. Knowing this, Streeten decided to study 13 conjunctival samples of PXF patients for its morphology and distribution of PXF material. Most of the samples showed signs of aging in the elastic fibers. The PXF material was found throughout the conjunctiva without affinity toward a specific structural area. PXF and elastotic material were generally found intermingled with each other which may suggest PXF to be a type of elastosis. Ultrastructural comparison of samples from severe elastosis of conjunctival pinguecula and pterygia with pseudoexfoliative conjunctiva showed great similarity in their structure and composition.5

Pseudoexfoliation Syndrome and its relation to Pigment Dispersion Syndrome

Pseudexfoliation and Pigment Dispersion syndrome, while they appear to be two separate diseases, actually have many similarities in common, such as pigment in the anterior chamber, increased pigmentation in the trabecular meshwork and iris
Both appear to have an increased risk of open angle glaucoma.19

Some differences are that PXF syndrome is more common in older patients while PDS is usually found in young, white males. PDS most commonly occurs bilaterally while pseudoexfoliation occurs unilaterally. Transillumination of the iris in PDS is seen in the midperiphery while in PXF it is only seen along the pupillary margin. While pigment dispersion is known to occur in both PDS and PXF, there is only minimal pigment attachment to the corneal endothelium in PXF unlike PDS.2

Effectivity of Laser Trabeculoplasty

Argon laser trabeculoplasty (ALT) is used in pseudoexfoliative glaucoma to lower IOP's. Bruisini studied its long term effectivity on lowering intraocular pressure and stopping the progression of glaucomatous damage to the eye and found that IOP's were successfully lowered to normal IOP levels on a long term basis. However, an acute and sometimes high pressure rise is known to occur in PXF glaucoma patients immediately after laser treatment. The IOP does stabilize, but not until after several hours or sometimes days.21

Brubaker's research found that patients with higher initial IOP's showed greater response to ALT and more PXF glaucoma patients were found to respond to treatment than either chronic simple glaucoma patients or open angle glaucoma patients.22
While long term reduction in intraocular pressure is found to be successful in pseudoexfoliative glaucoma, it does not stop the progression of visual field loss. 25 percent of those who underwent surgery still showed deterioration in visual field and all 7 patients with severe visual field loss eventually became blind even when normal IOP is maintained.21

Summary

Although there is still very little that is known on the etiology of Pseudoexfoliation syndrome, this consolidation of views may help us to get a better grasp of the disease process. In summary, we have found that PXF can vary widely in prevalence depending on population location and culture but it always seems to occur with old age which is indicative of an aging process. It has also been determined that there is a 25 percent chance of developing glaucoma bilaterally, assuming unilateral glaucoma and PXF of the fellow eye is present. Poor dilation and fragile lens zonules have been of concern when performing cataract surgery on PXF patients. Its association with pigment dispersion syndrome has also been discussed.

Of particular significance is the fact that even with ALT, visual field loss is still progressive in many patients with PXF glaucoma. Earlier detection of PXF and further study may be helpful in developing improved treatment procedures.


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