PSEUDOEXFOLIATIVE GLAUCOMA



Eye Learn

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Pseudoexfoliative glaucoma



- 1. Pseudo Exfoliative Syndrome- pathology, signs, complications & management. (2007) (2004)
- 2. Discuss the pathology, clinical features and management of pseudo exfoliation syndrome. D2013
- 3. a) Etiopathogenesis, clinical features and diagnosis of pseudoexfoliative glaucoma b) Give specific features of true exfoliation in eye 3+3+2+2 J2018

Introduction

- Exfoliative syndrome (previously or classically known as pseudoexfoliation syndrome) occurs when several ocular tissues synthesize an abnormal protein. This protein may obstruct the trabecular meshwork and cause glaucoma.
- Exfoliation syndrome and its associated glaucoma are known by a variety of other names, including pseudoexfoliation, senile exfoliation, senile uveal exfoliation, glaucoma capsulare, and iridociliary exfoliation.
- Pseudoexfoliative material (PXF), the presence of which in the eye is termed pseudoexfoliation syndrome (PXS), is a common cause of secondary open-angle glaucoma, but is easily overlooked if signs are mild.
- Pseudoexfoliation syndrome can present unilaterally or bilaterally and with varying degrees of asymmetry. Often, this disorder presents unilaterally, and the uninvolved eye manifests signs of the disease at a later time.
- It should be distinguished from true capsular exfoliation, which occurs due to chronic infrared exposure.

• Epidemiology

- This syndrome is strongly age related: it is rarely seen in persons younger than 50 years though after this age its prevalence increases rapidly and occurs most commonly in individuals older than 70 years(-90).
- It is more common in women than men.
- The prevalence is up to 5% in many older populations but is particularly common in Scandinavia (50%) and several other areas, including parts of Africa; rates of 25% or more have been reported in members of some ethnic groups with symptomatic cataract.
- The risk of progression to glaucoma also varies widely and can be as high as 40% of patients over a 10-year period.
- The prevalence of exfoliation syndrome in the Framingham study was 0.6% in patients younger than 65 years of age, 2.6% in patients 65–74 years of age and 5.0% in patients 75–85 years of age.
- In the Blue Mountains Eye Study, the exfoliation syndrome prevalence was 2.7%
- The incidence of glaucoma (PXG) at diagnosis of PXS is 15–30%, and the cumulative risk of eyes with PXS requiring glaucoma treatment may be as high as 60% at 5 years.

Genetics

- Most cases appear to be sporadic, but Allingham and associates found a series of Icelandic families in which there appears to be an X-linked inheritance pattern.
- In all cases in which a parent and child were found to have exfoliation syndrome, the parent was always the mother.
- Recently, a polymorphism in exon 1 of the LOXL1 gene has been found to be highly associated with exfoliative syndrome

Pathogenesis

• PXF is a grey-white fibrillary amyloid-like material; it may derive from abnormal extracellular matrix metabolism in ocular and other tissues. The material is deposited on various ocular structures including

1.	Skin of the eyelid	5.	Lens epithelium and capsule
2.	Conjunctiva and subconjunctival tissue.	6.	Zonular fibres,
3.	Iris pigment epithelium, iris stroma, iris blood vessels,	7.	Trabeculum
4.	Pupillary margin	8.	Ciliary epithelium,

Systemic associations

- PXF has been found in skin and visceral organs (skin, lung, heart, and liver.), leading to the concept of PXS as the ocular manifestation of a **systemic disorder**.
- PXS is associated with an increased prevalence of vascular (cerebrovascular diseases) disorders, hearing loss and Alzheimer disease.
- Plasma homocysteine tends to be higher than controls, and inadequate dietary folate intake (folate reduces homocysteine) may be a risk factor.
- Increased levels of plasma homocysteine have been associated with increased risk of cardiovascular disease.

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On microscopy

- The exfoliation material appears as a fibrillar protein arranged in an irregular meshwork.
- This material has been compared to zonules, basement membrane, microtubular constituents, and amyloid.
- At one time, many thought that all of the exfoliation material came from the lens capsule and epithelium.
- However, the material has a multifocal origin and has been found in the iris, ciliary epithelium, and conjunctiva as well as in ocular and orbital blood vessels.

Etiopathogenesis

- The etiopathogenesis is multifactorial, but in at least some populations almost all patients with PXS have certain single nucleotide polymorphisms (SNPs) in the LOXL1 gene, which is involved in elastin fibre production.
- However, the SNPs are very common in the general population and most individuals with them do not develop PXS, suggesting a multifactorial etiology for this disease.
- The exact mechanism by which LOXL1 mutations are related to pseudoexfoliation syndrome is unclear, but it likely involves the reduced or abnormal synthesis of elastin fibers.
- Schlotzer-Schredhardt and associates- Inhibitors of matrix metalloproteinases [tissue inhibitor of metalloproteinases (TIMPs)] have been found to be upregulated and actual matrix metalloproteins have been found to be downregulated in the aqueous humor of eyes with exfoliative syndrome compared to eyes without.
- This abnormal relationship leads to the development and precipitation of the exfoliative material and pigment that obstruct the trabecular meshwork.
- **Ho and colleagues** concluded that there is downregulation of proteolytic activity in the trabecular meshwork leading to clogging.
- Open-angle glaucoma associated with PXF is conventionally due to elevated IOP, likely mechanisms including trabecular obstruction by PXF and liberated iris pigment, with secondary degenerative outflow dysfunction. (PXF impede the outflow of aqueous through the trabecular meshwork or uveoscleral pathways)
- In addition, since elastin is an important component of the lamina cribrosa, pseudoexfoliation syndrome may increase the susceptibility of the optic nerve to injury. Elastin abnormality may affect the rigidity of the lamina cribrosa.
- This increased susceptibility may, in turn, contribute to the increased risk of development and progression of glaucoma in these patients, as was found in the Early Manifest Glaucoma Trial
- A high prevalence of glaucomatous optic neuropathy has been reported in eyes with visible PXF but normal IOP, and in fellow eyes of PXS with no visible PXF and apparently normal IOP.
- Aggressive investigation such as conjunctival biopsy will usually reveal subclinical PXF in fellow eyes.
- A few authorities have postulated an underlying defect of the outflow channels and supported this theory by finding a few patients with unilateral exfoliation and bilateral glaucoma.
- However, many patients with apparent unilateral disease have bilateral pseudoexfoliation that can be demonstrated by conjunctival biopsy.
- In addition, most patients with unilateral pseudoexfoliation syndrome have more abnormal aqueous humor dynamics in the affected eye.
- Finally, patients with exfoliation syndrome and glaucoma resemble the normal population rather than patients with POAG in their corticosteroid responsiveness.





Clinical features

• Diagnosis is usually incidental, though follows vision loss from advanced glaucoma more commonly than POAG.

1. Cornea.

- PXF may be deposited on the endothelium, and scattered pigment deposits are common.
- A vertical (Krukenberg) spindle may rarely form, similar to that seen in pigment dispersion syndrome.
- Endothelial cell abnormalities such as low density are more common than average.

2. Anterior chamber.

• PXF particles are sometimes seen; mild aqueous flare from an impaired blood-aqueous barrier is common.

3. Iris.

- Granular PXF deposits, pupillary ruff loss and patchy transillumination defects at the pupillary margin.
- The peripapillary iris has an irregular, moth-eaten pattern of transillumination.
- Fluorescein angiography of the iris reveals a decreased number of vessels, neovascularization, and leakage from the vessels.
- The pupil often dilates poorly, likely because of infiltration of fibrillar material into the iris stroma.

4. Lens.

- The classic characteristic of pseudoexfoliation syndrome is the deposition of fibrillar deposits in a "bull's-eye" pattern on the anterior lens capsule, which is best seen after pupillary dilation.
- The anterior lens capsule typically shows a central disc and a radially indented peripheral layer of PXF material, separated by a clear zone maintained by pupillary abrasion
- The central and peripheral zones can be entirely separate or can be joined by bridges of material.
- In some cases, the central disc is not present.
- Peripheral capsular deposition is often visible only with pupillary dilatation
- Deposits may be flaky, with scrolled edges.
- Cataract is more common than average.
- Phacodonesis (lens instability) due to Zonular weakness may be present, but spontaneous subluxation is rare.

5. Anterior chamber angle.

- Regular gonioscopy at least annually in most cases is important.
- Patchy trabecular and Schwalbe line hyperpigmentation is common, especially inferiorly. sometimes in a variegated fashion
- A Sampaolesi line is seen in PXF and other causes of a heavily pigmented angle: an irregular band of pigment running on or anterior to the Schwalbe line.
- Dandruff-like PXF angle deposits may be seen.
- There is an increased risk of angle closure and of post-surgical malignant glaucoma (cilio-lenticular block), probably due to zonular laxity.
- The zonular fibers in patients with pseudoexfoliation syndrome are often weak and may cause an anterior movement of the lens-iris interface, resulting in narrow angles.

6. **IOP.**

- In most eyes the presence of glaucomatous damage is associated with elevated IOP.
- The majority of patients have a chronic open-angle glaucoma that is usually unilateral at first.
- Occasionally the IOP may rise acutely despite a wide angle, mimicking acute angle closure.
- Clinically, this fibrillar extracellular material (Dandruff-like flakes) can be seen on the pupillary margin, zonular fibers of the lens, ciliary processes, inferior anterior chamber angle(trabecular meshwork), anterior and posterior iris., corneal endothelium, and the anterior hyaloid in aphakic eyes
- 7. Investigation is similar to that of POAG.

8. Prognosis.

- Pseudoexfoliation glaucoma differs from POAG in that it often presents unilaterally and with greater pigmentation of the trabecular meshwork.
- Prognosis is worse than POAG as the IOP is often higher and there are greater diurnal fluctuations in IOP in pseudoexfoliation glaucoma than in POAG.
- Severe damage may be present at diagnosis, or can develop rapidly.
- It is therefore important to monitor patients closely, and it may be prudent for review in patients with PXS to take place at intervals of no more than 6 months.

Treatment

1. Medical treatment is similar to that of POAG, but failure is more common.

2. Laser trabeculoplasty

- Laser trabeculoplasty is probably more effective than in POAG, with mean IOP reduction around 30% following SLT.
- Care should be taken not to apply excessive energy, as trabecular pigmentation may confer higher absorption; transient IOP spikes are not uncommon.
- Argon laser trabeculoplasty has its greatest pressure-lowering effect in exfoliation syndrome.
- Somewhat paradoxically, however, the ultimate success rate of ALT in patients with exfoliation syndrome may be lower than that in other conditions because the initial pressures are higher and because adjunctive medical therapy is less effective.
- Further, in many successfully treated eyes, the IOP rises again in 12–36 months.
- Filtering surgery has a high rate of success in this condition.

3. Phacoemulsification

- Alone may significantly lower IOP, though it may give better control combined with trabeculectomy.
- There is a higher risk of complications, due to poor mydriasis, increased fragility of the zonule and lens capsule, and endothelial deficiency
- Cataract surgery- risk of zonular dehiscence, vitreous loss, lens dislocation, and other complications intraoperatively
- There is also an increased risk of a postoperative IOP spike, postoperative corneal edema, capsular opacification, capsulorhexis contraction (capsular phimosis) and late IOL decentration or dislocation.
- 4. Filtration surgery in PXG has a similar success rate to POAG.

5. Trabecular aspiration

- It is a non-filtering procedure performed with a suction canula, to clear debris from the trabecular meshwork in cases of exfoliation syndrome.
- Alone it seems to confer at least a short-term benefit, and can be performed at the same time as other intraocular procedures.

• True exfoliation

- It is seen in glassblowers cataract
- It occurs due to infrared heat radiation to the eye causing changes in the lens proteins
- There occurs delamination of the anterior lens capsule.
- The anterior capsule splits into anterior and posterior part.
- It is not associated with glaucoma or rise in IOP

