Answer to Ophthaproblem *continued from* **page 683**

3. Pseudoexfoliation syndrome

Pseudoexfoliation (PEX) syndrome is a connective tissue disorder that results in the deposition of abnormal proteins in the extracellular matrix. Ocular manifestations include accumulation of abnormal fibrillar deposits on the anterior lens capsule and pupillary margin, which are visible on slit lamp examination. These fibrillar deposits are actually material produced by abnormal membranes of aging epithelial cells, and have been described as a "grey-white, fibrilogranular, extracellular, matrix material composed of a protein core surrounded by glycosaminoglycans."[1] There is often increased transillumination of the iris at the pupillary margin. This disorder has systemic manifestations, and pseudoexfoliative material might be found in vascular structures as well as visceral organs.[2] Of particular importance, PEX syndrome has been associated with an increased risk of abdominal aortic aneurysm.[3]

Pseudoexfoliation syndrome is found in populations around the world. Although PEX syndrome is highly prevalent among people of British ancestry, the prevalence of PEX syndrome is highest among Scandinavian populations.[4] Pseudoexfoliation syndrome prevalence is also age-related, increasing from 0.6% among those 52 to 64 years of age to 5% among those between 75 and 85 years of age.[5]

Pathogenesis

The molecular events underlying the deposition of proteins seen in PEX syndrome are only partly understood. Some research has been done on the role of homocysteine in PEX syndrome. There are also contrasting studies on the correlation between PEX syndrome and lower plasma levels of certain vitamins essential to homocysteine metabolism (ie, vitamin B6, vitamin B12, and folate).[6] Further research, however, is required.

Pseudoexfoliation syndrome can cause vision-threatening sequelae. In particular, owing to tissue alteration, patients are predisposed to secondary open-angle glaucoma and cataracts. Glaucoma arises from the accumulation of pseudoexfoliative material and pigmentary granules within the trabecular meshwork—the fluid drainage system of the eye. Because aqueous humour continues to be produced, the increased resistance to outflow induced by the pseudoexfoliative material causes the intraocular pressure (IOP) to rise. This in turn causes progressive loss of retinal ganglion cells, which form the optic nerve. This process is termed *glaucomatous optic neuropathy,* and is a common cause of blindness.

Recent studies have identified a single-nucleotide polymorphism in the lysyl oxidase–like protein 1 gene that demonstrates a strong association with cases of PEX glaucoma in a number of populations. The test is not diagnostic, as the alleles are found in many non-PEX glaucoma patients as well, suggesting other genetic or environmental factors affecting the expression of the lysyl oxidase–like protein 1 gene.[7]

Diagnosis

Because of its insidious onset and progression, PEX syndrome is often found incidentally on slit lamp examination; if not, it is not usually diagnosed until a very late stage when the patient develops symptoms of glaucoma, namely peripheral visual field constriction. Pseudoexfoliation syndrome usually begins unilaterally, but will become bilateral in 25% of such cases within 10 years. Moreover, the "normal" eye often has unnoticed but subtle PEX syndrome.[2]

On examination of an affected dilated eye, a deposit consisting of 3 zones can be observed in the anterior lens capsule: a central zone, containing disk-shaped, homogenous, white, flaky material; a relatively clear intermediate zone; and an outer peripheral zone also containing material.[2] This appearance is formed by the normal dilation and constriction of the iris, which causes the iris to rub on the lens and displace the fibrillar material in a circular ring. Atrophy of the iris dilator muscle is responsible for poor pupil dilation, which is most apparent upon pharmacologic dilation.

Pseudoexfoliation syndrome is also an important clinical diagnosis for patients undergoing cataract surgery. Not only does this disorder induce earlier onset of cataract, but it also causes increased zonular laxity and poor iris dilation. Lens zonules hold the lens in place, and good pupil dilation improves surgical visualization. The effect of PEX syndrome on the lens zonules and iris increases the risk of capsular rupture or zonular dehiscence during cataract surgery, which can induce sight-threatening complications.

Management

All patients with suspected cases of PEX syndrome on clinical examination should be referred to an eye care professional. If PEX is diagnosed early, and there is no increase in IOP, yearly monitoring of IOP, visual fields, and optic disks is the recommended approach. More frequent examinations are warranted if there are substantial PEX stigmata; or if the IOP increases upon successive examination, is approaching the upper limits of normal (21 mm Hg), or is very asymmetric (more than a 3–mm Hg difference).[2]

If the condition has resulted in secondary open-angle glaucoma with clinically apparent glaucomatous optic nerve damage or glaucomatous visual field defects, the patient should be treated similarly to those with primary open-angle glaucoma. Management of PEX glaucoma usually begins with IOP-lowering drugs; however, PEX glaucoma is more resistant to medical

therapy compared with primary open-angle glaucoma.[5] Laser trabeculoplasty, the use of laser energy to alter the trabecular meshwork of the eyes, has high success rates in PEX glaucoma, but its effects might wear off rapidly and cause IOP spiking. If medical or laser therapy fails to control the IOP, then advanced surgical interventions such as trabeculectomy or glaucoma drainage device implantation are required.[8]

Conclusion

Pseudoexfoliation syndrome is an age-related systemic disorder characterized by accumulation of abnormal proteins (pseudoexfoliative material). In the eye, these proteins are deposited on the anterior lens capsule and iris, as well as within the trabecular meshwork. This syndrome might insidiously progress to glaucoma and often results in blindness. Additionally, cataract surgery is a higher-risk procedure in patients with PEX syndrome than in patients without. Nevertheless, cataract surgery in most patients with PEX syndrome is uneventful. Patients with this quiet disease are often diagnosed incidentally or, unfortunately, when they present with visual symptoms of glaucoma, which become detectable to the patient only at advanced stages of the disease. Hence, early recognition and appropriate management of PEX syndrome and PEX glaucoma are important in the prevention of blindness.

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Competing interests
None declared

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