Pseudoexfoliation of lens capsule and glaucoma

Case report

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A woman aged 80 years was first seen in October 1973. She had been suffering from watering eyes and on one occasion, when wiping her right eye, had noticed that the vision of her left eye was blurred. In the past she had had an operation on her 'tear duct', pyelitis, and an operation for an abdominal cyst. Currently she was well apart from some rheumatoid arthritis of her hands.

Examination showed her visual acuity to be right 6/5, left 6/60. The right lens capsule showed pseudoexfoliation (Fig. 1) while the left lens capsule was quite unaffected (Fig. 2). Gonioscopy showed wide open angles without trabecular pigmentation. The intraocular pressure was right 18 mm and left 24 mm. The right optic disc was normal but the left showed glaucomatous cupping and new vessel formation. There were also several retinal haemorrhages characteristic of retinal branch vein thrombosis. There were no other significant clinical findings. In short, the findings were of an old woman with pseudoexfoliation of the right lens capsule and no glaucoma, glaucoma of the left eye without pseudoexfoliation, and an absence of typical trabecular pigmentation in either eye.

Discussion

Pseudoexfoliation of the lens capsule was first noted by Lindberg (1917) and more fully described by Vogt (1925), who also noted its association with glaucoma and coined the term 'glaucoma capsulare'. This association has been a challenge to successive generations of investigators. Vogt (1926) thought that the exfoliated material blocked the outlets of the angle and so caused glaucoma. He also considered the possibility of pseudoexfoliation being the result of glaucoma. Malling (1938) held that both the capsular changes and glaucoma were secondary to vascular changes in the uvea, whereas Bedell (1926) considered the relationship coincidental, and Trantas (1929) thought that the glaucoma was due to degenerative changes in the

excretory channels identical with the change in the lens capsule. Chandler and Grant (1965), and others, pointed to the increased trabecular pigmentation that is often associated with pseudoexfoliation and saw in it a cause of trabecular embarrassment. All these views imply that the glaucoma is secondary and different from chronic simple glaucoma.

Another puzzling fact about this condition is the great variation of its incidence in glaucoma patients in different countries. For example, its incidence among English glaucoma patients is given as 2 per cent while in Norway the figure is 93 per cent (Tarkkanen, 1962). Thomassen (1949), who examined patients in both countries, held that these were true differences. He found an incidence of 79 per cent in Oslo and of 2 per cent in London. If that was so, and the glaucoma is secondary, then, other things being equal, there should be an excess of glaucoma patients in Norway. There are many fallacies in comparing the results of different glaucoma surveys, but the following figures are available.

Bertelsen (1965) found an incidence of glaucoma in Norway of 1.7 per cent in the 50-59 age group and 3.3 per cent in the 60-69 age group. Wright (1966) in Bedford, England, found an incidence of 2.18 per cent in the 50-59 age group and of 2.58 per cent in the 60-69 age group, excluding ocular hypertensives who account for 0.20 per cent in the younger group and 2.44 per cent in the older. More recent investigations have thrown interesting sidelights on the older views as well as opening up new lines of inquiry.

Aasved (1971b) found that the incidence of pseudoexfoliation increases with age and with the severity of glaucoma. Apparently the clinics reporting a high incidence of pseudoexfoliation in Norway have particularly advanced cases referred to them. Aasved (1969) found the incidence of pseudoexfoliation in Birmingham to be of the same order of magnitude as in Norway. Similarly, Jones (1957), in London, found that of glaucoma patients undergoing surgery 5.5 per cent had pseudoexfoliation compared with 2 per cent of

glaucoma outpatients found by Thomassen (1949).

Aasved (1971c) also noted several interesting facets of the natural history of pseudoexfoliation. It increases intraocular pressure even in the absence of glaucoma. Patients who develop pseudoexfoliation while under observation tend to develop glaucoma at about the same time, so that there is no increase in the incidence of glaucoma with age as there is in patients without pseudoexfoliation (Aasved, 1971a). This is consistent with the findings of Tarkkanen (1962). Moreover, patients with pseudoexfoliation who have glaucoma tend to be younger than those who do not have glaucoma (Aasved, 1971c; Gillies, 1972; Tarkkanen, 1962). This also argues against a progressive onset of glaucoma.

There is evidence to suggest that the manifestations of the syndrome are more widespread than was once thought. Thus Ringvold (1973) found pseudoexfoliated material in the conjunctiva, Vannas (1969) found vascular anomalies in the irides of eyes with pseudoexfoliation, and Laatikainen (1971) found limbal circulatory abnormalities more often in such eyes. Evidence has also been presented against the view that the glaucoma is simply due to trabecular obstruction by pseudoexfoliation flakes or pigment. Tarkkanen (1962) found flakes in the angles of 46 per cent of the non-glaucomatous eyes and in only 50 per cent of the glaucomatous, and while the glaucomatous eyes tended to be more heavily pigmented 65 per cent were graded 1 or 2 on a scale of 4 and, perhaps more significantly, 8 per cent of the non-glaucomatous eyes had grade 3 pigmentation. Tarkkanen further points out that there is a genetic link between pseudoexfoliation and chronic simple glaucoma. Offspring of glaucomatous parents may have pseudoexfoliation and vice versa.

However, it seems that the most telling argument against the simple obstruction view is the fact that quite a number of patients with unilateral pseudoexfoliation have bilateral glaucoma (36 per cent of Tarkkanen's series of 187 patients). The converse is also true. Not all patients with pseudoexfoliation have glaucoma, and it is of interest to know whether non-glaucomatous eyes, either in the presence of pseudoexfoliation or in the other eye, have an increased tendency to glaucoma. This tendency has been assessed on the basis of steroid sensitivity.

Becker and Mills (1963) administered topical corticosteroids to 30 normal volunteers, of whom 40 per cent developed a rise of 6 mm or more in their intraocular pressure, while 90 per cent of 32 glaucoma suspects and 93 per cent of 44 glaucoma patients showed such a rise. (These data are extracted from Becker and Mills's Figs 1 and 7).

Armaly (1963) found that 9 (40 per cent) out of 22 normal volunteers over the age of 40 had a rise of intraocular pressure of 5 mm or more under similar conditions. Becker and Hahn (1964) found that after topical corticosteroids 32 per cent of normal volunteers, 92 per cent of glaucoma patients, 80 per cent of glaucoma suspects, and 73 per cent of offspring of glaucoma patients had a rise of 6 mm or more in their intraocular pressure.

We may summarize these results by saying that in a population of normal volunteers about one-third respond to steroids and that this proportion increases to over 90 per cent in chronic simple glaucoma patients, with intermediate values for glaucoma suspects. Gillies (1970) administered topical steroids to 38 non-glaucomatous eyes of 29 patients with pseudoexfoliation. There was a rise in pressure of 5 mm or more in five eyes (13 per cent). Tarkkanen and Horsmanheimo (1966) found that of 33 patients who had bilateral or unilateral non-glaucomatous pseudoexfoliation five (15 per cent) had a rise of 6 mm or more or a reduction in facility of outflow greater than 33 per cent.

It would seem, therefore, that these eyes are no more prone to glaucoma than average eyes, and if anything less so. Furthermore, Pohjola and Horsmanheimo (1971) found that of eyes with pseudoexfoliation that actually had glaucoma only 28 per cent responded to corticosteroids with a pressure rise of 5 mm or more (as against 90 per cent of chronic simple glaucoma eyes), and in all but one of the responders the glaucoma was bilateral.

These authors offer the following explanation. Patients with pseudoexfoliation may have one of two kinds of glaucoma, either primary chronic simple glaucoma, which is bilateral even with unilateral pseudoexfoliation and is steroid responsive, or a secondary glaucoma, which is non-steroid responsive and is confined to the pseudoexfoliated eye. Furthermore, the presence of the pseudoexfoliation gene is strongly contributory to the expression of chronic simple glaucoma, so that steroid-responders with pseudoexfoliation tend to develop manifest glaucoma, leaving only a small proportion of responders among the non-glaucomatous eyes.

Tarkkanen (1962) notes that patients with unilateral pseudoexfoliation and glaucoma, which would be classed by Pohjola and Horsmanheimo as secondary glaucoma, show a high proportion of males, relatively many myopes, a family history of glaucoma, marked pigmentary changes, and a large proportion of high initial intraocular pressures as compared with bilateral cases.

If we now look at Tarkkanen's overall figures with Pohjola and Horsmanheimo's views in mind

FIG. 1 Right eye: pseudoexfoliation of lens capsule

FIG. 2 Left eye: normal lens capsule

we see that 60 per cent of all patients with pseudoexfoliation have glaucoma. Of these some have chronic simple glaucoma and some have secondary glaucoma. The relative proportions of these conditions may be estimated from the distribution of glaucoma in patients with unilateral pseudoexfoliation (Table 19). There are 36 per cent of patients with bilateral glaucoma and 23 per cent with unilateral glaucoma. These figures can serve as a measure of the incidence of chronic simple glaucoma and secondary glaucoma respectively.

While the manner in which the secondary glaucoma is produced is not clear the association of chronic simple glaucoma in 37 per cent of cases of pseudoexfoliation also requires explanation. Such an explanation has been put forward by Tarkkanen (1962).

'The condition [pseudoexfoliation] may be associated with a gene bearing three characteristics. (1) An abnormality of the drainage mechanism of the aqueous,

similar to the one seen in chronic simple glaucoma. (2) Pseudoexfoliation. (3) Pigmentary disturbance. The variations in expression of the gene would explain why the three characteristics are occasionally found together, but sometimes only one or two of them are present.'

The subject of the present report may be viewed as illustrating the thesis of Pohjola and Horsmanheimo.

A search of the English-language literature discovered mention of only five other such cases, where one eye was affected by pseudoexfoliation only and the other by glaucoma only (Trantas, 1929 (two cases); Fahmy, 1936; Wilson, 1953; Good and Ratnaj, 1968). The rarity of this combination seems analogous to the rarity of unilateral chronic simple glaucoma. Leydhecker (1973) states that fewer than 0.1 per cent of cases remain unilateral 10 years after the onset of the disease. Possibly further follow-up would find the glaucoma in these cases becoming bilateral (indeed, Wilson's

patient had a pressure of 23 mm in the sound eye). When a little more advanced such bilateral cases would excite no undue interest. They are nevertheless worthy of attention, because they emphasize the fact that pseudoexfoliation and glaucoma,

even though closely associated, can arise independently.

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