Symposium on congenital anomalies of the eye associated with glaucoma

Chairman: Robert N. Shaffer

The symposium was opened by a brief report on the recent conference on oxygen use in premature infants. J. Everett Kinsey, Ph.D., and Arnall Patz, M.D., stated that more oxygen was being used at present in order to decrease infant deaths. Dr. Patz recommended routine ophthalmoscopy of premature infants receiving oxygen. If excessive oxygen is being given, the retinal arterioles will show extreme vasoconstriction. A decrease in oxygen is indicated. This practical method can be carried out by ophthalmologists or by the pediatricians, and it does not require a skilled pediatric team to extract arterial blood and analyze its oxygen count.

Congenital mesodermal anomalies and glaucoma

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The purpose of this paper is to review three congenital anomaly syndromes that have the following characteristics in common: genetic determination of the anomalies, predominant involvement of tissues of mesodermal derivation, and relative frequency of an associated glaucoma.

Mesodermal dysgenesis of the cornea and iris

Developmental ocular anomalies are the main characteristics of this syndrome (Axenfeld's syndrome, Rieger's syndrome), although associated dental and skeletal abnormalities (palate deformities, partial...
anodontia, dysgnathia, and so forth) have been reported. The defect is relatively rare and is transmitted as an autosomal dominant with a high penetrance rate and wide expressivity. Occasional sporadic cases, probably representing de novo mutations, also occur.

**Clinical characteristics.** The most consistent features of the syndrome are localized or diffuse hypoplasia of the anterior leaf of the iris, a prominent Schwalbe's line (so-called posterior embryotoxon [G. embryon; embryo; G. toxon, bow]), and persistent developmental iris stromal adhesions to peripheral cornea and Schwalbe's line and the trabecular meshwork.

Although the eye is usually normal in size, microcornea may occur, and buphthalmos may be seen if glaucoma supervenes early in life. Asymmetrical globe size and syndrome expression is not uncommon. A variety of pupillary and iris abnormalities may be seen consequent to the stromal hypoplasia and peripheral iris processes. Corectopia, dyscoria, and degrees of ectropion uveae may be present. Occasionally, the iris pigment epithelium is involved, with colobomas, partial aniridia, and pseudopolycoria resulting. True polycoria rarely occurs.

Anterior chamber angle findings are extremely variable, ranging from barely discernible and localized to extensive changes involving 360 degrees of the angle. The trabecular zone is widened, and Schwalbe's anterior border ring is prominent, frequently axially displaced, and visible to slit-lamp examination as a circumferential hyaline rod which in some cases appears to be detached from the back of the cornea. Nonprogressive and noninflammatory pleomorphic iris stromal adhesions bridge the angle and insert onto Schwalbe's line, and often onto the trabecular meshwork.

In a significant but undetermined percentage of cases, the dysgenesis of the anterior chamber angle structure impedes aqueous outflow, although the severity of the resultant glaucoma may not correlate well with the extent of the clinically observable angle aberrations. Probably more than 50 per cent of these patients seen by ophthalmologists have glaucoma. But they are necessarily a selected group, and the percentage would undoubtedly be lowered if the untroubled, asymptomatic, less involved individual were observed and diagnosed more frequently. As with other manifestations, glaucoma onset and severity is extremely variable. In one family we have observed patients with no glaucoma, glaucoma easily controlled medically, and glaucoma resulting in blindness despite intensive medical and surgical therapy. Glaucoma may be seen in infancy, but more often becomes manifest somewhat later in life, frequently before the age of thirty.

Various other ocular anomalies are found which are not an integral part of the syndrome. A number of corneal opacities and defects has been reported. When glaucoma occurs in infancy, classical ruptures in Descemet's membrane may result from corneal stretching. Except for epicapsular pigment stars, the crystalline lens is infrequently involved, although lens opacities, colobomas, and ectopia have been occasionally noted.

Strabismus and the spectrum of ametropias are frequent but nonspecific components of Axenfeld's syndrome. Compound myopic astigmatism is common when buphthalmos is present, and high refractive myopia may well result from microcornea. As might be predicted, asymmetrical involvement often results in the triad of anisometropia, refractive amblyopia, and strabismus. Along with others, we have also observed strabismus unrelated to refractive problems.

**Systemic hypoplastic mesodermal dystrophy**

In contrast to iridocorneal mesodermal dysgenesis, systemic as well as ocular abnormalities are prominent manifestations of Marfan's syndrome. The syndrome is uncommon, but by no means rare; and it is inherited as an autosomal dominant trait with fairly high penetrance and a broad...
range of expression. Sporadic cases do occur.

**Clinical characteristics.** The cardinal manifestations of Marfan’s syndrome are musculoskeletal, cardiovascular, and ocular.\(^6\)

Dolichomorphism is the characteristic skeletal feature of Marfan’s syndrome. Exaggerated limb length (dolichostenomelia) is frequent. Arachnodactyly may be striking, but is neither pathognomonic nor invariable. Other skeletal manifestations are manifold, including various rib cage deformities, dolichocephaly, kyphoscoliosis, and so forth.

Defective joint capsules, tendons, and ligaments result in hyperextensibility, flat feet, dislocations, and a gamut of typical deformities. Muscular hypotonia and sparse subcutaneous fat are secondary, associated findings.

Although the clinical importance of the various cardiovascular findings of Marfan’s syndrome cannot be overemphasized, detailed discussion is beyond the scope of this paper. Progressive degenerative changes in the wall of the aorta—and occasionally the pulmonary arteries—lead to ectasia, insufficiency and regurgitation, and dissecting aneurysms which may rupture.

Ectopia lentis is the signal ocular finding of Marfan’s syndrome, and is probably present in some 70 per cent of cases. Conversely, a high proportion of spontaneously dislocated lenses are found to have Marfan’s syndrome. Displacement of the small, globular lenses is usually bilateral and frequently in an upward direction.

Enlargement of the eye (megaloglobus), high myopia, and retinal detachment are other ocular stigmas of the syndrome. Miosis and poor response to mydriatics is probably explained by hypoplasia or absence of the dilator pupillae muscle.\(^7, 8\)

Glucoma due to poor aqueous outflow can be explained on the basis of anterior chamber angle anomalies.\(^8\) Additionally, displacement of the crystalline lens may result in phacogenic angle closure glaucoma. The use of miotics in the presence of the globular lens may increase pupillary block with a resultant “paradoxical” angle closure glaucoma. Mydriatic therapy would be indicated in such a situation.

It is important to remember that homocystinuria must be differentiated from Marfan’s syndrome.

**Systemic hyperplastic mesodermal dystrophy**

This rare syndrome (Weill-Marchesani syndrome\(^9, 10\)), which is the mesodermal antithesis of Marfan’s syndrome, may be more prevalent than the number of reported cases would indicate.\(^11\) In the limited number of cases studied, genetic transmission appeared to be either dominant or recessive with partial expression in the heterozygote.

**Clinical characteristics.** A brachymorphic habitus characterizes this syndrome. Typically, the patient has brachycephaly, short limbs, and pudgy hands and fingers.

There may be reduced joint motility and flexure deformities. (A patient of ours was operated upon to relieve “sclerosing tenosynovitis” of the flexor tendons of the hands.) Muscle mass and subcutaneous fat were well developed.\(^12\)

Microspherophakia, ectopia lentis, and lenticular myopia are characteristic ocular abnormalities of the Weill-Marchesani syndrome. In contrast to Marfan’s syndrome, bilateral dislocation of the lenses is reported to be in a downward direction.\(^11\) Other nonspecific ocular abnormalities may be present. We have observed an associated endothelial dystrophy of the cornea in one patient.

Phacogenic angle closure glaucoma is a common complication.\(^11\) While it would seem likely that glaucoma would also occur in the absence of angle closure, there has been insufficient documentation of this finding.

**Concluding remarks**

The three genetically determined syndromes reviewed in this paper have been categorized as “mesodermal anomalies.”
Nonetheless, associated ectodermal anomalies are also observed. Iris colobomas, partial aniridia, and lens opacities and ectopia have been documented in patients with Axenfeld’s syndrome. These abnormalities have been explained as resulting from the effect of the primary mesodermal disturbance on contiguous ectodermal structures. Zonular and lenticular anomalies are the most striking ocular defects in Marfan’s and the Weill-Marchesani syndromes. Again, a primary mesodermal defect of the ciliary body has been faulted. Indeed, the desire to tie all possible manifestations of these syndromes into one neat mesodermal package is quite understandable. Nonetheless, it would seem likely that at least some of these accompanying ectodermal defects are independently inherited. In Marfan’s syndrome, for example, it is suggested that a primary lesion of the zonule, ectopia lentis, and hypoplasia of the dilator pupillae muscle might be the polyphenic expression of a single gene.\textsuperscript{12}

Because of the variable expression of glaucoma complicating the predominantly mesodermal anomalies, few guidelines can be drawn concerning its management. In general, a conservative approach is indicated when glaucoma is not of the pupillary block or acute angle closure variety. Obviously the age at onset, severity, and many other factors must be weighed in determining the proper management course. When ectopia lentis provokes acute angle closure, a surgical approach is usually required. Individual circumstance determines whether iridectomy alone, lens extraction with iridectomy, or other surgical procedure is required. It can be said with certainty that management of these patients frequently challenges the ophthalmologist’s clinical acumen and surgical skills.

REFERENCES

4. Marfan, A. B.: Un cas de d\textsuperscript{\textsuperscript{o}}formation cong\textsuperscript{\textsuperscript{\textsuperscript{e}}}n\textsuperscript{\textsuperscript{\textsuperscript{e}}}nale des quatre membres plus pron\textsuperscript{\textsuperscript{\textsuperscript{c}}}nc\textsuperscript{\textsuperscript{\textsuperscript{e}}}e\textsuperscript{\textsuperscript{\textsuperscript{e}}}e par l\textsuperscript{\textsuperscript{\textsuperscript{e}}}all\textsuperscript{\textsuperscript{\textsuperscript{e}}}nglement des os, Bull. et m\textsuperscript{\textsuperscript{\textsuperscript{e}}}m. Soc. méd. hôp., 13: 220, 1896.