Mesoectodermal Dysgenesis: Familial Iris Anomaly

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Abnormalities of the anterior segment of the eye have been reported since the late nineteenth century. Axenfeld\(^1\) in 1920, and Rieger\(^2\) in 1935, were the first to more fully delineate these anatomic anomalies. In 1966 Reese and Ellsworth\(^3\) coined the term “anterior chamber cleavage syndrome” to represent congenital abnormalities of the anterior chamber characterized by iridocorneal adhesions, persistence of mesenchymal tissue in the anterior chamber angle, and defects of the cornea and lens. Cross and Maumenee,\(^4\) in 1973, referred to these anomalies by the term mesoectodermal dysgenesis. In 1975 Waring, Rodriguez, and Laibson\(^5\) introduced a simplified approach with an anatomic stepladder classification of the numerous peripheral and central malformations of the anterior chamber cleavage syndrome. For enhancing the learning process, this terminology has been accepted to include all possibilities of mesoectodermal dysgenesis of the anterior segment.\(^6\) We describe a family with unusual characteristics on this continuum (Fig. 1).

CASE REPORTS

**Patient No. 1**

The propositus (IV-5) was born on November 12, 1968, to a 25-year-old mother and a nonconsanguinous 26-year-old father. The pregnancy was uneventful with the exception of premature delivery. The birth weight was 1958 gm. He received oxygen during the neonatal period for three to four weeks.

Childhood and medical developmental histories revealed bilateral inguinal hernias requiring herniorrhaphy and agenesis of the left kidney. At his initial ophthalmic evaluation, abnormal irides were first noted. Physical examination at age 7.98 years revealed a head circumference of 52.3 cm (75 percentile), arm span of 124.1 cm, height of 119.3 cm (25 percentile), and an upper/lower body ratio of 0.96.\(^7\) Facial features did not suggest any recognizable syndrome (Fig. 2). Dental examination revealed six normal teeth per quadrant. Possible connective tissue abnormalities were suggested by the presence of well-healed bilateral herniorrhaphy scars and pedal arachnodactyly. The remainder of the examination was normal with the exception of the eyes.

Visual acuity, on April 25, 1974, was 20/30, OD, and 20/30, OS, with a refractive error of +3.50 + 0.50 x 90, OD, and +3.50 + 0.75 x 100, OS. The patient was orthophoric. The pupils were 2 mm and oval with a 3+ reaction to direct light; they dilated poorly with mydriatics and cycloplicans. Slit-lamp examination showed a white, granular deposit at the nasal limbus in the left cornea at the subepithelial-Bowman’s membrane levels. The irides showed prominent sphincter muscles and hypoplasia of the anterior stroma extending peripherally to the angle from the cusp (Fig. 3). The fundi were normal. On November 6, 1974, applanation pressures were: 20 mm Hg, OD, and 18 mm Hg, OS. The white, granular corneal deposits had increased to include nasal and temporal limbal areas of both eyes. Gonioscopy revealed normal anterior chamber angle structures. The major arterial circle of the iris, with its radial branches, was clearly visible secondary to the anterior iris stromal hypoplasia.

**Patient No. 2**

The father (III-1) was born on November 12, 1942, after an uneventful gestational period. Developmental and medical histories were normal. Physical examination at age 33.984 years showed a head circumference of 58.1 cm, arm span of 188.5 cm,
height of 178.7 cm, and a body ratio of 0.90. He had simian creases of both hands, as well as brachydactyly of the fifth fingers. Dental examination showed normally structured teeth with eight per quadrant. The remainder of the examination was normal except for a recently sustained leg injury and abnormal irides.

Ophthalmic examination showed a visual acuity of 20/20, OD, and 20/20 OS, with a refraction of +1.00 + 1.00 x 90, OD, and +1.50 + 1.50 x 90, OS. Intraocular pressure, by applanation tonometry, was 19 mm Hg, OD, and 19 mm Hg, OS. The pupils were 2 mm in diameter with a 2-3+ reaction to direct light; they dilated poorly to mydriatics and cycloplicics. Slit-lamp examination revealed a normal cornea. The iris showed a prominent sphincter with hypoplasia of the anterior iris stroma (Fig. 4). Gonioscopic of both eyes revealed normal anterior chamber angle structures and confirmed anterior stromal hypoplasia to the iris root. The fundi were normal.

Patient No. 3

The third son (IV-6) was born on September 23, 1970, after an uneventful gestation and delivery. The developmental and medical histories were normal. Physical examination at age 6.121 years showed a head circumference of 53.1 cm (75 percentile), arm span of 113.8 cm, height of 111.1 cm (25 percentile), and a body ratio of 1.01. The teeth were normal in appearance, and there were five per quadrant. There was brachydactyly of the fifth fingers. The remainder of the examination was normal except for the eyes.

The visual acuity was 20/40, OD, and 20/40, OS, with a refractive error of +2.00 + 2.50 x 80, OD, and +1.00 + 2.50 x 90, OS. The pupils were about 2 mm and oval; they reacted 3+ to direct light and dilated poorly with mydriatics and cycloplicics. Applanation tonometry showed intraocular pressures to be 20 mm Hg, OD, and 21 mm Hg, OS. Slit-lamp examination on November 6, 1976, revealed white, granular deposits
at the subepithelial-Bowman’s membrane levels at the nasal and temporal limbal areas of the left eye which were not present on initial examination in October of 1973. The iris had a moderately prominent sphincter with anterior stromal hypoplasia extending to the iris root by gonioscopy in both eyes. Again, the major arterial circle, with its radial vessels, was visible. The angle structures were normal. The fundi were normal.

Patient No. 4

The daughter (IV-7) was born prematurely on May 13, 1972. Her birth weight was 2270 mg, and she received oxygen therapy for a short period of time. Her childhood developmental and medical histories were normal. Physical examination at age 4.485 years showed a head circumference of 50.5 cm (50 percentile), arm span of 97 cm, height of 102 cm (about 35 percentile), and a body ratio of 54:48. There were five normal teeth in each quadrant. The head showed prominence of the frontal bone. She had brachydactyly of the five fingers. The remainder of the examination was normal except for the eyes.

The visual acuity was 20/40, OD, and 20/40, OS, with a refractive error of −0.50 + 2.50 x 90, OD, and −0.50 + 2.50 x 90, OS. The pupils were 2 mm in diameter and oval; they reacted 3+ to direct light and dilated poorly with mydriatics and cycloplegics.

Fig. 3. Prominence of the iris sphincter muscle and hypoplasia of the anterior iris stroma in the propositus (IV-5).

Fig. 4. Similar iris appearance of the father (III-1).

Tactile pressures were normal for both eyes; the parents refused sedation for accurate intraocular pressures recording. Slit-lamp examination revealed a normal cornea. The iris showed a prominent sphincter and hypoplasia of the anterior iris stroma with radial iris vessels easily seen. The child would not cooperate for gonioscopy. The fundi were normal.

COMMENTS

The embryologic development of the anterior chamber angle was originally thought to be an atrophic process in the mesenchymal tissues. This is in ill repute today. In 1955 Allen, Burian, and Braley presented the theory that the cleavage resulted from a period of extensive unequal growth between the mesenchymal tissue of the trabecular tissue and the iris-ciliary body tissue mass. In 1971 Smelser and Ostonis suggested the process of a gradual rarefaction of the reticular mesenchyme of the trabecular area. Continuing investigation of the embryologic etiology of the anterior chamber cleavage syndrome is being carried out. This may one day change the current thoughts and classifications.
Posterior embryotoxon, Axenfeld's anomaly, Rieger's anomaly and iridogoniodygenesis are included in the peripheral abnormalities of the anterior chamber cleavage syndrome. Known by many eponyms, posterior embryotoxon is a distinct, whitish-gray opacity at the level of Descemet's membrane representing a prominent and anteriorly placed Schwalbe's line. Incidence is reported as high as fifteen percent of normal eyes, and it has a familial occurrence. Posterior embryotoxon is an entity unto itself. When associated with glaucoma, additional ocular abnormalities, such as iris atrophy, corectopia, polycoria, and extensive remnants of the pupillary membrane, may occur. Histologically, a central collagen core with reticulin fibers and a basement membrane-like substance is seen. This is surrounded by Descemet's membrane and bounded internally by corneal endothelium.

A prominent Schwalbe's ring with attached iris strands is known as Axenfeld's anomaly. These strands range from fine processes to a broad lattice-like membrane. Rarely, these strands may originate from the iris collarette and produce a distorted pupil. About 50 percent of patients with Axenfeld's anomaly develop glaucoma at an early age, and this frequently goes unrecognized. Inheritance is usually autosomal dominant.

A prominent Schwalbe's line with iris strands and a hypoplastic iris stroma is Rieger's anomaly. The stromal hypoplasia may be either progressive or nonprogressive with and without the presence of glaucoma. Associated ocular findings include slit-like pupils, polycoria (true or pseudo), corectopia, persistent pupillary membrane, microcornea (real or pseudo), megalocornea, cornea plana, colobomas, ectopia lentis, and lens capsule stars. Glaucoma occurs in 60 percent of these patients and usually occurs before the age of 30 years. When associated with systemic abnormalities, it is known as Rieger's syndrome. Frequent dental anomalies include: hypodontia, anodontia, and maxillary hypoplasia with malocclusion. Retarded bone growth and mental retardation can also be present. About seventy (70%) percent of patients with this anomaly inherit it as an autosomal dominant trait with high penetrance and extremely variable expressivity.

Iridogoniodygenesis describes patients with hypoplastic anterior iris stroma and iris strands in the angle without a prominent Schwalbe's line. Most cases have been described by Jerndal from an autosomal dominant Swedish pedigree. All patients over the age of eight years had glaucoma. Associated ocular findings include megalocornea and corectopia.

Hypoplastic anterior iris stroma, in the absence of a prominent Schwalbe's line, iris processes, and glaucoma seen in this pedigree, lacks an eponym. These findings are seen in the father (III-1), two sons (IV-5, IV-6), and one daughter (IV-7). There is a vague history of ocular abnormalities in the father's brother (III-3) and in the father's maternal grandmother (I-2), neither of which is available for examination. The propositus (IV-5) had unilateral renal agenesis and bilateral inguinal hernias requiring repair. The father (III-1) and two siblings (IV-6, IV-7) had brachydactyly of the fifth fingers. All of these findings represent mesodermal abnormalities. It is interesting to note that no family member has developed glaucoma, although each should be regularly examined for this because of its increased incidence at any age in the anterior chamber cleavage syndrome.

One can infer genetic inheritance from the pedigree. X-linked transmission is excluded because of the male-to-male transmission. Recessive inheritance can be presumably excluded because this is a structural abnormality, there is no consanguinity, and three-fourths of the siblings are affected. The pedigree suggests autosomal dominant inheritance of a structural abnormality. The final mode of inheritance will be determined in the future generation.

It is important to differentiate the ocular findings in this family from other disorders with similar iris changes. Xeroderma pigmentosa has a variable age of onset, affects all layers of the iris (usually inferiorly), is autosomal recessive, and has associated lid and skin tumors. The etiology of essential iris atrophy is unknown, and it is associated with almost 100 percent incidence of glaucoma. Chandler's syndrome occurs in the third to fourth decade, is unilateral, has an endothelial dystrophy, and has a frequent association with glaucoma. The entity that most closely resembles this family is congenital stromal hypoplasia of the iris. As classically described, it has an extremely high incidence of glaucoma and angle anomalies, neither of which is present in this family.
However, both have autosomal dominant transmission.

We have presented the main peripheral abnormalities of the anterior chamber cleavage syndrome and a family with a new and unusual presentation. Using the purist's approach, this family represents a point on the spectrum of mesoectodermal dysgenesis or anterior chamber cleavage syndrome, to which it is more conveniently referred.

SUMMARY

A family is described with hypoplasia of the anterior iris stroma, no angle anomalies, and no glaucoma. The pedigree is suggestive of an autosomal dominant mode of inheritance. This is compared to the main peripheral malformations of the anterior chamber cleavage syndrome and other disease entities with similar iris changes. The pedigree represents a point on the continuum of mesoectodermal dysgenesis or anterior chamber cleavage syndrome.

REFERENCES


