EOPS 63rd ANNUAL MEETING

Date of Meeting: 11th to 14th June 2024
Location: Basal, Switzerland
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Material Submitted: 1 x H&E

Title: Anterior segment dysgenesis and Persistent Primary Hyperplastic Vitreous

Clinical History: This 9-year-old female was born with congenital cataract. She had a right lensectomy age one month and persistent primary hyperplastic vitreous was identified. The right eye was then affected by secondary glaucoma.

By age 7 she was persistently rubbing the right eye, and it was painful and watery with developing corneal decompensation. Due to persistent problems with a buphthamic eye the decision was taken for enucleation age 9.

She has reduced vision in the left eye with nystagmus. There are no other systemic abnormalities.

Ocular Pathology:
Macro*:* The specimen consists of an enlarged right eye 24 mm AP by 24 mm horizontally by 24 mm vertically with 2 mm optic nerve attached. The cornea is cloudy and measures 15 x 14 mm. The sclera is thinned. There are no shadow is on transillumination. The globe is opened in the horizontal plane. The anterior chamber is deep and there are strands arising from the iris crossing the anterior chamber. There is no identifiable lens. In the posterior segment there is a strand of tissue extending from the optic nerve head across the vitreous to form of white plaque in the place of the lens.

Microscopy: The corneal epithelium is oedematous but intact. There are several breaks in Bowman's layer with scarring of the superficial stroma. The posterior pigment epithelium is adherent to the posterior corneal surface and there are 2 strands of iris covered on both sides by pigment epithelium extending across the centre of the anterior chamber. Behind this is a plaque formed of fibrous tissue and adipose tissue within which there are entrapped remnants of lens capsule. This fibrous tissue is contiguous with ciliary processes. Superiorly there is no identifiable trabecular meshwork although there is a potential canal of Schlemm. Inferiorly the trabecular meshwork is covered by a layer of posterior pigment epithelium and an endothelial downgrowth.

In the posterior segment the retina shows advanced, glaucomatous atrophy with complete loss of the ganglion cell layer. A persistent primary hyperplastic vitreous containing a central blood vessel crosses from the optic disc head and extends to behind the lens plaque. The choroid is thin as is the sclera. There is complete loss of the pre-laminar region of the optic disc with bowing of the lamina cribrosa posteriorly and atrophy of the retrolaminar region with sagging meninges.

Summary of Findings: There is significant anterior segment dysgenesis and persistent hyperplastic fetal vasculature. There is adhesion of iris strands to the cornea causing corectopia. There are secondary retinal changes of glaucoma and cupping of the optic disc with thinning of the sclera.
Overall, the anterior chamber changes could fit with the spectrum of Axenfeld-Rieger anomaly.

Discussion:
Background: Axenfeld Rieger anomaly/syndrome (ARS) is a heterogenous group of conditions characterized by anterior segment dysgenesis of the eye which may be associated with systemic

congenital abnormalities[1]. Axenfeld described the condition in 1920 in a patient with anterior displacement of Schwalbe's line (posterior embryotoxon) and corectopia[2]. In 1934, Rieger described two patients with "mesodermal dysgenesis" consisting of iris hypoplasia, pseudopolycoria, and posterior embryotoxon[3]. Given the phenotypic similarities, these cases described by Axenfeld and Rieger are considered part of a group of disorders known as Axenfeld Rieger Syndrome.

Ocular Manifestations: In a mild form there is a thickened periphery of Descemet's membrane (Schwalbe's line) which is bow-shaped when visible clinically (by gonioscopy), hence the term embryotoxon (Greek: *toxon*—a bow). Strands of tissue derived from the iris may be present in the chamber angle. This peripheral malformation is referred to as Axenfeld's anomaly when iridocorneal strands are localised to the anteriorly displaced Schwalbe's line, but the drainage system is unaffected and the intraocular pressure is normal. If there is evidence of glaucoma the condition is classified as Axenfeld's syndrome.

The addition of "iris hypoplasia" and an irregular pupil (corectopia) to the changes described for Axenfeld's syndrome is known as Rieger's anomaly. Where there are additional skeletal, facial, and dental abnormalities the term Axenfeld-Rieger syndrome (Rieger's syndrome) is applied.

Other ocular structures can show abnormalities. Congenital and early-onset cataracts, as in this case, are common[1]. These can be associated with persistent fetal vasculature, as in this case[3, 4]. Peter's anomaly and sclerocornea can also co-exist[5]. Optic nerve and chorioretinal colobomas have been reported as has hypoplasia of the optic nerve and foveal hypoplasia[3].

Genetics and Pathogenesis: ARS occurs in 1 of 100,000–200,000 live births. Mutations in the *PITX2* and *FOXC1* genes, which are crucial for normal embryologic development of the anterior segment and other organs affected in ARS, account for 40–60% of cases[6]. Vision loss is most commonly due to glaucoma, as in this case, which affects more than 50% of individuals with ARS.

Comparison with other cases: This case shows some similarities to a case reported by Rohrbach *et al*[7]. In this case there was a corneal staphyloma with anterior chamber agenesis and microphakia. There was an adherent layer of pigment epithelium on the posterior cornea similar to this case which they believed was derived from ciliary epithelium. Karin Loëffler also presented another similar case of unilateral congenital corneal staphyploma where the inner corneal surface was covered by a thin layer of pigmented tissue with broad anterior synechia extending from the central cornea towards some lens remnant[8].

Summary: This case shows features of complex anterior chamber dysgenesis with congenital cataract and persistent hyperplastic primary vitreous.

References

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