A case of Axenfeld-Rieger syndrome (ARS) with asymmetric ocular phenotypes and left glaucomatous optic atrophy

Athul Suresh Puthalath, Ajai Agrawal, Rimpi Rana, Ramanuj Samanta

DESCRIPTION
A 27-year-old woman presented with loss of vision in the left eye (LE) since early childhood. Her best-corrected visual acuity at presentation was 20/20 in the right eye (RE) and no light perception in LE. Intraocular pressure (IOP) was 20 mm Hg and 28 mm Hg in RE and LE, respectively. Further evaluation revealed megalocornea with measured corneal diameter of 14 mm in both eyes. Anterior segment photo slit-lamp images (Topcon DC-4, Topcon Medical Systems, Oakland, New Jersey) of RE showed iris stromal hypoplasia, multiple atrophic patches, ectropion uveae, corectopia, partial loss of pupillary ruff (figure 1A) and prominent posterior embryotoxon in the inferior part (figure 1B). LE showed an oblique band of hypoplastic iris tissue with exposed bare posterior pigmented epithelium and inferotemporal corectopia (figure 1C–D). Transillumination of LE showed multiple iris defects and prominent equator of the lens nasally (figure 1E).

Gonioscopic low magnification (16×) images (figure 1F–I) of RE revealed posterior embryotoxon with attached iris strands and peripheral anterior synechiae (yellow arrows). High magnification (25×) gonioscopic image (figure 1J) of the inferior angle of RE showed a large iris strand extending from the iris surface to anteriorly placed Schwalbe’s line. Bare iris vessels were also noted traversing the surface. The fundus showed a vertical cup to disc ratio of 0.6:1 in RE and a total glaucomatous optic atrophy in LE. Systemic evaluation revealed maxillary hypoplasia, broad nasal bridge, oligodontia, and an operated atrial septal defect.

Considering the ocular and systemic features, a diagnosis of Axenfeld-Rieger syndrome (ARS) was made. Absence of a central corneal opacity ruled out Peters anomaly, and the systemic features seen in Peters plus such as cleft lip/palate, short stature, abnormal ears and mental retardation were also absent in our patient.1 Even though our patient had abnormal dentition and Axenfeld-Rieger anomaly similar to SHORT syndrome, there were no other systemic findings suggestive of SHORT syndrome.2

The patient was started on a combination of topical brimonidine (0.2%) and timolol (0.5%) two times per day in RE. Poor prognosis was explained to the patient. At 3-month follow-up, her IOP in RE remained controlled on two topical antiglaucoma medications. She was advised 6-weekly IOP monitoring and regular systemic evaluation.

ARS occurs secondary to genetic mutations vital for ocular development, with majority having mutations in transcription factors PITX2 and FOXC1. It is a fully penetrant, multigenic syndrome with variable expressivity. Inheritance is autosomal dominant in 70% and sporadic in 30%. It has both ocular and systemic manifestations. Ocular findings in ARS can affect the cornea (megalocornea and posterior embryotoxon), iris (mild to severe degenerative changes like hole formation, corectopia and ectropion uveae) and anterior chamber angle (anterior insertion of the iris, tissue strands from the peripheral iris to the prominent Schwalbe’s line). Systemic features include craniofacial dysmorphism (hypertelorism, telecanthus, flat nasal bridge, mid-facial hypoplasia), dental malformations (hypodontia, anodontia or peg-shaped teeth), umbilical defects (redundant umbilical skin) and cardiac defects.3–5

The phenotypes between the two eyes of an affected individual of ARS are usually similar.
while few cases reported asymmetrical phenotypes.\textsuperscript{7–10} A significant phenotypic variability was observed in cases of ARS with PITX2 mutations.\textsuperscript{7} Kelberman \textit{et al}.\textsuperscript{8} have reported phenotypic variability of ARS in different affected members of a family and have shown increased phenotypic severity with digenic inheritance. Other reported asymmetric phenotypes of ARS in the same individual include unilateral detached Schwalbe’s line suspended in the anterior chamber of one patient\textsuperscript{9,10} and unilateral aniridia in another patient.\textsuperscript{10}

The most severe ocular phenotype associated with ARS is early-onset glaucoma, which affects more than 50\% of patients with ARS.\textsuperscript{4} Treating glaucoma is the primary aim in patients with ARS. Medical management can be tried but is usually unrewarding, necessitating surgical interventions. In the index report, we have demonstrated the anterior segment and gonioscopic features of ARS with asymmetric ocular phenotypic presentation, although vision in LE could not be salvaged due to late presentation.

**Patient’s perspective**

I lost my vision in the left eye in childhood. I came for opinion about my right eye. Eye doctors evaluated both of my eyes and told that my left eye has irreversible damage. I have also been explained that, I might need glaucoma surgery in right eye in future if my eye pressures are not controlled with medication.

**Learning points**

- Axenfeld-Rieger syndrome (ARS) can present with asymmetric ocular phenotypes.
- Monitoring and control of intraocular pressure in patients with ARS are of utmost importance as delay in treatment can lead to irreversible damage.
- All patients with such ocular features should be thoroughly examined systemically to look for any coexistent systemic abnormalities.

**REFERENCES**


**ORCID iDs**

Athul Suresh Puthalath http://orcid.org/0000-0002-0483-7014
Ramanuj Samanta http://orcid.org/0000-0002-9737-8346

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