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

Athul Suresh Puthalath ¹, Ajai Agrawal, Rimpi Rana, Ramanuj Samanta ²

Ophthalmology, All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand, India

Correspondence to
Dr Ramanuj Samanta;
ramanuj.samanta@gmail.com

Accepted 24 June 2020

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, 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, microdontia 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 in LE. 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 periumbilical skin) and cardiac defects.^{3–5}

The phenotypes between the two eyes of an affected individual of ARS are usually similar,⁶

Figure 1 Anterior segment photograph of RE shows iris stromal hypoplasia, multiple atrophic patches, ectropion uveae (A) and prominent posterior embryotoxon in the inferior part (red arrows; B). LE shows inferotemporal corectopia (C), exposed bare posterior pigmented epithelium (white arrows; D), and multiple iris defects on transillumination (blue arrows; E). Gonioscopy of RE (F–I) shows posterior embryotoxon with attached iris strands and peripheral anterior synechiae (yellow arrows); high magnification image of the inferior angle of RE (J) shows a large iris strand extending from the iris surface to anteriorly placed Schwalbe's line and bare iris vessels. LE, left eye; RE, right eye.

© BMJ Publishing Group Limited 2020. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Puthalath AS, Agrawal A, Rana R, et al. *BMJ Case Rep* 2020;**13**:e237224. doi:10.1136/bcr-2020-237224

Images in...

while few cases reported asymmetrical phenotypes.^{7–10} A significant phenotypic variability was observed in cases of ARS with PITX2 mutations.⁷ Kelberman *et al*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 patient⁹ and unilateral aniridia in another patient.¹⁰

The most severe ocular phenotype associated with ARS is early-onset glaucoma, which affects more than 50% of patients with ARS.³ 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.

Twitter Athul Suresh Puthalath @asputhalath

Contributors ASP: data acquisition, data analysis, drafting of the manuscript, approval of the final version of the manuscript. AA: conception and design of the study, data interpretation, drafting of the manuscript, approval of the final version of the manuscript. RR: data acquisition, data analysis and interpretation, drafting of the manuscript, approval of the final version of the manuscript. RS: conception of study, data interpretation, drafting and critical revision of the manuscript, approval of the final version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iDs

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

REFERENCES

- 1 Bhandari R, Ferri S, Whittaker B, *et al*. Peters anomaly: review of the literature. *Cornea* 2011;30:939–44.
- 2 Klatka M, Rysz I, Kozyra K, *et al*. Short syndrome in a two-year-old girl – case report. *Ital J Pediatr* 2017;43:44.
- 3 Shields MB, Buckley E, Klintworth GK, *et al*. Axenfeld-Rieger syndrome. A spectrum of developmental disorders. *Surv Ophthalmol* 1985;29:387–409.
- 4 Song W, Hu X. The rare Axenfeld-Rieger syndrome with systemic anomalies: a case report and brief review of literature. *Medicine* 2017;96:e7791.
- 5 Souzeau E, Siggs OM, Zhou T, *et al*. Glaucoma spectrum and age-related prevalence of individuals with FOXC1 and PITX2 variants. *Eur J Hum Genet* 2017;25:839–47.
- 6 Hjalt TA, Semina EV. Current molecular understanding of Axenfeld-Rieger syndrome. *Expert Rev Mol Med* 2005;7:1–17.
- 7 Perven R, Lloyd IC, Clayton-Smith J, *et al*. Phenotypic variability and asymmetry of Rieger syndrome associated with PITX2 mutations. *Invest Ophthalmol Vis Sci* 2000;41:2456–60.
- 8 Kelberman D, Islam L, Holder SE, *et al*. Digenic inheritance of mutations in FOXC1 and PITX2: correlating transcription factor function and Axenfeld-Rieger disease severity. *Hum Mutat* 2011;32:1144–52.
- 9 Parikh RS, Parikh SR, Debashish B, *et al*. Unusual presentation in Axenfeld-Rieger syndrome. *Indian J Ophthalmol* 2011;59:312–4.
- 10 Law SK, Sami M, Piri N, *et al*. Asymmetric phenotype of Axenfeld-Rieger anomaly and aniridia associated with a novel PITX2 mutation. *Mol Vis* 2011;17:1231–8.

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.

Copyright 2020 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

Customer Service

If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow