

Get Clarity On Generics

Cost-Effective CT & MRI Contrast Agents

**FRESENIUS
KABI**

WATCH VIDEO

AJNR

Neuroimaging Findings in Axenfeld-Rieger Syndrome: A Case Series

Samuel White, Ajay Taranath, Prasad Hanagandi, Deepa A. Taranath, Minh-Son To, Emmanuelle Souzeau, Owen M. Siggs and Jamie E. Craig

This information is current as
of August 24, 2025.

AJNR Am J Neuroradiol 2023, 44 (10) 1231-1235

doi: <https://doi.org/10.3174/ajnr.A7995>

<http://www.ajnr.org/content/44/10/1231>

Neuroimaging Findings in Axenfeld-Rieger Syndrome: A Case Series

 Samuel White,  Ajay Taranath,  Prasad Hanagandi,  Deepa A. Taranath,  Minh-Son To,  Emmanuelle Souzeau,  Owen M. Siggs, and Jamie E. Craig



ABSTRACT

SUMMARY: Axenfeld-Rieger syndrome is an autosomal dominant condition associated with multisystemic features including developmental anomalies of the anterior segment of the eye. Single nucleotide and copy number variants in the paired-like homeodomain transcription factor 2 (*PITX2*) and forkhead box C1 (*FOXC1*) genes are associated with Axenfeld-Rieger syndrome as well as other CNS malformations. We determined the association between Axenfeld-Rieger syndrome and specific brain MR imaging neuroradiologic anomalies in cases with or without a genetic diagnosis. This case series included 8 individuals with pathogenic variants in *FOXC1*; 2, in *PITX2*; and 2 without a genetic diagnosis. The most common observation was vertebrobasilar artery dolichoectasia, with 46% prevalence. Other prevalent abnormalities included WM hyperintensities, cerebellar hypoplasia, and ventriculomegaly. Vertebrobasilar artery dolichoectasia and absent/hypoplastic olfactory bulbs were reported in >50% of individuals with *FOXC1* variants compared with 0% of *PITX2* variants. Notwithstanding the small sample size, neuroimaging abnormalities were more prevalent in individuals with *FOXC1* variants compared those with *PITX2* variants.

ABBREVIATION: ARS = Axenfeld-Rieger syndrome

Axenfeld-Rieger syndrome (ARS) is an autosomal dominant genetic condition associated with multisystemic features. It is characterized primarily by ocular features that result from developmental anomalies of the anterior segment of the eye, including posterior embryotoxon (a thickened and anteriorly displaced Schwalbe ring), iris hypoplasia, corectopia (displaced pupil), pseudopolycoria (additional pupillary opening), and iridocorneal adhesions.^{1,2} The developmental anomalies of the structures allowing drainage of the aqueous humor lead to an increased risk of secondary glaucoma. Commonly reported systemic features include facial dysmorphism; dental, umbilical, cardiovascular,

and endocrinological anomalies; hearing impairment; and developmental delay.^{2,3}

ARS has been associated with variants in the paired-like homeodomain transcription factor 2 (*PITX2*) and forkhead box C1 (*FOXC1*) genes.⁴⁻⁶ *PITX2* belongs to the homeobox gene family and is fundamental to the embryonic development of several tissues, including an essential role in left-right patterning.^{7,8} *FOXC1* encodes a forkhead family transcription factor and is also involved in embryonic development.^{9,10} Pathogenic and likely pathogenic variants in *FOXC1* and *PITX2* have been reported in ~40% of individuals with a clinical diagnosis of ARS,^{11,12} with unique ocular and systemic phenotypes associated with each gene.¹³⁻¹⁶

Variants in both *FOXC1* and *PITX2* have also been associated with a range of CNS malformations, including hydrocephalus,¹⁶⁻¹⁸ classic commissural agenesis (corpus callosum agenesis),¹⁷⁻¹⁹ and cerebellar malformations (Dandy-Walker phenotype,²⁰ mega cisterna magna, and cerebellar vermis hypoplasia).^{18,21,22} More recently, cerebral small-vessel disease has been reported in individuals with *FOXC1* or *PITX2* variants, with the presence of WM hyperintensities, dilated perivascular spaces, and lacunar infarcts on MR imaging.^{23,24}

Here, using a series of ARS cases with accompanying MR imaging of the brain, we systematically determined the association between ARS and specific neuroradiologic anomalies in cases with or without a genomic diagnosis.

Received February 2, 2023; accepted after revision August 16.

From the Robinson Research Institute (S.W.), Faculty of Medicine and Health Sciences, University of Adelaide, Adelaide, South Australia, Australia; Department of Radiology (A.T.), Women's and Children's Hospital, Adelaide, South Australia, Australia; Department of Neuroradiology (P.H.), King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia; Department of Ophthalmology (D.A.T., M.-S.T., E.S., O.M.S., J.E.C.), Flinders University, Bedford Park, South Australia, Australia; and Garvan Institute of Medical Research (O.M.S.), Darlinghurst, New South Wales, Australia.

This work was supported by the Australian National Health and Medical Research Council Centres of Excellence Research Grant (APP116360). J.E.C. was supported by an Australian National Health and Medical Research Council Practitioner Fellowship (APP1154824). E.S. was supported by an Early Career Fellowship from the Hospital Research Foundation, and O.M.S. was supported by a Snow Fellowship.

Please address correspondence to Samuel White, MD, Robinson Research Institute, Ground Floor, Norwich Centre, 55 King William Str, North Adelaide, South Australia 5006, Australia; e-mail: s.white@adelaide.edu.au

 Indicates open access to non-subscribers at www.ajnr.org

<http://dx.doi.org/10.3174/ajnr.A7995>

Table 1: Cohort demographics^a

	All	FOXC1 Variant	PITX2 Variant	No Genetic Diagnosis
Prevalence in overall cohort (No.) (%)	NA	8 (61.5)	2 (16.7)	2 (16.7)
Sex, female (No.) (%)	9 (75)	6 (75.0)	2 (100)	1 (50)
European ancestry (No.) (%)	100 (100)	8 (100)	2 (100)	2 (100)
Age (yr)				
Mean	37.3 (SD, 21.1)	29.2 (SD, 16.1)	51.8 (SD, 3.04)	10.6 (SD, 14.6)
Range	8–73	8–49	48–54	0–31

Note:—NA indicates not applicable.

^a Both sex and ancestry were self-reported.

Table 2: Mean globe parameters

Parameter	Mean Length (mm)				General Population ^{27,28}
	All (n = 12)	FOXC1 Variant (n = 8)	PITX2 Variant (n = 2)	No Genetic Diagnosis (n = 2)	
Anterior-posterior diameter of globe	22.1	22.4	24.0	20.1	24.2
Transverse diameter of globe	22.9	23.5	24.0	20.7	24.2
Anterior chamber depth	2.37	2.62	1.89	1.51	2.62

MATERIALS AND METHODS

Subjects, Genetic Testing, and Neuroimaging

The study was conducted in accordance with the revised Declaration of Helsinki. Ethics approval was obtained from the Southern Adelaide Clinical Research Ethics Committee, and all participants or their caregivers provided written informed consent. Individuals with a clinical diagnosis of ARS were drawn from the Australian and New Zealand Registry of Advanced Glaucoma as previously described.²⁵ *FOXC1* and *PITX2* genetic testing was performed in a National Association of Testing Authorities–accredited laboratory by Sanger sequencing or multiplex ligation-dependent probe amplification as previously described.^{16,26} Brain MRIs were assessed by 2 pediatric neuroradiologists (A.T. and P.H.) blinded to the genetic results of each participant.

RESULTS

Twelve individuals with ARS were included. The mean age at evaluation was 37.3 (SD, 21.2) years (range, 2 months–73 years), 77% (10/13) were female, and all were of European ancestry (Table 1). Eight individuals had heterozygous pathogenic or likely pathogenic variants in *FOXC1* (including 7 with sequence variants and 1 with a full gene deletion), 2 had heterozygous pathogenic or likely pathogenic variants in *PITX2*, and 2 had no genetic diagnosis despite testing.

Globe and Optic Chiasm

Mean globe parameters are outlined in Table 2 and are compared with ocular biometry from the general population.^{27,28} A thin optic chiasm was reported in 42% (5/12) of the cohort. Both individuals with *PITX2* variants had optic chiasm thinning, whereas only 38% (3/8) of those with *FOXC1* variants had a thin optic chiasm (Fig 1A and Table 3).

Cortex

Five subjects had nonspecific WM hyperintensities. Other WM changes included reduced WM volume ($n = 1$) and delayed

myelination ($n = 1$). Prominent perivascular spaces were noted in 3 individuals. Four patients had corpus callosal thinning. Three individuals had colpocephaly/ventriculomegaly, and another had a ventriculoperitoneal shunt. Other corpus callosal abnormalities included thickening of the splenium ($n = 1$) and genu ($n = 1$). The prevalence of prominent perivascular spaces in the *FOXC1* variant group was 38% (3/8). Corpus callosum thinning was observed in 38% (3/8) of *FOXC1* variants (Fig 1B). Thirty-eight percent (3/8) of individuals with *FOXC1* variants had ventriculomegaly or a ventriculoperitoneal shunt in situ, whereas none (0/2) of the *PITX2* variant group had a ventricular abnormality.

Cerebellum

Hemispheric or global cerebellar hypoplasia was reported in 42% (5/12) of subjects (Fig 1C). Superior vermian hypoplasia was identified in 1 patient, and inferior vermis hypoplasia, in another. Other cerebellar findings included tonsillar ectopia (defined as inferior tonsillar location 3–5 mm below the plane of foramen magnum) ($n = 1$) and mega cisterna magna (defined as distance from the posterior aspect of the cerebellar vermis to the inside of the occipital bone of >10 mm) ($n = 1$) (Fig 1C). One of the 2 individuals with *PITX2* variants had superior vermian hypoplasia, and 38% (3/8) of the *FOXC1* variant group had global or hemispheric cerebellar hypoplasia.

Brainstem

An oblong pons was observed in 3 patients. Three subjects had brainstem indentation secondary to tortuous vertebral arteries. Another individual had medullary elongation. Brainstem indentation secondary to tortuous vertebral arteries was observed in 38% (3/8) of individuals with *FOXC1* variants. No brainstem abnormalities were reported in the *PITX2* variant group.

Vessels

Twenty-five percent (3/12) of individuals had circle of Willis abnormalities on MRA. Vertebrobasilar artery dolichoectasia was reported in 6 patients (Fig 1D). Four of these 6 individuals also had anterior circulation dolichoectasia. All 3 patients with circle

of Willis abnormalities on MRA had *FOXC1* variants, accounting for 38% of this group. Most (75%) of the *FOXC1* variant group had vertebrobasilar artery dolichoectasia. Of these patients, two-thirds also had anterior circulation dolichoectasia.

Other Findings

Absent or hypoplastic olfactory bulbs were reported in 50% (6/12) of subjects (Fig 1E). Other findings included cochlear nerve

hypoplasia ($n = 1$), a widened opercula ($n = 1$), hippocampal malrotation ($n = 1$), and bilateral absent posterior semicircular canals ($n = 1$). Absent or hypoplastic olfactory bulbs were reported in 63% (5/8) of subjects with *FOXC1* variants but in none (0/2) of the subjects with *PITX2* variants. Except for 1 subject with right unicoronal craniosynostosis, most of the cohort did not have craniofacial dysmorphism. The pituitary gland and hypothalamus were normal across the cohort. There was no abnormality of the deep gray nuclei. No dental abnormalities were observed.

DISCUSSION

This case series reviewed the neuroradiologic features of 12 individuals diagnosed with ARS, comprising 8 individuals with *FOXC1* variants, 2 with *PITX2* variants, and 2 with unsolved genetic defects. No single anatomic abnormality was observed in most individuals. The most common observation was vertebrobasilar artery dolichoectasia (50% prevalence), which was associated with anterior circulation dolichoectasia in most cases. Other prevalent abnormalities included WM hyperintensities (42%), hemispheric or global cerebellar hypoplasia (42%), corpus callosal thinning (33%), and ventriculomegaly (25%). Optic chiasm thinning was observed in both members of the *PITX2* variant group and in 38% of the *FOXC1* variant group. Vertebrobasilar artery dolichoectasia was reported in 75% of individuals with *FOXC1* variants compared with 0% of individuals with *PITX2* variants. Similarly, while 63% of individuals with *FOXC1* variants had absent or hypoplastic olfactory bulbs, they were not observed in any of the individuals with *PITX2* variants. Circle of Willis abnormalities on MRA and ventricular abnormalities both had a prevalence of 38% in the *FOXC1* group compared with 0% in the *PITX2* group.

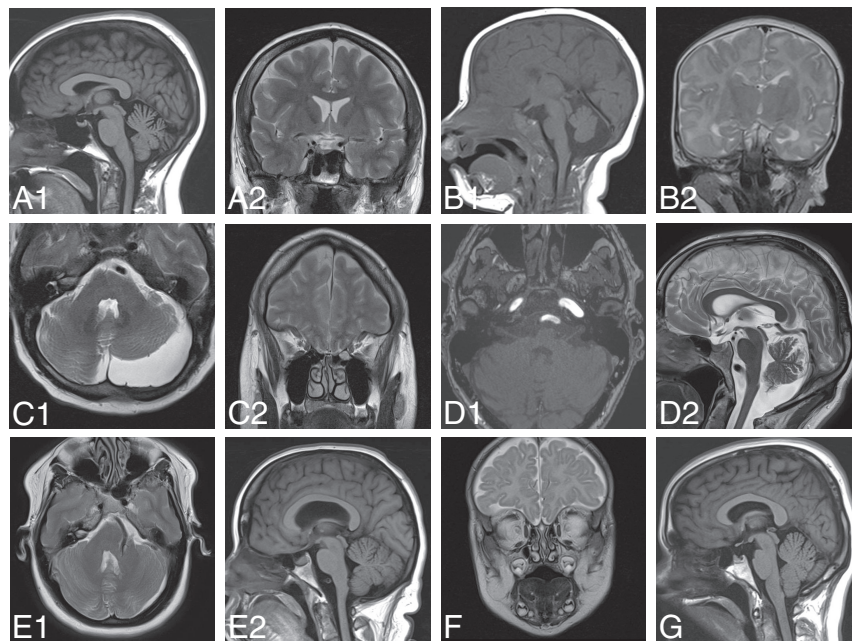


FIGURE. A, A 49-year-old woman with a *PITX2* mutation had superior vermian volume loss on the T1-weighted sagittal image (A1) and optic chiasm thinning on the T2-weighted coronal image (A2). B, A 2-month-old girl with an unsolved mutation had inferior vermian hypoplasia and a widened tegmentovermian angle on the T1-weighted sagittal image (B1) and malrotated hippocampi on the T2-weighted coronal image (B2). C, A 43-year-old man with a *FOXC1* mutation had mega cisterna magna and an ectatic basilar artery and a hypoplastic left cerebellar hemisphere on the T2-weighted axial image (C1) and hypoplastic olfactory bulbs on the T2-weighted coronal image (C2). D, A 46-year-old man with a *FOXC1* mutation had a tortuous basilar artery and an ectatic cavernous segment of the left ICA on axial TOF angiography (D1); a short mesencephalon with loss of the normal relationship among the mesencephalon, pons, and medulla; loss of volume in the superior vermis and ectatic basilar artery; and flow void seen end-on on the T2-weighted sagittal image (D2). E, A 41-year-old woman with a *FOXC1* mutation had a tortuous basilar artery flow void on the T2-weighted axial image (E1), a short mesencephalon with loss of the normal relationship among the mesencephalon, pons, and medulla, and bowing of the corpus callosum secondary to ventriculomegaly on the T1-weighted sagittal image (E2). F, A 3-month-old boy with an unsolved mutation had absent olfactory bulbs on the T2-weighted coronal image. G, A 31-year-old woman with an unsolved mutation had a thickened splenium and tonsillar ectopia on the T1-weighted sagittal image.

Table 3: Prevalence of neuroradiologic anomalies^a

(N (%))	All	<i>FOXC1</i>	<i>PITX2</i>	No Genetic Diagnosis
Thin optic chiasm	5/12 (41.7)	3/8 (37.5)	2/2 (100)	0/2 (0.0)
Nonspecific WM hyperintensities	5/12 (41.7)	4/8 (50.0)	1/2 (50.0)	0/2 (0.0)
Corpus callosal thinning	4/12 (33.3)	3/8 (37.5)	0/2 (0.0)	1/2 (50.0)
Ventriculomegaly or ventriculoperitoneal shunt	4/12 (33.3)	3/8 (37.5)	0/2 (0.0)	0/2 (0.0)
Hemispheric or global cerebellar hypoplasia	5/12 (41.7)	3/8 (37.5)	1/2 (50.0)	0/2 (0.0)
Oblong pons	3/12 (25.0)	2/8 (25.0)	0/2 (0.0)	1/2 (50.0)
Brainstem indentation secondary to tortuous vessels	3/12 (25.0)	3/8 (37.5)	0/2 (0.0)	0/2 (0.0)
Circle of Willis abnormalities	3/12 (25.0)	3/8 (37.5)	0/2 (0.0)	0/2 (0.0)
Vertebrobasilar artery dolichoectasia	6/12 (50.0)	6/8 (75.0)	0/2 (0.0)	0/2 (0.0)
Absent/hypoplastic olfactory bulb	6/12 (50.0)	5/8 (62.5)	0/2 (0.0)	1/2 (50.0)

^a Data are (No.) (%).

Mean globe parameters were smaller in the cohort without a genetic diagnosis. Although we acknowledge the very small sample size, this group might have an underlying genetic etiology that also impacts globe development, though this remains to be validated. No individuals with *FOXC1* or *PITX2* variants had craniofacial dysmorphism or abnormalities of the hypothalamus, pituitary, deep gray nuclei, or dentition.

The specific endocrinologic manifestations of ARS have not been comprehensively reported in the literature. Santini et al²⁹ have described a patient with growth hormone deficiency associated with ARS. Notably, growth hormone deficiency is a prevalent feature among individuals with septo-optic dysplasia,³⁰ which, like ARS, often involves olfactory bulb–tract hypoplasia.³¹

While there have been several isolated ARS neuroimaging case studies reported,^{32–34} to our knowledge, there is only 1 case series (Reis et al³⁵) that characterized the genetic and phenotypic features of an ARS cohort comprising 128 individuals with *FOXC1* or *PITX2* variants, including 18 with neuroimaging. The authors observed WM hyperintensities in 94% of *FOXC1* variants and 50% of *PITX2* variants³⁵ (compared with 50% for both *FOXC1* and *PITX2* variant groups in our study). Seventy-one percent of individuals with *FOXC1* variants had colpocephaly/ventriculomegaly (compared with 25% in our study). Reis et al also reported a 31% prevalence of arachnoid cysts in the *FOXC1* variant group, which was not assessed in our case series. Most interesting, the same study observed no correlation between the extent of neuroimaging anomalies and the presence or severity of cognitive impairment in patients with *FOXC1* variants.

Due to the nature of the imaging technique used in this study (MR imaging of the brain), we were not able to reliably detect extracerebral abnormalities such as craniofacial dysmorphism and dental anomalies, which are more sensitively detected by physical examination and specific dental imaging modalities such as orthopantomogram. Reis et al³⁵ reported classic dental anomalies such as hypodontia/oligodontia and microdontia in 91% of individuals with *PITX2* variants, with similar anomalies reported in 100% (23/23) of an Australian *PITX2* cohort¹⁶ drawn from the same registry as the current study. In contrast, these classic dental anomalies were considerably less common among the *FOXC1* group, who had a tendency to present with more atypical anomalies such as enamel hypoplasia/frequent caries (16%) or dental crowding (16%).³⁵ In a similar vein, while craniofacial dysmorphism was not observed on MR imaging of the brain in any of the individuals included in our case series, features such as thin upper lip and maxillary hypoplasia were reported in 78% of individuals with *FOXC1* variants and 93% of individuals with *PITX2* variants in 1 previous study,³⁵ and in another study (which included all cases described here), hypertelorism/telecanthus and low-set ears were found to be more prevalent in those with *FOXC1* variants compared with those with *PITX2* variants.¹⁵

This case series was limited by its small cohort size ($n = 12$), particularly with respect to the *PITX2* variant group ($n = 2$), which like other ARS case series precluded statistical comparisons.³³

CONCLUSIONS

This study is novel in its description of the relative prevalence of neuroimaging findings among patients with *FOXC1* and *PITX2*

variants, and overall, we observed that the *FOXC1* variant group had a higher prevalence of most (70%) neuroimaging abnormalities assessed (Table 3). The most common observation was vertebrobasilar artery dolichoectasia, which was reported in 75% of individuals with *FOXC1* variants compared with 0% of individuals with *PITX2* variants.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

REFERENCES

- Shields MB, Buckley E, Klintworth GK, et al. Axenfeld-Rieger syndrome: a spectrum of developmental disorders. *Surv Ophthalmol* 1985;29:387–409 [CrossRef Medline](#)
- Alward WL. Axenfeld-Rieger syndrome in the age of molecular genetics. *Am J Ophthalmol* 2000;130:107–15 [CrossRef Medline](#)
- Fitch N, Kaback M. The Axenfeld syndrome and the Rieger syndrome. *J Med Genet* 1978;15:30–34 [CrossRef Medline](#)
- Semina EV, Reiter R, Leysens NJ, et al. Cloning and characterization of a novel bicoid-related homeobox transcription factor gene, RIEG, involved in Rieger syndrome. *Nat Genet* 1996;14:392–99 [CrossRef Medline](#)
- Nishimura DY, Swiderski RE, Alward WL, et al. The forkhead transcription factor gene FKHL7 is responsible for glaucoma phenotypes which map to 6p25. *Nat Genet* 1998;19:140–47 [CrossRef Medline](#)
- Mears AJ, Jordan T, Mirzayans F, et al. Mutations of the forkhead/winged-helix gene, FKHL7, in patients with Axenfeld-Rieger anomaly. *Am J Hum Genet* 1998;63:1316–28 [CrossRef Medline](#)
- Kitamura K, Miura H, Miyagawa-Tomita S, et al. Mouse *Pitx2* deficiency leads to anomalies of the ventral body wall, heart, extra- and periorbital mesoderm and right pulmonary isomerism. *Development* 1999;126:5749–58 [CrossRef Medline](#)
- Lu MF, Pressman C, Dyer R, et al. Function of Rieger syndrome gene in left-right asymmetry and craniofacial development. *Nature* 1999;401:276–78 [CrossRef Medline](#)
- Kume T, Deng K, Hogan BL. Murine forkhead/winged helix genes *Foxc1* (*Mf1*) and *Foxc2* (*Mfh1*) are required for the early organogenesis of the kidney and urinary tract. *Development* 2000;127:1387–95 [CrossRef Medline](#)
- Kume T, Jiang H, Topczewska JM, et al. The murine winged helix transcription factors, *Foxc1* and *Foxc2*, are both required for cardiovascular development and somitogenesis. *Genes Dev* 2001;15:2470–82 [CrossRef Medline](#)
- D'haene B, Meire F, Claerhout I, et al. Expanding the spectrum of *FOXC1* and *PITX2* mutations and copy number changes in patients with anterior segment malformations. *Invest Ophthalmol Vis Sci* 2011;52:324–33 [CrossRef Medline](#)
- Reis LM, Tyler RC, Volkmann Kloss BA, et al. *PITX2* and *FOXC1* spectrum of mutations in ocular syndromes. *Eur J Hum Genet* 2012;20:1224–33 [CrossRef Medline](#)
- Prem Senthil M, Knight LSW, Taranath D, et al. Comparison of anterior segment abnormalities in individuals with *FOXC1* and *PITX2* variants. *Cornea* 2022;41:1009–15 [CrossRef Medline](#)
- Knight LS, Ruddle JB, Taranath DA, et al. Childhood and early onset glaucoma classification and genetic profile in a large Australasian disease registry. *Ophthalmology* 2021;128:1549–60 [CrossRef Medline](#)
- Souzeau E, Siggs OM, Pasutto F, et al. Gene-specific facial dysmorphism in Axenfeld-Rieger syndrome caused by *FOXC1* and *PITX2* variants. *Am J Med Genet A* 2021;185:434–39 [CrossRef Medline](#)
- 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 [CrossRef Medline](#)
- Maclean K, Smith J, St Heaps L, et al. Axenfeld-Rieger malformation and distinctive facial features: clues to a recognizable 6p25 microdeletion syndrome. *Am J Med Genet A* 2005;132A:381–85 [CrossRef Medline](#)

18. Delahaye A, Khung-Savatovsky S, Aboura A, et al. **Pre- and postnatal phenotype of 6p25 deletions involving the FOXC1 gene.** *Am J Med Genet A* 2012;158A:2430–38 [CrossRef Medline](#)
19. Raybaud C. **The corpus callosum, the other great forebrain commissures, and the septum pellucidum: anatomy, development, and malformation.** *Neuroradiology* 2010;52:447–77 [CrossRef Medline](#)
20. Whitehead MT, Barkovich MJ, Sidpra J, et al. **Refining the neuroimaging definition of the Dandy-Walker phenotype.** *AJNR Am J Neuroradiol* 2022;43:1488–93 [CrossRef Medline](#)
21. Idrees F, Vaideanu D, Fraser SG, et al. **A review of anterior segment dysgeneses.** *Surv Ophthalmol* 2006;51:213–31 [CrossRef Medline](#)
22. Aldinger KA, Lehmann OJ, Hudgins L, et al. **FOXC1 is required for normal cerebellar development and is a major contributor to chromosome 6p25.3 Dandy-Walker malformation.** *Nat Genet* 2009;41:1037–42 [CrossRef Medline](#)
23. Cellini E, Disciglio V, Novara F, et al. **Periventricular heterotopia with white matter abnormalities associated with 6p25 deletion.** *Am J Med Genet A* 2012;158A:1793–97 [CrossRef Medline](#)
24. French CR, Seshadri S, Destefano AL, et al. **Mutation of FOXC1 and PITX2 induces cerebral small-vessel disease.** *J Clin Invest* 2014;124:4877–81 [CrossRef Medline](#)
25. Souzeau E, Goldberg I, Healey PR, et al. **Australian and New Zealand Registry of Advanced Glaucoma: methodology and recruitment.** *Clin Exp Ophthalmol* 2012;40:569–75 [CrossRef Medline](#)
26. Siggs OM, Souzeau E, Pasutto F, et al. **Prevalence of FOXC1 variants in individuals with a suspected diagnosis of primary congenital glaucoma.** *JAMA Ophthalmol* 2019;137:348–55 [CrossRef Medline](#)
27. Augusteyn RC, Nankivil D, Mohamed A, et al. **Human ocular biometry.** *Exp Eye Res* 2012;102:70–75 [CrossRef Medline](#)
28. Hashemi H, Khabazkhoob M, Miraftab M, et al. **The distribution of axial length, anterior chamber depth, lens thickness, and vitreous chamber depth in an adult population of Shahroud, Iran.** *BMC Ophthalmol* 2012;12:50 [CrossRef Medline](#)
29. Santini AJ, Canales Ramos NM, Burgos Ortega NI, et al. **MON-257 Axenfeld-Rieger syndrome: an uncommon cause of growth hormone deficiency.** *J Endocr Soc* 2020;4(Suppl 1):MON-257 [CrossRef](#)
30. Koizumi M, Ida S, Shoji Y, et al. **Endocrine status of patients with septo-optic dysplasia: fourteen Japanese cases.** *Clin Pediatr Endocrinol* 2017;26:89–98 [CrossRef Medline](#)
31. Benson JC, Nascene D, Truwit C, et al. **Septo-optic dysplasia: assessment of associated findings with special attention to the olfactory sulci and tracts.** *Clin Neuroradiol* 2019;29:505–13 [CrossRef Medline](#)
32. Whitehead M, Choudhri A, Salim S. **Magnetic resonance imaging findings in Axenfeld-Rieger syndrome.** *Clin Ophthalmol* 2013;7:911–16 [CrossRef Medline](#)
33. Kumar M, Chambers C, Dhamija R. **Axenfeld-Rieger syndrome and leukoencephalopathy caused by a mutation in FOXC1.** *Pediatr Neurol* 2017;66:113–14 [CrossRef Medline](#)
34. Annakie D, Gasimova U, Shafi M, et al. **Brain matter white changes in Axenfeld-Rieger syndrome: things to keep in mind.** *Turk J Neurol* 2022;28:124–26 [CrossRef](#)
35. Reis LM, Maheshwari M, Capasso J, et al. **Axenfeld-Rieger syndrome: more than meets the eye.** *J Med Genet* 2023;60:368–79 [CrossRef Medline](#)