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DIAGNOSIS AND TREATMENT OF AXENFELD-RIEGER SYNDROME

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ABSTRACT

Introduction: Axenfeld-Rieger syndrome (ARS) is a rare congenital disorder characterized by anterior segment dysgenesis and diverse systemic anomalies. Mutations in genes such as PITX2 and FOXC1 are most commonly implicated in its pathogenesis. The condition significantly affects vision, primarily due to structural disruption of the visual axis and the high incidence of secondary glaucoma.
Aim of the study: The purpose of this study is to provide an updated overview of Axenfeld-Rieger syndrome, with emphasis on its historical background, genetic mechanisms, clinical manifestations, and current therapeutic strategies.
Research materials and methods: A systematic review of scientific and medical literature was conducted using PubMed and Google Scholar databases.
Conclusions: Genetic testing and comprehensive clinical evaluation are crucial for accurate diagnosis and optimal management of ARS. Due to its multisystem nature, care should be coordinated within a multidisciplinary framework. Early recognition of glaucoma and other systemic manifestations is essential to improve long-term outcomes.

KEYWORDS

Axenfeld-Rieger Syndrome, PITX2 Mutations, FOXC1 Mutations, Secondary Glaucoma, Anterior Chamber Malformations, Iridocorneal Angle Anomalies

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Introduction:

German doctor Theodor Axenfeld during an examination of a patient in 1920 noticed a bright line in the posterior segment of the cornea, near to the limbus. Additionally, he observed that tissue filaments extended from the white line to the peripheral part of the iris, which passed through the iridocorneal angle. He named this condition 'embryotoxon cornea posterius"

A few years later, Herwigh Rieger described comparable findings in several patients in the anterior chamber of the eye also accompanied by iris lesions such as corectopia, atrophy or pseudopolycoria. He called them collectively 'mesodermal dysgenesis of the cornea and iris'. He also reported extraocular anomalies of the tooth or craniofacial development. [1234]

Over the years, multiple classifications have been proposed in an attempt to systematise the wide range of abnormalities. Some divided them into four subgroups - Axenfeld anomaly (AA), Axenfeld syndrome (AS), Rieger anomaly (RA) and Rieger syndrome (RS). Others, however, split the symptoms into two categories: Axenfeld-Ringer syndrome (with systemic symptoms) and Axenfeld-Ringer anomaly (without systemic symptoms). These subdivisions, nevertheless, proved to be impractical due to the phenotypic similarities between the disorders. A name of Axenfeld-Rieger syndrome was considered to be more adequate and logical. At the same time, it emphasises the fact that symptoms belong to a spectrum. Furthermore, reports of modern molecular genetics show that those disorders are genetically alike. [1 3]

Genetic Discoveries

ARS is a heterogeneous condition inherited in an autosomal dominant manner. Most frequent genetic mutations involve the following known genes: the PITX2 gene located on chromosome 4q25 and a mutation in the FOXC1 gene on chromosome 6q25. In fact, they may be present in up to half of ARS cases. [5] Genetic linkage analysis has shown that deletion of 13q14 region can also cause ARS but so far no particular gene has been identified. [6] There have been few cases of patients with deletion of the PAX6 gene at the 11p13 region [7] and deletion of the 16q23-q24 region. [8] Although there is wide knowledge of underlying factors, many cases of ARS have not been successfully identified with a genetic causative factor. [5]

PITX2 and FOXC1 - defects

PITX2 (Pituitary homeobox 2) gene encodes a homedomain transcription factor. Currently 87 genetic mutations associated with ARS have been identified including missense, nonsense, splice-site, and deletions/insertions/ duplications.[1] Point mutations like frameshift, missense and nonsense mutations are the most common mutations of PITX2. Some studies also reported chromosomal aberrations such as interstitial deletions or translocations involving chromosome 4q25. DNA rearrangements involving the PITX2 often result in extraocular deformities in addition to ocular findings.[9]

FOXC1 (Forkhead box protein C1) gene is a part of winged helix family of transcription factors. FOXC1 include activation and inhibitory domains. Its 110-amino-acid forkhead domain, binds to specific sites in the DNA and activate target genes. Studies suggest that FOXC1 play a great role in embryogenesis, cardiac, renal, skeletal, ocular and cerebral morphogenesis and tumour development. [10] FOXC1 mutations include intragenic frameshift, missense and nonsense alleles as well as intragenic deletions, duplications and insertions. The presence of segmental and telomeric chromosomal rearrangements of the chromosome 6p25 region of the FOXC1 gene was also observed.[11] Phenotypes of ARS patients who have FOXC1 mutations usually presented ocular manifestations without extraocular findings although some cases with systematic abnormalities exist. The differences between phenotypes among patients are mostly due to the size of deletion and affected genes.

Pathomechanism of PITX2 an FOXC1 mutations

Patients with alleles of the PITX2 or FOXC1 genes associated with ARS present complete penetrance meaning that ocular changes will be manifested in all phenotypes. Meanwhile, the expressivity is variable and depends on the mutation type. ARS-associated symptoms present in patients will occur with varying frequency and severity.[12]

Expression of the genes PITX2 and FOXC1 occur during early embryogenesis of neural crest cells. To be more specific, two major genes are expressed in cranial and cardiac neural crest subpopulations.[13] Cranial subpopulation of neural crest cells contributes to the formation of the frontonasal prominence, pharyngeal arches, and periocular mesenchyme (POM). POM gives rise to the development of important parts of the anterior segment of the eye such as the cornea, sclera, trabecular meshwork, iris and aqueous outflow pathways. [14] Cardiac neural crest subpopulation affects further development of the cardiovascular system. [15]

Researches based on animal models have shown that loss of PITX2 and FOXC1 gene expression can cause apoptosis of neural crest cells. The consequences of this situation would be developmental anomalies of the craniofacial bones and defects of cornea, iris, and iridocorneal angle development, microphthalmia and colombas. Cardiovascular malformations have also been observed. Complete deletion or non-expression of genes resulted in lethal cardiovascular defects but in the heterozygote state characteristic ocular anomalies appeared . [13] [16] Additionally, glaucoma phenotypes are more often associated with FOXC1 mutations.

It has been proven that a gene dosage model is involved in the pathogenesis of the syndrome, meaning that every abnormal level of proteins formed during transcription have an impact on ARS phenotypes. It is considered that the main pathomechanism of ARS is haploinsufficiency. Gain-of-function mutations like duplication of FOXC1can also cause ARS.[17] Two contrasting mutations can give a similar phenotype. The reason why this happens is because PITX2 binds with FOXC1 and supress activation of potential FOXC1 target genes. Deletion of PITX2 cause activation of FOXC1 target genes leading to ARS. Duplication of FOXC1 lifts the inhibitory effect of PITX2 leading to outcome. It highlights the importance of balanced gene expression. [18]

Epidemiology

The incidence of ARS is estimated at 1 in 200 000 live births. The syndrome occurs regardless of gender and race.[919] Since ARS is a congenital disorder, first symptoms are usually noticed in young patients already. However, the symptoms may appear later, for example, when glaucoma develops.

Ocular and non-ocular symptoms

Spectrum of symptoms seen among patients with ARS is quite wide. Those can be divided into ocular and extraocular findings. Ocular alterations typically occur bilaterally sometimes asymmetrically. Rarely, they are found only in one eye. The lesions involve the cornea, iris, and the iridocorneal angle.

Cornea

One of the main ocular malformations present in patients with Axenfeld-Rieger syndrome is posterior embryotoxon meaning prominent and anteriorly displaced Schwalbe's line. Histopathology identifies this tissue as dense collagen and ground substance associated with a layer of spindle cells.[9] Under slit-lamp biomicroscopy, it can look anything between a non-continous fine line running along the corneal limbus to a sharp white line. Identification of embryotoxon posterior facilitates the diagnosis of ARS, however, it is not mandatory for the diagnosis. The abnormality may occur in up to 15% of the normal population without clinical significance. [4] [20]

Iris

Changes that can be noticed may be barely visible and thus overlooked during slit-lamp examination. An iris may be thinned (hypoplasia), a pupil may be positioned differently (corectopia), or multiple holes may be present giving the illusion of numerous pupils (polycoria). Photophobia and cosmetic problems might occur in some patients due to pupil changes. [9] Other changes observed in ARS patients are iris adhesions, vascular layer extensions from the iris on to the trabecular meshwork (iris processes or strands) or even absence of iris (aniridia).[21]

Iridocorneal angle abnormalities and risk of glaucoma

One of major glaucoma risk factor is Schlemm's canal blockage. It interferes with aqueous outflow which contributes to increased intraocular pressure. Ocular hypertension eventually leads to damage of the optic nerve and blindness. Secondary glaucoma affects both eyes but may manifest with varying severity in each eye.[22] In patients with ARS it is mainly attributed to congenital malformations of the iridocorneal angle. Non-retraction of the neural crest-derived cell layer results in a reduction of the intertrabecular spaces that thicken the trabecular meshwork. Thus, a barrier for the free circulation of the aqueous fluid is created.[23] Iris biding strands are unlikely to be the reason for impaired aqueous outflow since cutting the strands apparently hasn't helped with effective control of eye pressure.[22] ARS patients have approximately a 50% chance of developing glaucoma during their lifetime. In comparison with primary infantile glaucoma, it appears later in life. Symptoms observed in children include enlargement of the eyeball (buphthalmos), larger corneal diameter and axial length, Descemet's tears, corneal edema, increased intraocular pressure and optic nerve cupping.[21] The age of glaucoma onset ranges from early childhood to adulthood which needs to be taken into consideration during systematic follow-up appointments.

Other less common eye findings

In some cases described in the literature, patients with ARS showed the presence of strabismus related anomalous insertions of the extraocular muscles, hypertelorism cataract, Optic nerve colobomas, hypoplasia, and dysplasia, foveal hypoplasia, and atrophy, and chorioretinal colobomas. [242526]

Systematic findings

Although ocular symptoms come to the forefront, non-ocular symptoms may help in the diagnosis. The most common systemic defects involve the cranofacial, dental and umbilical area. Midface lesions include maxillary and mandibular hypoplasia, hypertelorism, increased distance between the inner corners of the eyelids, prominent forehead,thin upper lip, flat nasal bridge. Due to decreased numbers of odonoblasts and cementoblasts during embryogenesis, thickened frenulum, microdontia, oligodontia or hypodontia may be present. [27] However, the most common dental feature is absence of lateral mandibular incisors. Congenital heart defects such as aortic and mitral valve stenosis as well as cardiovascular outflow tract hypoplasia have been observed in 25% of patients.[28] [29]Umbilical anomalies manifest as redundant periumbilical skin, umbilical or inguinal hernia. [30] Skeletal malformations include joint hypermobility or degeneration, scoliosis, hip anomalies, clubfoot, flattening of the femoral and humeral epiphyses, femoral neck length reduction, vertebrae changes. [31] [32] Other malformations include pituritary defects, grow retardation, hypospadia, hearing loss. [3334] Some studies show that developmental delay and neuropsychiatric problems can also be present in ARS patients. [35]

Diagnosis

Patients with Axenfield-Rieger syndrome undergo a series of medical tests. The clinical diagnosis is based on ophthalmological and clinical examinations as well as a genetic tests can be considered.

During assessment, visual acuity, fixation behaviour, biomicroscopy of the anterior segment, intraocular pressure measurement, gonioscopy and ophthalmoscopy are performed. Gonioscopy is used to visualize the open iridocorneal angle. It allows to identify potential disorders of the aqueous outflow. Posterior embryotoxon is usually noticed during slit-lamp examination but sometime gonioscopy is required especially when iris strands goes through the angle structures.[36] Due to the fact that patients have the potential to develop glaucoma, it is important to systematically evaluate the intraocular pressure, optic nerve disc and retinal nerve fiber layer from an early age. Moreover, visual fields measurements are taken. Considering the fact that ARS occurs among young patients, it is possible to face difficulties during the examination as a result of poor cooperation. Sometimes a general anesthesia may be required. It is important to keep in mind that additional disorders such as craniofacial malformations can increase the risk of anaesthetic complications.[2137] Doctors should remain watchful for extraocular symptoms since they may possibly be in need of specialized coordinated care including ophthalmologists, dentists, cardiologists, neurologists. Some patients will also require a surgical treatment. [38 3639].

Genetic testing helps to confirm the suspected clinical diagnosis of ARS and allows to choose an appropriate management. However, the absence of specific mutation does not exclude the diagnosis of ARS.

Treatment

Medical approach to each patient should be unique due to the different phenotypes of ARS. Treatment in patients with glaucoma is initiated with medications that reduce intraocular pressure. Medications of choice are beta blockers, carbonic anhydrase inhibitors, and prostaglandin analogs. Attention should be given to the side effects of these drugs. Alpha agonists have the potential to increase cardiac outflow exacerbating cardiovascular problems.[40] Unfortunately, above mentioned medications are usually ineffective and surgery must be undertaken. Surgical treatment involves trabeculectomy with antifibrotics such as mitomycin C or placement of a glaucoma drainage device (GDD resulting in long-term normalization of intraocular pressure [22] Recently minimally-invasive glaucoma surgery is being developed. Trabeculectomy requires frequent postoperative monitoring. The procedure may be linked to long-term consequences such as risk of bleb-related infections and later even loss of vision.[26,41] Literature reports the use of laser therapy such as laser iridotomy, laser trabeculoplasty, and laser cyclo-ablation[42]. In addition, patients with ARS may require a special treatment of other conditions, such as sensorineural hearing loss, cardiac or endocrine dysfunctions, craniofacial and orthopedic problems.

Conclusions

Axenfeld-Reiger syndrome is a multi-dimensional disorder that requires involvement of multiple specialists during the diagnostic and therapeutic process. Spectrum of both ocular and non-ocular symptoms is significant therefore it requires careful analysis and examination. Watchful attention is recommended since there are phenotypes with subtle abnormalities, invisible at first glance, which can cause diagnostic difficulties. Over the past few years, understanding of the ARS pathogenesis has increased significantly. Molecular genetics allowed to identify more and more causative mutations. The number of available methods of diagnosis and treatment has also increased. Due to the high percentage of people with ARS who develop glaucoma, it is important to put great emphasis on regular monitoring of ocular pressure and optic nerve evaluation. Early detection of glaucoma allows early treatment and avoids severe consequences such as vision loss.

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REFERENCES

1. Seifi M, Walter MA. Axenfeld-Rieger syndrome. *Clin Genet*. 2018;93(6):1123-1130. doi:10.1111/cge.13148
2. Shields MB, Buckley E, Klintworth GK, Thresher R. *A Spectrum of Developmental Disorders*. Vol 29.
3. Chang TC, Summers CG, Schimmenti LA, Grajewski AL. Axenfeld-Rieger syndrome: New perspectives. *British Journal of Ophthalmology*. 2012;96(3):318-322. doi:10.1136/bjophthalmol-2011-300801
4. Alward WLM. *PERSPECTIVE Axenfeld-Rieger Syndrome in the Age of Molecular Genetics*.; 2000.
5. Michels K, Bohnsack BL. Ophthalmological Manifestations of Axenfeld-Rieger Syndrome: Current Perspectives. *Clinical Ophthalmology*. 2023;17:819-828. doi:10.2147/OPTH.S379853
6. Philli JC, Bono EA Del, Haines JL, et al. *A Second Locus for Rieger Syndrome Maps to Chromosome 13q14*. Vol 59.; 1996.
7. Riise R, Storhaug K, Brøndum-Nielsen K. Rieger syndrome is associated with PAX6 deletion. *Acta Ophthalmol Scand*. 2001;79(2):201-203. doi:10.1034/j.1600-0420.2001.079002201.x
8. Werner W, Kraft S, Callen DF, Bartsch O, Hinkel GK. A small deletion of 16q23.1-->16q24.2 [del(16)(q23.1q24.2).ish del(16)(q23.1q24.2)(D16S395+, D16S348-, P5432+)] in a boy with iris coloboma and minor anomalies. *Am J Med Genet*. 1997;70(4):371-376.
9. Tümer Z, Bach-Holm D. Axenfeld-Rieger syndrome and spectrum of PITX2 and FOXC1 mutations. *European Journal of Human Genetics*. 2009;17(12):1527-1539. doi:10.1038/ejhg.2009.93
10. Lehmann OJ, Sowden JC, Carlsson P, Jordan T, Bhattacharya SS. Fox's in development and disease. *Trends in Genetics*. 2003;19(6):339-344. doi:10.1016/S0168-9525(03)00111-2
11. Gould DB, Jaafar MS, Addison MK, et al. Phenotypic and molecular assessment of seven patients with 6p25 deletion syndrome: Relevance to ocular dysgenesis and hearing impairment. *BMC Med Genet*. 2004;5(1):17. doi:10.1186/1471-2350-5-17
12. Hjalt TA, Semina E V. Current molecular understanding of Axenfeld-Rieger syndrome. *Expert Rev Mol Med*. 2005;7(25). doi:10.1017/S1462399405010082
13. French CR. Mechanistic Insights into Axenfeld–Rieger Syndrome from Zebrafish foxc1 and pitx2 Mutants. *Int J Mol Sci*. 2021;22(18):10001. doi:10.3390/ijms221810001
14. Williams AL, Bohnsack BL. The Ocular Neural Crest: Specification, Migration, and Then What? *Front Cell Dev Biol*. 2020;8. doi:10.3389/fcell.2020.595896

15. Stoller JZ, Epstein JA. Cardiac neural crest. *Semin Cell Dev Biol*. 2005;16(6):704-715. doi:10.1016/j.semcdb.2005.06.004
16. Chen L, Gage PJ. Heterozygous *Pitx2* Null Mice Accurately Recapitulate the Ocular Features of Axenfeld-Rieger Syndrome and Congenital Glaucoma. *Investigative Opthalmology & Visual Science*. 2016;57(11):5023. doi:10.1167/iovs.16-19700
17. Holmberg J, Liu CY, Hjalt TA. PITX2 Gain-of-Function in Rieger Syndrome Eye Model. *Am J Pathol*. 2004;165(5):1633-1641. doi:10.1016/S0002-9440(10)63420-7
18. Berry FB, Lines MA, Oas JM, et al. Functional interactions between FOXC1 and PITX2 underlie the sensitivity to FOXC1 gene dose in Axenfeld–Rieger syndrome and anterior segment dysgenesis. *Hum Mol Genet*. 2006;15(6):905-919. doi:10.1093/hmg/ddl008
19. Dinalli Francisco A, Sande Miguel T, Luiza Mansur Souto A, Almeida da Costa D, Bastos Pereira M. Axenfeld-Rieger Syndrome: Case Report. *Ophthalmology Research: An International Journal*. Published online March 12, 2022:8-12. doi:10.9734/or/2022/v16i230229
20. Sim KT, Karri B, Kaye SB. Posterior embryotoxon may not be a forme fruste of Axenfeld-Rieger's Syndrome. *Journal of American Association for Pediatric Ophthalmology and Strabismus*. 2004;8(5):504-506. doi:10.1016/j.jaapos.2004.06.012
21. Khandwala NS, Ramappa M, Edward DP, Mocan MC. Axenfeld–Rieger syndrome in the pediatric population: A review. *Taiwan J Ophthalmol*. Published online November 24, 2023. doi:10.4103/tjo.TJO-D-23-00089
22. Zepeda EM, Branham K, Moroi SE, Bohnsack BL. Surgical outcomes of Glaucoma associated with Axenfeld-Rieger syndrome. *BMC Ophthalmol*. 2020;20(1):172. doi:10.1186/s12886-020-01417-w
23. Idrees F, Vaideanu D, Fraser SG, Sowden JC, Khaw PT. A Review of Anterior Segment Dysgeneses. *Surv Ophthalmol*. 2006;51(3):213-231. doi:10.1016/j.survophthal.2006.02.006
24. Gołaszewska K, Dub N, Saeed E, Mariak Z, Konopińska J. Axenfeld-Rieger syndrome combined with a foveal anomaly in a three-generation family: a case report. *BMC Ophthalmol*. 2021;21(1):154. doi:10.1186/s12886-021-01899-2
25. Ramesh P V, Devadas AK, Varsha V, et al. A rare case of unilateral Axenfeld–Rieger anomaly associated with optic disc coloboma: A multimodal imaging canvas. *Indian J Ophthalmol*. 2022;70(7):2645-2647. doi:10.4103/ijo.IJO_2950_21
26. Park SW, Kim HG, Heo H, Park YG. Anomalous Scleral Insertion of Superior Oblique in Axenfeld-Rieger Syndrome. *Korean Journal of Ophthalmology*. 2009;23(1):62. doi:10.3341/kjo.2009.23.1.62
27. Badnaware S, Srivastava VK, Chandel M, Gupta P, Fulzele P. Dental and Craniofacial Manifestation of Axenfeld-Rieger Syndrome: A Case Report. *Cureus*. Published online June 29, 2022. doi:10.7759/cureus.26442
28. Mammi I, Giorgio P De, Clementi M, Tenconi R. Cardiovascular anomaly in Rieger Syndrome, Heterogeneity or contiguity? *Acta Ophthalmol Scand*. 1998;76(4):509-512. doi:10.1034/j.1600-0420.1998.760424.x
29. Valikodath N, Johns JA, Godown J. Cardiac anomalies in Axenfeld–Rieger syndrome. *Cardiol Young*. 2023;33(7):1229-1231. doi:10.1017/S1047951122003857
30. Ali Z, Charan P, Said JM, Stark Z. Axenfeld–Rieger syndrome as rare cause of umbilical abnormality. *Ultrasound in Obstetrics & Gynecology*. 2019;54(2):276-277. doi:10.1002/uog.20129
31. Dunbar AC, McIntyre GT, Laverick S, Stevenson B. Axenfeld–Rieger syndrome: a case report. *J Orthod*. 2015;42(4):324-330. doi:10.1179/1465313315Y.0000000017
32. Kannu P, Oei P, Slater HR, Khammy O, Aftimos S. Epiphyseal dysplasia and other skeletal anomalies in a patient with the 6p25 microdeletion syndrome. *Am J Med Genet A*. 2006;140A(18):1955-1959. doi:10.1002/ajmg.a.31411
33. Grosso S, Farnetani MA, Berardi R, et al. Familial Axenfeld-Rieger anomaly, cardiac malformations, and sensorineural hearing loss: A provisionally unique genetic syndrome? *Am J Med Genet*. 2002;111(2):182-186. doi:10.1002/ajmg.10493
34. Yamazaki H, Nakamura T, Hosono K, et al. Sensorineural hearing loss and hypoplastic cochlea in Axenfeld-Rieger syndrome with FOXC1 mutation. *Auris Nasus Larynx*. 2021;48(6):1204-1208. doi:10.1016/j.anl.2020.07.006
35. Saffari A, Ziegler A, Merkenschlager A, et al. Axenfeld-Rieger Anomaly and Neuropsychiatric Problems—More than Meets the Eye. *Neuropediatrics*. 2020;51(03):192-197. doi:10.1055/s-0039-3402037
36. Reis LM, Maheshwari M, Capasso J, et al. Axenfeld-Rieger syndrome: more than meets the eye. *J Med Genet*. 2023;60(4):368-379. doi:10.1136/jmg-2022-108646
37. Zamora EA, Tripathy K, Salini B. *Axenfeld-Rieger Syndrome*.; 2024.
38. Cazzolla AP, Testa NF, Spirito F, et al. Axenfeld–Rieger syndrome: orthopedic and orthodontic management in a pediatric patient: a case report. *Head Face Med*. 2022;18(1):25. doi:10.1186/s13005-022-00329-y
39. Valikodath N, Johns JA, Godown J. Cardiac anomalies in Axenfeld–Rieger syndrome. *Cardiol Young*. 2023;33(7):1229-1231. doi:10.1017/S1047951122003857
40. Aantaa R, Jalonen J. Perioperative use of α2-adrenoceptor agonists and the cardiac patient. *Eur J Anaesthesiol*. 2006;23(5):361-372. doi:10.1017/S0265021506000378
41. DeBry PW. Incidence of Late-Onset Bleb-Related Complications Following Trabeculectomy With Mitomycin. *Archives of Ophthalmology*. 2002;120(3):297. doi:10.1001/archopht.120.3.297
42. Meyer JJ, Lawrence SD. What's new in laser treatment for glaucoma? *Curr Opin Ophthalmol*. 2012;23(2):111-117. doi:10.1097/ICU.0b013e32834f1887