Case Report

Axenfeld-Rieger syndrome – report of a rare case and review

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ABSTRACT

A typical case of Axenfeld-Rieger syndrome (ARS), a rare autosomal dominant condition manifesting with ocular, craniofacial, and dental abnormalities, is presented. The patient showed dental features such as oligodontia, microdontia, abnormally shaped teeth, hyperplastic maxillary labial frenum, and maxillary retrognathism. Early diagnosis of the syndrome from its dentofacial manifestations and a multidisciplinary approach is required for the management of patients with ARS.

Key words: Axenfeld Rieger syndrome, Hyperplastic maxillary frenum, Hypertelorism, Oligodontia

Axenfeld-Rieger syndrome (ARS) is a rare autosomal dominant disorder with an incidence of 1: 200,000 [1]. There are no definitive data on the gender and racial prevalence of ARS [2]. The craniofacial malformations of this syndrome include maxillary hypoplasia, hypertelorism, a broad nasal bridge, and an enlarged sella turcica. The face appears to be flattened, with a prominent forehead and a flat, broad nasal root, widely spaced eyes, a broad flat bridge of the nose, and a protruding lower lip. Dental alterations include hypodontia, microdontia, abnormally shaped teeth, enamel hypoplasia, hyperplastic maxillary labial frenum, and delayed eruption.

In this paper, we report the case of a 14-year-old patient with ARS. This case report presents a brief description of ARS with the characteristics of craniofacial and dental findings.

CASE REPORT

A 14-year-old female patient came to the Department of Oral Medicine and Radiology, Tamil Nadu Government Dental College and Hospital with the chief complaint of an absence of the upper front teeth. The patient was diagnosed with glaucoma during a routine eye check-up at school. Family history revealed that the patient was born by full-term vaginal delivery from non-consanguineous parents. There was no family history of similar complaints.

On general examination, the patient was calm, conscious, and cooperative with normal stature. The patient was moderately built and moderately nourished with a normal gait. No signs of anemia, cyanosis, jaundice, clubbing, and pedal edema were noted. The pulse rate was 80 beats/minute, the respiratory rate was 14 cycles/min, the blood pressure was 110/70 mmHg, the temperature was 97.6 F, and the height and weight of the patient were 132 cm and 40 kg, respectively. The patient had extra folds of skin around her belly button (redundant periumbilical skin) (Fig. 1a). Extraoral examination revealed that the patient had a symmetrical face with a convex profile. The patient had hypertelorism, flat and broad nasal bridge, and protruded lower lip (Fig. 1b). The patient had normal eyelid, clear conjunctiva, and bilateral microcornea (Fig. 2). Intraoral examination revealed that the patient presented with mixed dentition. There were several missing teeth (18, 17, 15, 14, 13, 12, 22, 23, 24, 24, 27, 28, 38, 37, 35, 33, 32, 45, 47, 48) suggestive of oligodontia. The patient had microdontia, maxillary hypoplasia, altered morphology of the maxillary central incisors, and midline diastema with hyperplastic maxillary labial frenum and anterior crossbite (Fig. 3). The ophthalmic examination done by the ophthalmologist revealed posterior embryotoxon in the anterior chamber of eye, bilateral iris stromal atrophy, bilateral correctopia, polycoria, and pigments over the left lens (Fig. 4).

Orthopantomogram (OPG) and lateral cephalogram were taken for the patient. OPG revealed the presence of erupted 16, 55, 11, 21, 64, 65, 26, 36, 75, 34, 31, 41, 42, 43, 44, 85, 46 teeth. There were many missing teeth suggestive of oligodontia. Resorption of roots of 55, 64, 75, and 85 was noted. Altered morphology of 11 and 21 were noted. Microdontia with short roots of 32, 41, 42, and 43 was noted. Large pulp chambers of 34 and 44 were noted (Fig. 5a). Lateral cephalogram revealed the presence of maxillary hypoplasia, Class I molar relation, and a Class III incisor relation (Fig. 5b). Based on the clinical dental and ocular findings along

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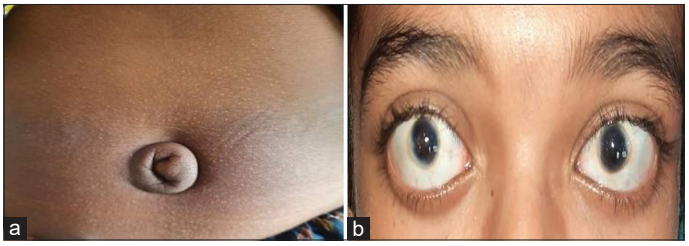

Figure 1: (a) Redundant periumbilical skin (b) hypertelorism and bilateral microcornea

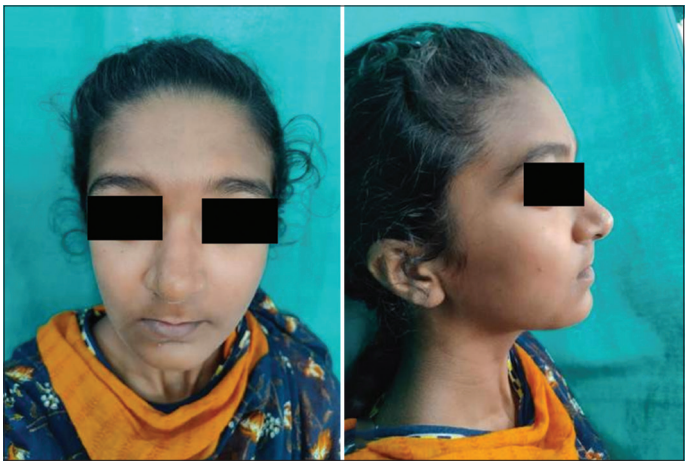

Figure 2: Extraoral images of patient showing broad nasal bridge, convex profile, a recessive upper lip, and a protrusive lower lip

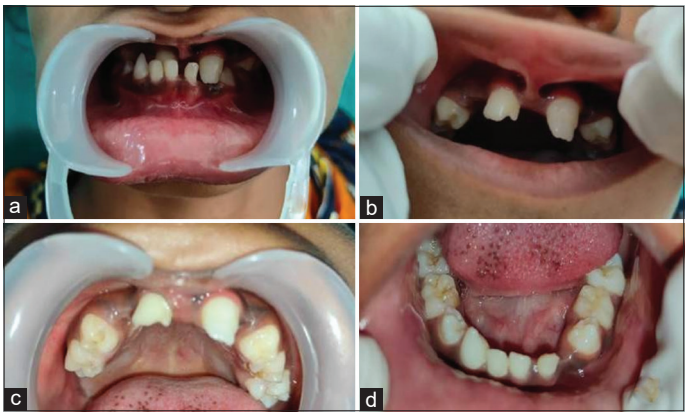

Figure 3: (a) Microdontia, anterior crossbite, (b) hyperplastic maxillary labial frenum, (c) maxillary arch, and (d) mandibular arch

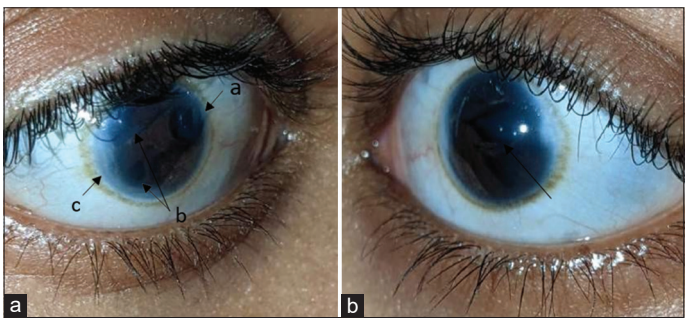

Figure 4: (a) Correctopia, (b) polycoria, and (c) posterior embryotoxon of the right eye; (b) irregular shaped pupils of left eye

with the radiological features, a final diagnosis of ARS was made.

The patient was advised for orthodontic correction of maxillary retrognathism using surgically assisted maxillary advancement, followed by extraction of the deciduous teeth and dental rehabilitation using fixed prosthodontic rehabilitation. Furthermore, the patient was emphasized on the need for regular check-ups with the ophthalmologist to evaluate the intraocular pressure and to prevent vision loss.

DISCUSSION

ARS is a rare autosomal dominant disorder. It was first described by Theodor Axenfeld, a German ophthalmologist in 1920 who described features such as posterior embryotoxon and iris strands adherent to the anteriorly displaced Schwalbe's line [3]. In 1935, Rieger described patients with congenital iris abnormalities including iris hypoplasia, correctopia, and polycoria which was described as Rieger anomaly [4]. Rieger anomaly with associated systemic findings, such as dental and facial bone defects including maxillary hypoplasia, umbilical abnormalities, or pituitary involvement is known as Rieger syndrome. The combination of Axenfeld anomaly and Reiger syndrome is collectively known as ARS [4,5]. Ozeki *et al*. reported that Axenfeld anomaly accounted for 71%, Rieger anomaly accounted for 10% while Reiger syndrome covered 19% of all ARS cases [5].

The mutation in genes forkhead box C1 (FOXC1, chromosomes 6p25) and pituitary homeobox 2 (PITX2, chromosomes 4q25) encoding transcription factors may lead to ARS. Another locus related to ARS has been identified located at chromosome 13q14 [6]. ARS is believed to be caused by a developmental arrest in the third trimester of gestation causing abnormal neural crest (NC) cell migration. NC cell migration is integral to craniofacial, dental, and ocular development [5].

The ocular features of ARS include a clear to white line in the peripheral cornea due to the anterior displacement of Schwalbe's line, termed posterior embryotoxon, bilateral microcornea, refers to the small cornea with a horizontal diameter of <10 mm, and the displacement of the pupil from the central position (correctopia). Defects of the iris range from mild stromal thinning to marked atrophy with extra holes in the iris (polycoria). More than half of the patient with ARS develop glaucoma which is difficult to control and often lead to significant optic nerve damage and visual loss [7]. Our patient had intraocular pressure of 43 mm of Hg and 32 mm of Hg in the right and left eyes respectively and is under treatment of tab. Acetazolamide 250 mg twice daily, tab. Ranitidine 150 mg twice daily and topical eye drops Brimonidine and Timolol twice daily, and Dorzolamide twice daily. The Craniofacial features of ARS include a prominent forehead, hypertelorism, telecanthus, maxillary hypoplasia, and a flattened mid-face with a broad, flat nasal bridge, thin recessive upper lip, protrusive lower lip, and an enlarged sella turcica. Dental anomalies of ARS include microdontia, hypodontia, oligodontia, anodontia, and cone-shaped teeth have been reported [8]. Class III incisor relationship on a Class III skeletal base with maxillary retrognathia has also been reported. Abdominal defects of involution of the skin leading to redundant periumbilical skin have been reported [8,9]. Additional features that may be seen

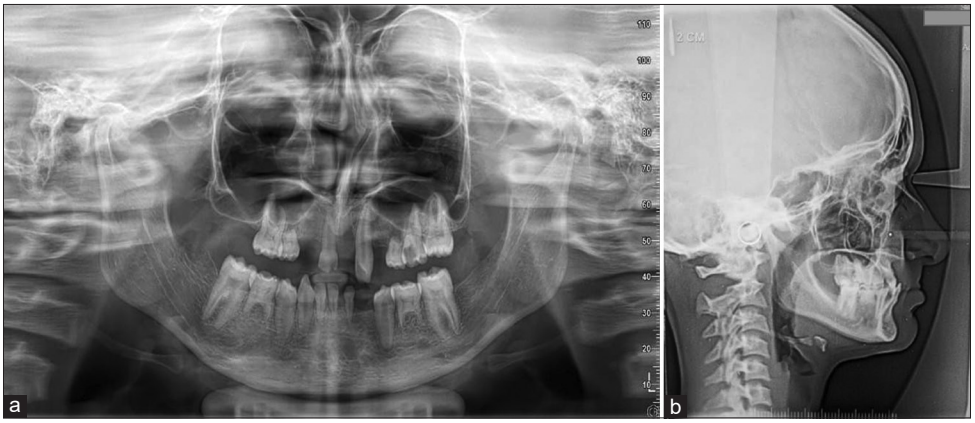

Figure 5: (a) absence of tooth buds of permanent dentition (hypodontia), small sized teeth (microdontia), short roots, and resorption of roots of retained deciduous teeth. (b) Class I molar relation and a Class III incisor relationship and maxillary hypoplasia

with ARS may include small anal stenosis, hypospadias, pituitary gland abnormalities, arachnoid cysts, growth retardation, and heart defects [8].

The differential diagnosis of the syndrome mainly includes oculodentodigital dysplasia, an autosomal dominant disorder characterized by pigmentary retinopathy, iris coloboma, congenital cataract, glaucoma, microcornea, microphthalmos, thin nose with narrow nostrils and hypoplastic alae, abnormality of fourth and fifth fingers, and hypoplastic dental enamel [10]. The other differential diagnosis includes Iridocorneal Endothelial syndrome, Peter's anomaly, aniridia (Iris hypoplasia), congenital ectropion uvea, and posterior polymorphous dystrophies [5].

The management of ARS includes early diagnosis to prevent vision loss due to glaucoma. Multidisciplinary dental management is required for aesthetic and functional correction. Orthodontic correction using MBT pre-adjusted edge-wise fixed appliance followed by Le Fort 1 advancement osteotomy has been reported [1]. Distraction following Le Fort 1 advancement with an external frame followed by the fixed prosthodontic appliance is required for a functional and esthetic occlusion [11].

CONCLUSION

ARS is a rare entity; only a few cases have been reported in the Indian population. The dental physician would play a key role in differentiating *de novo* hypodontia from that which is syndrome-related. Early diagnosis of the dental, craniofacial, and systemic presentation of ARS could prevent the devastating ocular effects of infantile glaucoma.

REFERENCES

1. Dunbar AC, McIntyre GT, Laverick S, Stevenson B. Axenfeld-Rieger syndrome: A case report. J Orthod 2015;42:324-30.
2. Cazzolla AP, Testa NF, Spirito F, Di Cosola M, Campobasso A, Crincoli V, *et al*. Axenfeld-Rieger syndrome: Orthopedic and orthodontic management in a pediatric patient: A case report. Head Face Med 2022;18:25.
3. Axenfeld T. Embryotoxon cornae posterius. Ber Deutsch Ophthalmol Ges 1920;42:301-2.
4. Rieger H. Dysgenesis mesodermalis corneae et iridis. Z Augenheilkd 1935;86:333.
5. Ozeki H, Shirai S, Ikeda K, Ogura Y. Anomalies associated with Axenfeld-Rieger syndrome. Graefes Arch Clin Exp Ophthalmol 1999;237:730-4.
6. Tumer Z, Bach-Holm D. Axenfeld-Rieger syndrome and spectrum of PITX2 and FOXC1 mutations. Eur J Hum Genet 2009;17:1527-39.
7. Shields MB, Buckley E, Klintworth GK, Thresher R. Axenfeld-Rieger syndrome. A spectrum of developmental disorders. Surv Ophthalmol 1985;29:387-409.
8. Seifi M, Walter MA. Axenfeld-Rieger syndrome. Clin Genet 2018;93:1123-30.
9. Song W, Hu X. The rare Axenfeld-Rieger syndrome with systemic anomalies: A case report and brief review of literature. Medicine (Baltimore) 2017;96:e7791.
10. American Academy of Ophthalmology. Retina and vitreous. In: 2009-2010 Basic and Clinical Science Course. Sec. 12. California, United States: American Academy of Ophthalmology; 2017-2018. p. 256.
11. Bender CA, Koudstaal MJ, van Elswijk JF, Prahl C, Wolvius EB. Two cases of axenfeld-rieger syndrome, report of the complex pathology and treatment. Cleft Palate Craniofac J 2014;51:354-60.

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