Case Report

JRAD Journal of Research and Advancement in Dentistry

J Res Adv Dent 2018;7:3:34-39.

# Axenfeld-Rieger Syndrome with Novel Findings of Unilateral Stahl Ear Deformity and Mandibular Condyle Hypoplasia: A Case Report

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## ABSTRACT

**Background**: Axenfeld-Rieger syndrome is a rare genetic condition characterized by ocular, dental, craniofacial, periumbilical and other variable systemic abnormalities. A young female presented for replacement of missing teeth. She had negligible previous dental attendance, impaired vision consequential to pediatric glaucoma and displayed craniofacial anomalies, dental anomalies, oligodontia and periumbilical redundant skin. A diagnosis of Axenfeld-Rieger syndrome was made. Unilateral Stahl ear deformity and mandibular condyle hypoplasia were noted. Dental prostheses and genetic counseling were provided. A missed case of Axenfeld-Rieger syndrome was diagnosed prosthodontically treated and novel findings were noted.

**Keywords:** Axenfeld-Rieger Syndrome, oligodontia, Stahl ear, condyle hypoplasia, PITX2.

## INTRODUCTION

**Axenfeld-Rieger syndrome(ARS)** refers to a rare spectrum of congenital, inherited developmental disorders mainly affecting the anterior segment of the eye and variable systemic features reportedly having an incidence of 1:2,00,000. [1] This syndrome has been extensively researched and reviewed in the fields of genetics and ophthalmology since the first descriptions by Axenfeld in 1920 and Rieger in 1935.[2-5]

Alward in an excellent review in 2000 suggested that the various conditions previously diagnosed separately as Rieger syndrome (RS) (ocular abnormalities, umbilical hernia and dental anomalies), Axenfeld syndrome (AS)(anterior segment defect with systemic signs), Axenfeld anomaly (AA) (anterior segment defect), Rieger anomaly (RA) (anterior segment with iris defects), iridogoniodysgenesis syndrome (IGDS), iridogoniodysgenesis anomaly (IA), familial glaucoma iridogoniodysplasia (FGI), and iris hypoplasia (IH) be denoted by the umbrella term ARS [2].

The ocular features are variable and often overlapping, though the main feature is a malformation of the components of the anterior segment of the eye such as iris, angle, cornea including iris strands connecting the iridocorneal angle to the trabecular meshwork and a prominent, anteriorly displaced Schwalbe's line (posterior embryotoxon), iris hypoplasia, abnormal situation of pupil (corectopia), more than one pupil in an eye (polycoria), microcornea with opacity and glaucoma [2]. Fifty percent of ARS patients develop glaucoma (neural retinal death), with resulting visual-field loss or blindness[2].Defects in other organ systems, typically the teeth and umbilicus, are also often part of ARS[2]. The traits of ARS conditions display a wide range of variability in severity and manifestation.[4]

**Received:** Jan. 5, 2018: **Accepted:** Feb. 18, 2018
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pISSN 2278-0076
eISSN 2321-9270

The systemic signs include abnormality of the cardiovascular outflow tract, midface hypoplasia, a broad flat nasal root, maxillary and occasionally mandibular hypoplasia, hypertelorism (excessive distance between two eyes) and telecanthus (abnormally increased distance between the medial canthi of the eyelids), microdontia (abnormally small teeth), hypodontia (having fewer teeth than normal), skeletal anomalies, and hearing loss[2-4].

## CASE DESCRIPTION

A twenty-eight year old visually-impaired female, accompanied by her mother, presented for the replacement of multiple missing teeth. The main motivation was to improve her facial appearance for matrimonial alliance. She reported that though she had a full complement of primary dentition, many of her permanent dentition had never erupted. She had undergone root canal therapy in tooth #37 and extraction of tooth #47 due to decay.

Past ophthalmic history revealed early onset glaucoma for which she had been unsuccessfully and intermittently treated with drug therapy. The consequences of the absolute glaucoma were a blind and painful left eye which had to be enucleated at the age of five years and ciliary staphyloma in the right eye which showed progressive deterioration of vision till she was completely visually-impaired by the age of twenty three years.

In the clinical interview, her mother reported that she was the third child of healthy unrelated parents and born at full term following an uncomplicated pregnancy. She had no immediate postnatal complications or feeding difficulty, but had a history of delayed acquisition of developmental milestones, particularly in the domains of gross motor and language.

She appeared to be of short stature, normal intelligence and had obvious craniofacial dysmorphology. She had a broad forehead, small jaws, mid-face hypoplasia, broad flat nasal root, thin upper lip vermillion and everted lower lip (Figure 1 and 2). Both her ears were low-set, with large lobules and showed deficient and poorly developed helical rims without the tight furls usually present in normally formed ears. The right ear showed a Stahl ear deformity i.e. the existence of a third crus that traverses the scapha, the absence of the superior crus of the antihelix, a broadened scapha, and unfolded, long helical rim (Figure 3).

Intraoral examination revealed a total of twelve teeth present in the mouth. Teeth missing were right permanent second molar, all maxillary and mandibular second premolars, all permanent maxillary and mandibular canines, maxillary lateral and all mandibular incisors. The only maxillary central incisor present (on the right side) and was peg-shaped. All teeth present were smaller than normal indicating microdontia and the molars had abnormal occlusal morphology indicating taurodontism. Bilaterally primary mandibular canines were present, over-retained, hypermobile and had receding gingivae. One permanent mandibular central incisor was rotated, hypermobile and periodontally compromised. The alveolar crests in edentulous areas were thin and atrophic.

The severe hypodontia was evident on orthopantograph(OPG). Also evident on the OPG, was the hypoplasia of the left mandibular condyle, which was confirmed by the mandibular deviation on opening to the left (Figure 4). A history of childhood glaucoma, typical craniofacial findings, severe hypodontia and microdontia pointed towards a diagnosis of ARS. An ophthalmological evaluation revealed characteristic Axenfeld anomaly and confirmed the diagnosis of ARS. Ophthalmoscopy and slit-lamp examination (Figure 5) of the right eye showed the following findings:

- Microcornea and correctopia
- No perception of light
- Peripheral vascularisation and hazy cornea with peripheral anterior synechiae suggestive of Axenfeld anomaly
- Shallow anterior chamber
- Irregular iris, iris hypoplasia, pupil with altered flow probably complicated cataract
- Huge eyeball with ciliary and equatorial staphyloma
- Nystagmoid movement
- digitally tension normal

The left ocular cavity was empty and without an ocular prosthesis.

Further physical examination revealed the typical umbilical finding of redundant periumbilical skin

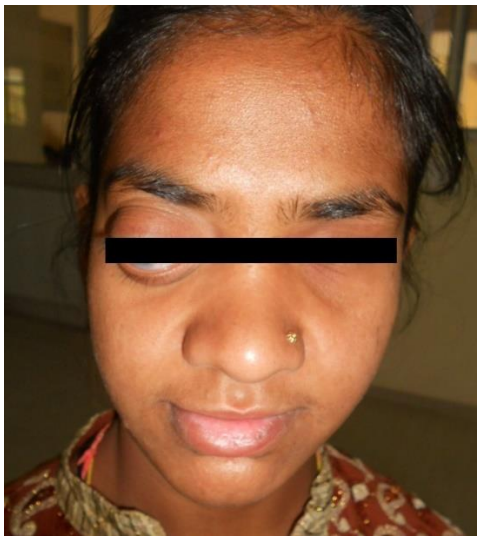

Fig 1: Face front view without prostheses.

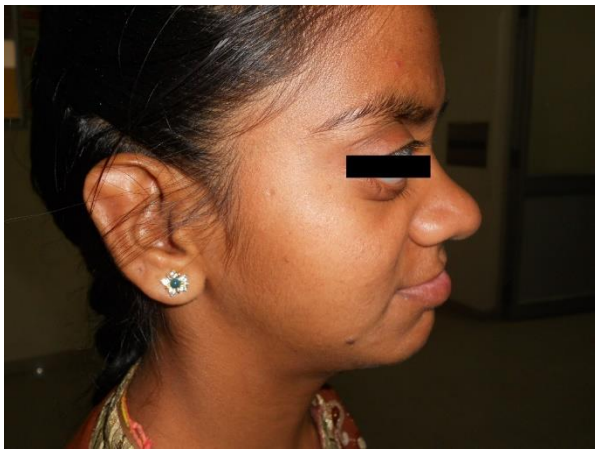

Fig 2: Face profile view without prostheses.

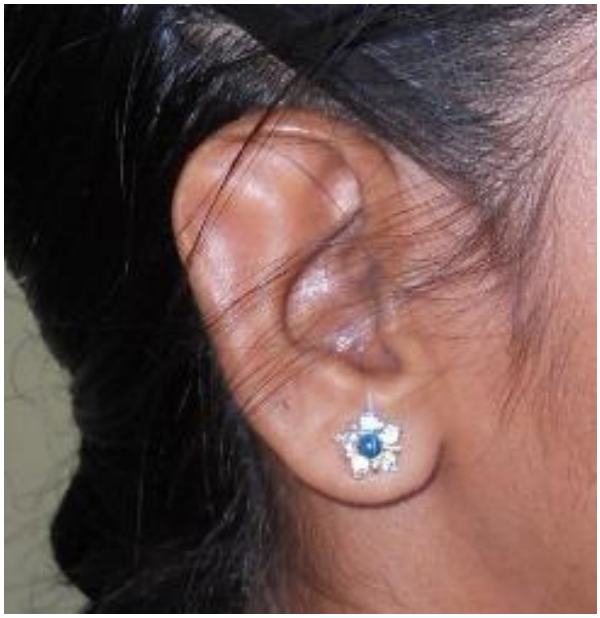

Fig 3: Stahl ear deformity.

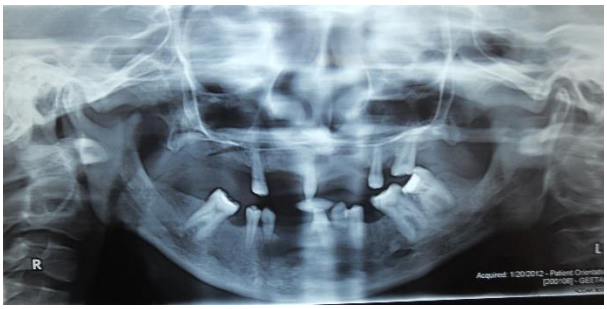

Fig 4: Orthopantograph.

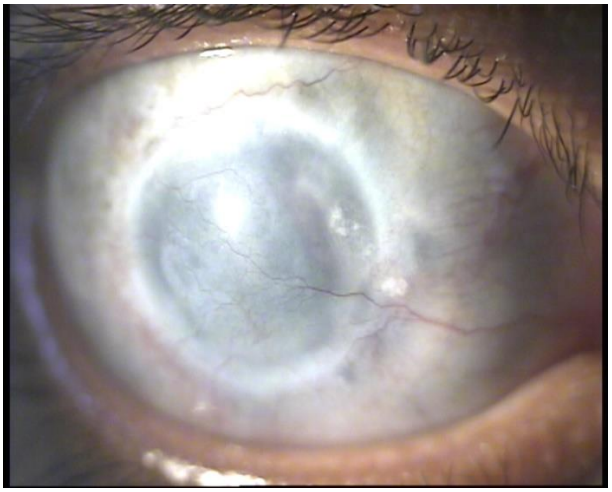

Fig 5: Slit-lamp examination of the right eye.

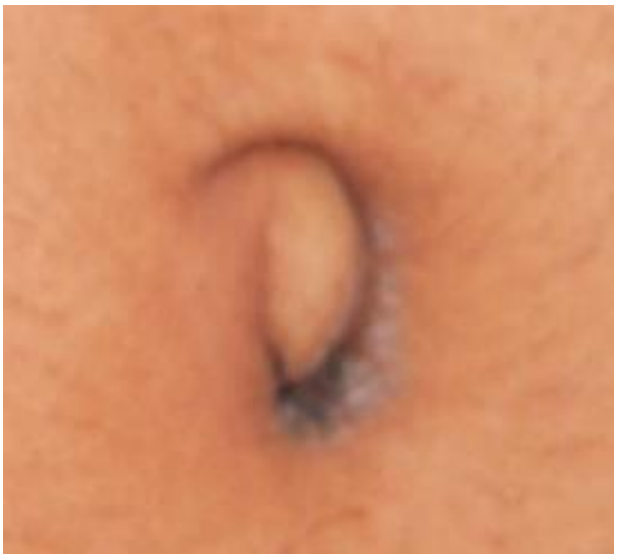

Fig 6: Redundant periumbical skin

(Figure 6). After the establishment of the ARS diagnosis, the patient was thoroughly examined for the systemic findings of ARS. Abdomen and pelvic ultrasound and trans-thoracic echocardiography were normal. Endocrinological tests as well as MRI of brain also did not reveal any abnormality. There

was no otologic, neurologic, skeletal or dermatologic abnormality found. Genetic testing was considered not feasible due to the high cost. The typical clinical findings were conclusive of a diagnosis of ARS.

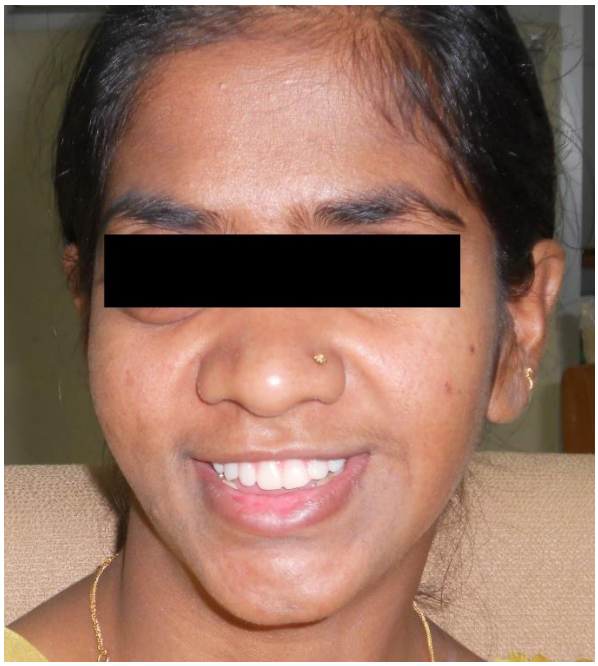

Fig 7: Face front view with prostheses.

The patient's family was screened for signs of ARS and they were found to be free of related abnormalities. The aims of dental treatment were restoration and maintenance of function and dentofacial aesthetics by the replacement of missing teeth and providing upper labial support. Implants were ruled out because of the poor alveolar ridges, fear of surgery and poor economical condition. Over-retained primary teeth and periodontally weak mandibular central incisor were extracted. Patient insisted on having a fixed prosthesis in at least one arch.

An acrylic tooth-supported overdenture in the maxillary arch over cast-metal copings and fixed porcelain-fused-to-metal prostheses in the mandibular arch utilizing the remaining teeth as abutments were planned and delivered. The prostheses improved her ofacial appearance and self-esteem (Figure 7). She was put on a periodic recall maintenance program. She was counseled that her offspring had 50% risk of being born with this syndrome.

## DISCUSSION

Early recognition of the syndrome and referral during childhood to a specialized oral and maxillofacial surgery, special dental care, and orthodontic unit provide the optimal starting point for this complex treatment[6]. Her mother had never sought advice for her severe hypodontia or craniofacial dysmorphology until the prospects of marriage were near. Had the syndrome been diagnosed earlier, careful counseling, prevention, management and monitoring through the course of this syndrome by a multidisciplinary special care team could have been provided.

Further examinations of the pedigree often disclose the autosomal dominant inheritance pattern (seventy percent), though sporadic cases of ARS do occur [7]. Our case appears to be sporadic in nature. It has been proposed that the anterior segment of the eye develops from mesenchyme of neural crest origin which migrates centrally from the rim of the optic cup, and that the anterior segment dysgenesis abnormalities, apart from aniridia which is of non-neural crest origin, represent a neurocristopathy, or primary developmental disorder of the neural crest[8].

Three chromosomal loci (4q25, 6p25,13q14) and two genes (PITX2 and FOXC1) have been linked to ARS. Recent single autosomal recessive case of a child with characteristic anterior chamber anomalies and umbilical findings was identified to be a compound heterozygote for mutations in CYP1B1. [9] In particular PITX2 is expressed in cranial neural crest and mesoderm-derived cells, which form tissues that interact with the developing eye.[10] PITX2 is required for pharyngeal arch development and subsequent jaw and dental formation[11]. PITX2 disruption is primarily associated with ARS with typical ocular anomaly accompanied by dental and umbilical defects and FOXC1 disruption primarily results in ARS with heart or hearing defects or an isolated ocular phenotype[5]. Therefore, we suspect the role of PITX2 disruption in our case.

The unilateral condylar hypoplasia of the left side appears to be of primary type as no history of trauma, infection, radiotherapy or childhood arthritis could be elicited. Congenital (primary) condylar hypoplasia is characterized by unilateral or bilateral underdevelopment of the mandibular

condyle and usually occurs as a part of some systemic condition originating in the first and second branchial arches[12].

During the fifth or sixth week of development, the early auricle arises from a series of paired mesenchymal condensations referred to as the 6 hillocks of His (auricular hillocks). It is generally accepted that the first three hillocks arise from the first branchial arch and lead to the development of the tragus, helical root and helical crus, respectively. The last 3 hillocks are thought to be second branchial arch derivatives that ultimately become the antihelix, antitragus, and lower helix and lobule. The early embryonic pinna begins caudal to the growing mandible, near the base of the neck. However, as synchronous first arch derivatives develop (mandible), the auricle is displaced more cephalad and posterior. By the end of the second trimester, the pinna will reach its adult location at the side of the head. It follows then that in syndromes with proposed arrested development of first and second branchial arch derivatives , the auricle is retroverted, malformed, and set in lower and more anterior position than the normal adult configuration. These deformities are frequently accompanied with middle ear malformations as its components also arise from the first and second pharyngeal arches[13]. However, no such syndrome includes Stahl ear deformity as seen in this case as a part of its typical clinical characteristics. Several theories exist on the etiology of Stahl ear, including developmental error during the 3rd embryologic month as the helix and scaphoid fossa mature, deforming pressure in utero, abnormal prechondral growth, failed embryologic regression, and abnormal transverse intrinsic muscle orientation [14]. Further research with this background of knowledge is required to analyse the etiopathogenesis of Stahl ear and condylar hypoplasia in the present case of ARS.

## CONCLUSION

Young patients with a congenital ocular abnormalities such as iris anomalies or early onset glaucoma should be examined for craniofacial , and dental anomalies as well as evaluated further for systemic abnormalities. The treating facility should have a ready protocol of management of patients with congenital anomalies including multidisciplinary special care and genetic testing. Conversely, every patient of oligodontia should receive an ophthalmic evaluation to rule out anterior segment dysgenesis. A missed case of Axenfeld-Rieger syndrome was thus diagnosed prosthodontically treated and novel findings were noted.

**Clinical significance**

1. Early diagnosis and multidisciplinary care improve the overall medical, ophthalmological and dental prognosis.

2. Our case has unilateral Stahl ear deformity on the right side, primary unilateral condylar hypoplasia on the left side and no associated middle ear abnormality. Such a combination of features, especially in concurrence with ARS has not been published till date. In this context, our case is an important addition to the literature.

## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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