Axenfeld-Rieger Syndrome: Report on dental and craniofacial findings

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Axenfeld-Rieger syndrome is a rare autosomal dominant disorder characterized by various ocular and extraocular malformations. Dental abnormalities are considered as definitive features for the diagnosis and differentiation of Rieger syndrome from other anterior chamber of the eye malformations. A case of Rieger syndrome with distinct dental and craniofacial anomalies is described. Significant cranio-dento-facial findings that have been observed are, teeth with short and dilacerated roots, hyperplastic frenums and underdeveloped maxilla. There was an anterior crossbite, bilateral posterior openbite and moderate to severe anterior crowding.
J Clin Pediatr Dent 30(1): 83-88, 2005

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INTRODUCTION

Axenfeld-Rieger syndrome is a rare genetic disorder characterized by malformations of the anterior chamber of the eye (goniodysgenesis) and hypodontia. It may also be accompanied by a spectrum of dental, craniofacial and somatic anomalies. The manifestations of this syndrome are variably expressed and therefore distinct from a less severe condition of ocular manifestations (Axenfeld anomaly) and other a closely related conditions.[1] Some authors have been proposed that Axenfeld anomaly, Rieger anomaly and Rieger syndrome represent a single condition to be designated as Axenfeld-Rieger syndrome.[1, 2] However recent genetic studies have proved that they are different.[3-5] The incidence of Axenfeld-Rieger syndrome in the general population has been estimated to be 1:200,000.[6] It is an autosomal dominant condition with considerable variability of expression.[1,7,8]

The purpose of this report is to present a case of Axenfeld-Rieger syndrome and its characteristic cranio-dento-facial findings. The issues related to diagnosis, management of dental problems and malocclusion will bee discussed.

REVIEW OF LITERATURE

Rieger first described mesodermal dysgenesis in 1934 as an eye malformation involving the cornea and iris.[9] Since more than a number of cases have been reported with major involvement of the eye, craniofacial, dental and somatic anomalies. A summary of the characteristics Systemic, Ocular, Craniofacial and Dental findings abstracted from the review of the literature is given below.

***General Appearance*:** Patient displaying an old appearance is characteristic. Hypoplasia of the maxilla is common and leads to a mild prognathic profile.[10] A shortened philtrum, a pronounced lower lip and a receding upper lip are also significant findings.[11,12] Telecanthus, a wide nasal bridge and occasional mandibular hypoplasia are also present in some patients.[1] Another common feature of this syndrome is skeletal growth deficiency which may be noted both by underdeveloped maxilla and stature deficiency. Short body stature and delayed bone age are thought to be related to growth hormone deficiency.[7,13] Shields et al found an "empty" sella turcica in Rieger syndrome patients, which may be related to growth hormone deficiency.[1] Empty sella is thought to result from herniation of the arachnoid membrane through the diaphragma sella causing an enlargement of the sella.[14] Although empty sella has been found to occur in Rieger's patients, it is not constantly associated with the pituitary dysfunction.[15]

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Systemic Findings: Many systemic developmental defects are also seen in Rieger syndrome patients which include anal atresia and stenosis,[16,17] cardiovascular disorders,[18-20] atresia of the lacrimal duct,[21] malformations of the hand,[11,19,20,22-25] the foot,[11,23,24] the leg[11,19,25] and the hip,[11,17,21] hypermobility of the joints,[19,20] scoliosis,[22] kyphosis,[11,16] mental retardation,[11,17,21,26] myopathy,[27,28] ear and nose abnormalities,[11,19,28] inguinal hernia,[7,8,11,20,29] sternum anomalies,[11,12,19,24,30] kidney malformation,[17,28] congenital deafness,[11,31] lipodystrophy[19,20] and Meckel's diverticulum.[32,33]

Ocular Features: The ocular involvement is usually bilateral and is characterized by a triad i.e. hypoplasia of the iris, anterior synechiae (iridocorneal adhesion) and a prominent anteriorly displaced Schwalbe's line.[18] The various eye defects cause increased intraocular pressure resulting in glaucoma in approximately 50% of patients.[1] Presence of corneal defects, papillary anomalies, cataracts, marked ametropia and onset of the juvenile glaucoma are also other significant findings in many patients.[1,11] The ocular manifestations of this disease are the result of partial or complete hypoplasia of the anterior stromal leaf of the iris.[10]

Dental Features: The significant dental characteristics are hypodontia of the primary and / or permanent dentition and microdontia (barrel or conical shaped teeth) of the mandibular primary incisors.[1,7,10,22,34] The hypodontia varies from a single missing tooth to multiple missing teeth (20 or more). Maxillary incisors and canines are most often absent, with premolars occasionally missing.[18,29] Missing primary and/or permanent teeth may be the initial clue in the diagnosis of Axenfeld-Rieger syndrome. Other associated tooth abnormalities are enamel hypoplasia, delayed eruption, taurodontism, misshapen teeth and shortened roots.[7,10-12,22,23,29] In some patients hyperplastic frena are also present.[10,12,34]

ETIOLOGY

Initially the etiology of the Rieger syndrome was attributed to mesodermal dysgenesis.[11] Recent evidence supports that it is an ectodermal tissue defect.[1,10,13] It is theorized that there is developmental arrest of tissue derived from neural crest ectoderm during third trimester of pregnancy.[1,30] This disturbance promotes retention of primordial endothelial layer of the iris and anterior chamber angle and accounts for iridic adhesions and hypoplasia and an abherent Schwalber's line. It is known that the neural crest cells are involved in facial bone formation, therefore their developmental disturbance may explain the morphologic abnormalities of the maxilla, mandible, hypertelorism, teeth, empty sella and the failure of involution of the periumbilical skin.[1,30]

CASE REPORT

An 11-years old Indian male patient NC was referred from department of Opthalmology to the department of Dental Surgery for orthodontic therapy to correct the malalignment of his upper and lower front teeth. The patient was examined clinically and a thorough family and medical history was recorded. On the basis of clinical findings and family and medical history, the diagnosis of Axenfeld-Rieger syndrome was made.

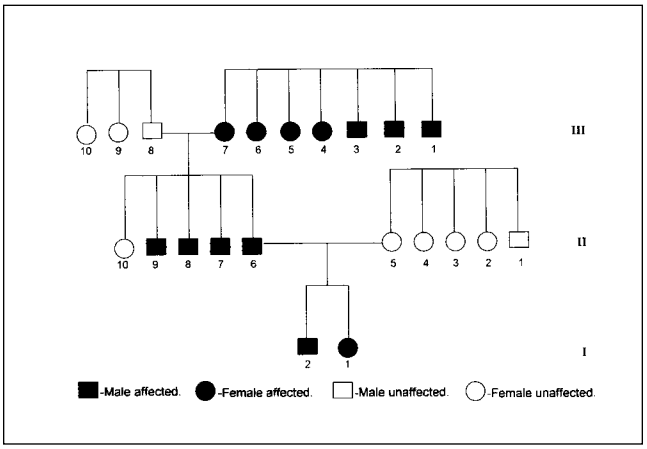

Figure-1. Pedigree analysis of three generations of the Axenfeld-Rieger syndrome family revealed an autosomal dominant mode of inheritance with variable expressivity.

The family pedigree is shown in Figure-1. The sister (**I.**1) of patient NC (**I.**2) had also similar problems. The NC's mother (**II.**5) was clinically normal but his father AC (**II.**6) was found to have the same problem. The AC had three brothers (**II.**7, **II.**8, **II.**9) and one sister (**II.**10). All the brothers (**II.**7, **II.**8, **II.**9) of AC had same problem but his sister (**II.**10) was clinically normal. It was also noted that the mother (**III.**7) of AC had same dental and eye problems. She (**III.**7) had also three brothers (**III.**1, **III.**2, **III.**3) and three sisters (**III.**4, **III.**5, **III.**6), and all had same problems. Few affected individuals in the **II** and **III** generation were completely edentulous and had been treated for eye problems secondary to Rieger anomaly. None of the examined members had involution of the periumbilical skin and all were of normal height and weight for their ages, indicating normal growth.

Patient's past medical and dental history suggested that patient NC had undergone adenoidectomy at the age of 9 years. He is also undergoing treatment for short sightness in the department of ophtalmology for the last 2 years. The shape of all primary teeth was apparently normal but their eruption was late.

Clinical examination of NC revealed apparently symmetrical face with a relatively straight facial profile (Fig-2A and 2B). Lips were competent and lower lip was slightly everted. Intraoral examination revealed presence of all the permanent teeth except second and third molars in all quadrants. The shapes of all permanent teeth were apparently normal (Fig-3A, 3B and 3C). The height of the clinical crown was average for all the teeth except mandibular premolars. The width of

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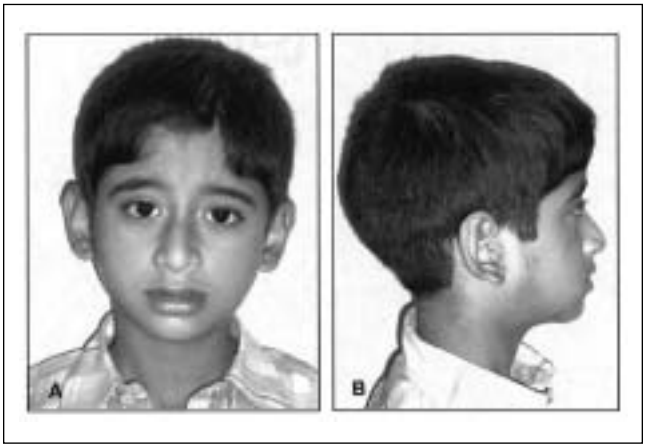

Figure 2. Extra-oral photographs (A,B) showing apparently symmetrical face, straight profile with everted lips giving an older appearance.

attached gingiva in all teeth was less than normal. Maxillary and mandibular labial frenums were large. Attachment of the upper and lower labial frenums were low and high respectively. The upper incisors were in crossbite. In maxillary and mandibular anterior segment moderate to severe crowding was present (Fig-3D and 3E). In both the sides of mandibular arch, approximately 2mm space was present distal to the canine and between premolars. Bilateral open bite in the premolar and molar region with lateral tongue thrusting was also a characteristic finding.

A Panoramic radiograph (Fig-4) showed congenital absence of the lower third molars. The shape of the all permanent teeth was abnormal and their roots were very short. The roots of the mandibular left canine and premolars were curved. The height of the mandibular body was very thin.

Table-1- Angular and linear cephalometric parameters for NC.

Parameters	Normative value	Measurement for NC
SNA Angle	82.920	77 0
SNB Angle	79.900	80 0
ANB Angle	3.020	-3 0
Frankfort-Mandibular Plane (FMA) Angle	22.820	16 0
Y-Axis Angle (FH Plane x S-Gn)	62.410	50 0
Craniomandibular Angle (SN-GoGn)	27.240	26 0
Anterior Cranial Base Length (S-N)	72.71mm	67.25mm
Effective Maxillary Length (Co-A)	94.61mm	75.41 mm
Maxillary Base Length (PNS-A)	47.78mm	43.59mm
Effective Mandibular Length (Co-Pog)	124.30mm	94.18mm
Mandibular Base Length (Go-Pog)	75.78mm	58.89mm
Upper Anterior Facial Height (N-ANS)	53.16mm	46.44 mm
Lower Anterior Facial Height (ANS-Me)	70.34mm	46.32 mm
Total Anterior Facial Height (N-Me)	118.48mm	92.76 mm
Total Posterior Facial Height (S-Go)	89.56mm	63.30 mm
Facial Height Ratio	75.74 %	68.24 %

Lateral cephalogram with teeth in occlusion (Fig-5A and 5B) revealed overall decrease in craniofacial

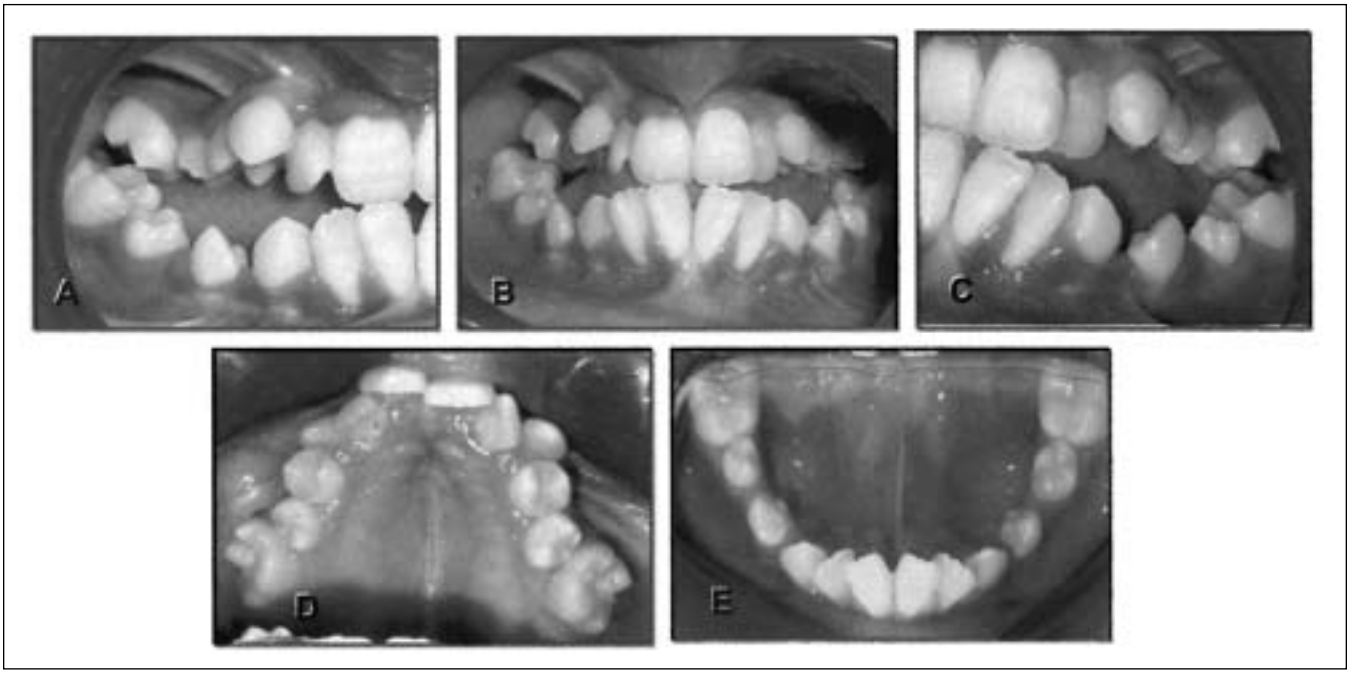

Figure 3. Intra-oral photographs (A-E) of the patient showing hyperplastic labial frenums(A), anterior crossbite (A), bilateral posterior openbite (B,C) and crowding in the anterior segments (D,E).

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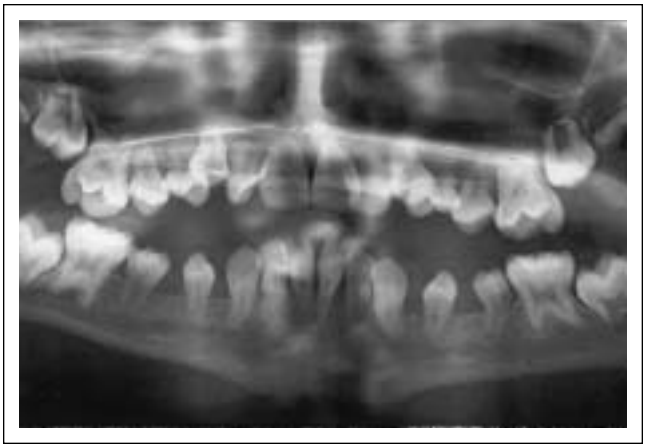
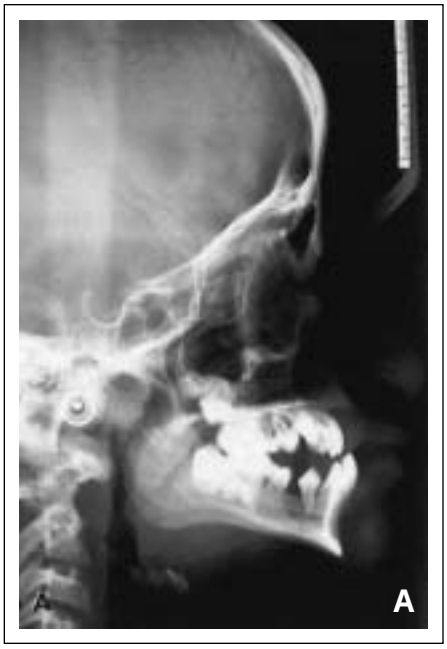


Figure-4 - Panoramic radiograph showing abnormal shape of all permanent teeth with short roots and dilacerated root in mandibular left canine and premolars.

dimensions with hypoplasia of the maxilla. The mandible was normally positioned in relation to the anterior cranial base with forward and upward rotation. The maxillary incisors were proclined and mandibular incisors were uprighted. Both posterior and anterior facial heights were decreased. Few important cephalometric parameters are shown in Table-1. Skeletal maturation of the patient (Cervical Vertebral Maturation Index) was Stage-1, which is far less for his chronological age. The morphology of the sella turcica was typical but relatively larger.

DISCUSSION

Malformation of the anterior chamber of the eye and various dental, craniofacial and somatic anomalies are characteristics of Axenfeld-Rieger syndrome.[3,12,18,35-38] When only eyes are involved, the condition is known as Rieger anomaly or Axenfeld anomaly.[4,15,35,36,39] The extraocular features help to distinguish the Axenfeld-Rieger syndrome from the Rieger anomaly and other disorders in which goniodysgenesis is a component.[12,34,39] As various characteristics of Rieger syndrome are overlapped, it has been proposed that Rieger anomaly and Rieger syndrome represent a single condition to be designated as Axenfeld-Rieger syndrome.[1,29] But recent genetic studies proved that they are different.[3-5] Axen-



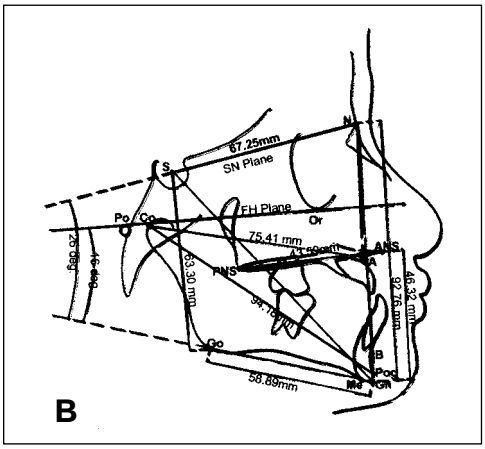


Figure 5. Lateral Cephalogram(A) with teeth in occlusion showing relatively large sella turcica, hypoplasia of the maxilla, slightly excessive mandibular length, decreased anterior facial height, proclined maxillary incisors, uprighted mandibular incisors and anterior crossbite. B. Tracing of lateral cephalogram with few important linear and angular measurements (See table-1).

feld-Rieger syndrome is described as an autosomal dominant condition with variable expressivity and pen-

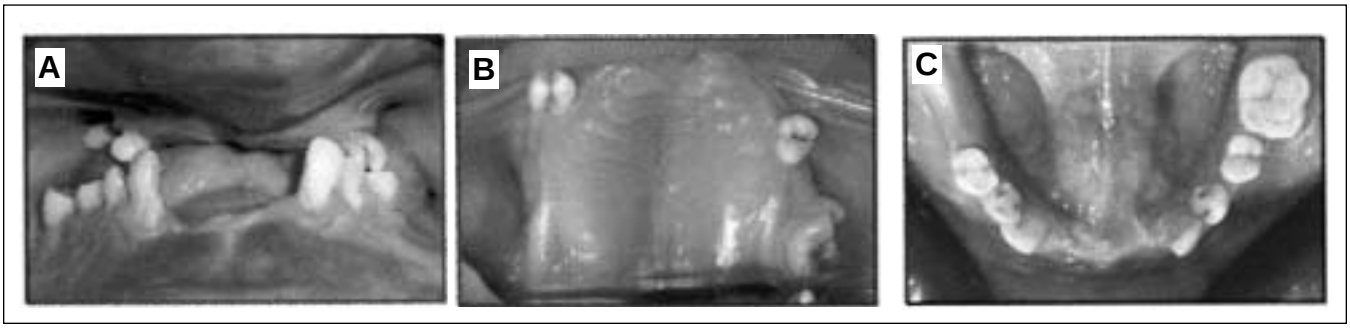


Figure 6. Intra-oral photographs (A-C) of the patient's father showing only three teeth in the maxillary arch and seven teeth in the mandibular arch.

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etrance.[6] The present case report study also appeared to demonstrate an autosomal dominant inheritance of the trait with variable expression of the ocular and extraocular manifestations. The reduced penetrance was demonstrated by the unaffected sister (**II.**10) of AC.

In the present case report, the patient had all the anterior teeth in both the jaws. Drum et al concluded that clinically observed maxillary deficiency existed because of alveolar hypoplasia resulting from missing teeth.[34] In the present study posterior facial height was almost normal and this finding was consistent with Drum et al.[34] However anterior facial height was decreased and could be due to the partial eruption of the premolars and molars. The lateral tongue thrust was secondary to the posterior openbite. Dilacerated roots in few teeth and generalized shortened roots in the present case were also reported by several authors.[7,10-12,22,23,29,34]

The shape of the sella turcica in the present case was apparently normal but the size was relatively large. Abnormalities of the sella turcica with deficiencies of growth hormone have been reported in association with Axenfeld-Rieger syndrome.[7,20] But in the present study the height of all affected individuals in the family was within normal limits indicating potentially normal hormonal level.

ISSUES RELATED TO THE DENTAL HEALTH

Several case reports have been shown in the literature discussing the ocular, dental, craniofacial and other somatic features. However none of the authors discussed issues related to the dental and or orthodontic treatment.

Issues related to early tooth loss - It is a major issue in patients with Rieger syndrome. In the present study few individuals of generation-II (age range of 35-45 yrs) and all the individuals of generation-III (age range 60-74 yrs) were already completely edentulous. Patient's father who is 35 yrs old had only three teeth in the maxilla and seven teeth in the mandible (Fig-6A, 6B and 6C). Early loss of the teeth is mostly because of the short roots and scanty attached gingiva leading to rapid periodontal bone loss.

Issues of dental treatment in young individuals- The patients with Rieger syndrome have inherent decreased height of the alveolar process. These patients are extremely prone to periodontal breakdown and early tooth loss, which is coupled with scanty attached gingiva and short roots. Hence it is of paramount important that all efforts on meticulous oral hygiene and prevention of gingival disease should be implemented both in terms of personal and professional care.

Issues related to early Orthodontic intervention- Esthetics is one of the primary requirements for any patient. However the short length of the roots governs provision of orthodontic treatment in these patients. This treatment is difficult to carry out due to a decrease in alveolar bone height and abnormal root curvatures that causes significant tooth movement. Abnormal jaw growth is a common characteristic in patients with Rieger syndrome. Thus the use of dentofacial orthopedics to modify or to reduce the severity of developing skeletal abnormalities during primary dentition or in the mixed dentition could be one of the orthodontic treatment options. Orthodontic treatment for minimum tooth movement along with meticulous oral hygiene should be considered in Axenfeld-Rieger syndrome patients.

Option of Surgical Orthodontics- In certain situation the abnormal jaw growth may be very severe or patients may consider orthodontic care during post adolescent period. In these patients orthognathic surgery may be considered.

Option of implant prosthesis- Tooth loss in Rieger syndrome patients may not be possible to avoid. The alveolar bone support is usually very poor, thus provision of fixed prostheses may not possible. In some favorable situations dental implants can be considered for restoration of missing teeth. However we could not find any case reports of implant prosthesis in Axenfeld-Rieger syndrome.

SUMMARY

Many dental and craniofacial characteristics of this case report are classical to Axenfeld-Rieger syndrome. However, localized hypodontia, which is a classical extraocular characteristic of Axenfeld-Rieger syndrome, was absent in this case. All possible modalities of dental treatments were considered for the wellbeing of patient.

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