Case Report

Axenfeld-Rieger Syndrome: Dentofacial Manifestation and Oral Rehabilitation Considerations

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Abstract: *Axenfeld-Rieger syndrome is a rare genetic disorder characterized by ocular and dental abnormalities. This case demonstrates a comprehensive review of the syndrome's clinical and dental features and describes a case of a 13-year-old boy presenting with it. The patient showed severe hypodontia, microdontia, and short roots. Different treatment options are discussed. Early diagnosis and an interdisciplinary approach are necessary to provide the best short- and long-term treatment plans, as well as treatment and follow-up for individuals with the syndrome. (Pediatr Dent 2011;33: 440-4) Received March 16, 2010 / Last Revision June 22, 2010 / Accepted July 17, 2010*

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Axenfeld-Rieger syndrome (**ARS**) is a rare genetic disorder characterized by ocular and dental abnormalities. The prevalence of the ARS in the general population has been estimated at 1:200,000,[1-3] and no racial or sexual predilection has been reported.[3] Dental and craniofacial anomalies are the main characteristic of this syndrome; however, very few case reports are documented in the dental literature.[1-8]

ARS patients are generally asymptomatic and the diagnosis is based upon findings from routine biomicroscopic and gonioscopic evaluations. They usually suffer from hypoplastic growth of the maxilla, leading to a mild prognathic profile,[3,6,8] shortened philtrum, pronounced lower lip, and a receding upper lip.[1,3,5] Significant dental characteristics prevalent in these patients include hypodontia of the primary and/or permanent dentition, varying from a single missing tooth to multiple missing teeth (≥20), and microdontia (barrel, conical, or peg-shaped teeth) of the primary mandibular incisors.[5,6,8-11] Maxillary incisors and canines are the teeth most often absent, with premolars occasionally missing.[4,5,12] Other associated tooth abnormalities are enamel hypoplasia, delayed eruption, taurodontism, malformed teeth, and shortened roots.[1,3-6,9,10] The shortened root length is the reason for the common phenomenon of early loss of teeth with this anomaly.

Apart from the craniofacial and dental features of the syndrome, there is a wide variety of systemic developmental defects seen in ARS patients, including: anal atresia and stenosis; cardiovascular disorders; atresia of the lacrimal duct; malformations of the hand, foot, leg, and hip; hypermobility of the joints; scoliosis; kyphosis; mental retardation; ear and nose abnormalities; kidney malformation; congenital deafness; and failure of the periumbilical skin to involute.[1,3] In many cases, ocular involvement is usually bilateral and manifests a triad of features: partial or complete hypoplasia of the iris, causing the eyes to appear dark; anterior synechiae (abnormality of the angle structure with congenital iris adhesion); and a prominent anteriorly displaced Schwalbe's line.[5,8,12]

The purpose of this paper was to present a case report of a patient with a variant of Axenfeld-Rieger syndrome and review appropriate dental management considerations.

Case report

A 13-year-old male Israeli patient was referred from a pool of high-risk patients from the dental clinic at Barzilai Medical Center, Ashkelon, Israel, to the Orthodontic and Craniofacial Center at the Rambam Health Care Campus, Haifa, Israel, for an orthodontic examination. The patient's complaints included functional and esthetic impairment due to the bizarre shape of his teeth.

At 7-years-old, the patient was examined clinically by a pediatric dentist who suspected a syndromatic condition due to tooth size and shape anomalies, the relationship of the maxilla and mandible, and eye abnormalities. After consulting with his pediatrician, the pediatric dentist referred the patient to a clinical geneticist who examined the boy and recorded his family medical history. DNA testing did not reveal any mutations in the familiar genes, known for causing ARS or in any other tested or suspected genes. The family pedigree (Figure 1) revealed that the patient's aunt had retinoblastoma during her childhood. All other members of the patient's family were clinically normal. Based only on the phenotype, the diagnosis of

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the pediatrician and geneticist was ARS with Peter's anomaly (a rare form of anterior eye segment dysgenesis).

A clinical examination at 13 years of age revealed normal cognitive and physical development for age. The auricle of the left ear protruded, causing apparent asymmetry of the auricular position between both sides. The face appeared symmetrical with a relatively straight facial profile and a prognathic tendency (Figure 2a-b). Bilateral mild enophthalmus was evident with hypoplasia of the left orbit. His left eye presented with abnormal cleavage of the anterior chamber, resulting in opacification of the left eye cornea in accordance with Peter's anomaly. The nasal bridge was wide and cylindrically shaped, the philtrum was slightly short, and a mild telecanthus was evident. His lips were thin and competent, with the lower lip slightly everted and pronounced, and the upper lip slightly receded. The patient displayed a characteristic appearance of an old man with an edentulous facade when smiling and speaking, without incisor crown exposure.

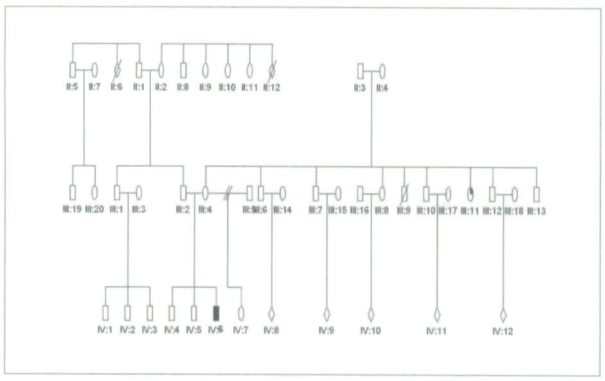


Figure 1. Patient's family pedigree.

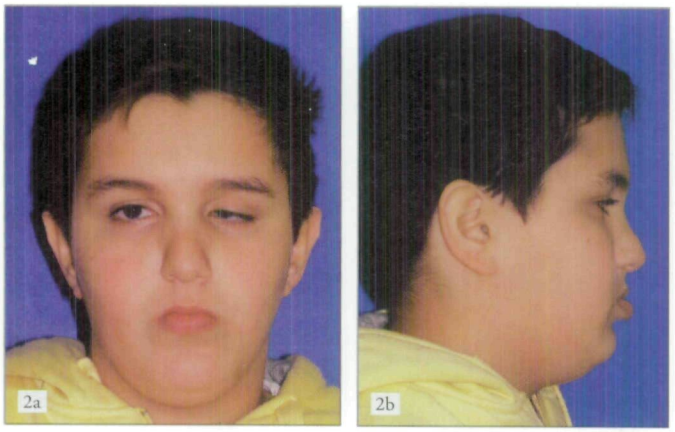


Figure 2. Extraoral photographs of the patient's (a) frontal repose and (b) profile appearance (right).

An intraoral examination revealed microstomia with oligodontia and a malformed permanent dentition. Clinical crowns were very short (2-4 mm length), resulting in a short face appearance, decreased freeway space, and overclosure. All teeth were very small with marked spaces between them and with normal enamel (Figure 3a-e). The maxillary central incisors were located in the position of the lateral incisors and were conical in shape.

The intercuspal occlusion of these teeth presented an anterior cross bite with overclosure relationships, resulting in reduction of the freeway space (Figure 3d, 3e, 4a). At the rest position, an anterior and bilateral posterior open bite was recorded with bilateral tongue thrusting in between the maxillary and mandibular premolar and molar regions, and the tongue reclined over the occlusal surfaces (Figure 3c). A lateral cephalogram taken with a horseshoe bite wax corrected the mandible's position; consequently, the relationships to the cranium could be traced and recorded (Figure 4b). These relationships are discussed later in this paper.

A panaromic radiograph (Figure 5) showed congenital absence of the mandibular permanent central incisors and all second premolars, and the mandibular left first premolar. All permanent teeth were extremely spaced and abnormally small with short crowns. The roots were very short, and in the panoramic radiographic, the true relation between the size of the crown and the root can be seen. This is true for the length of the root as well, indicating an early developmental completion time. Taurodontism could be noticed in the permanent

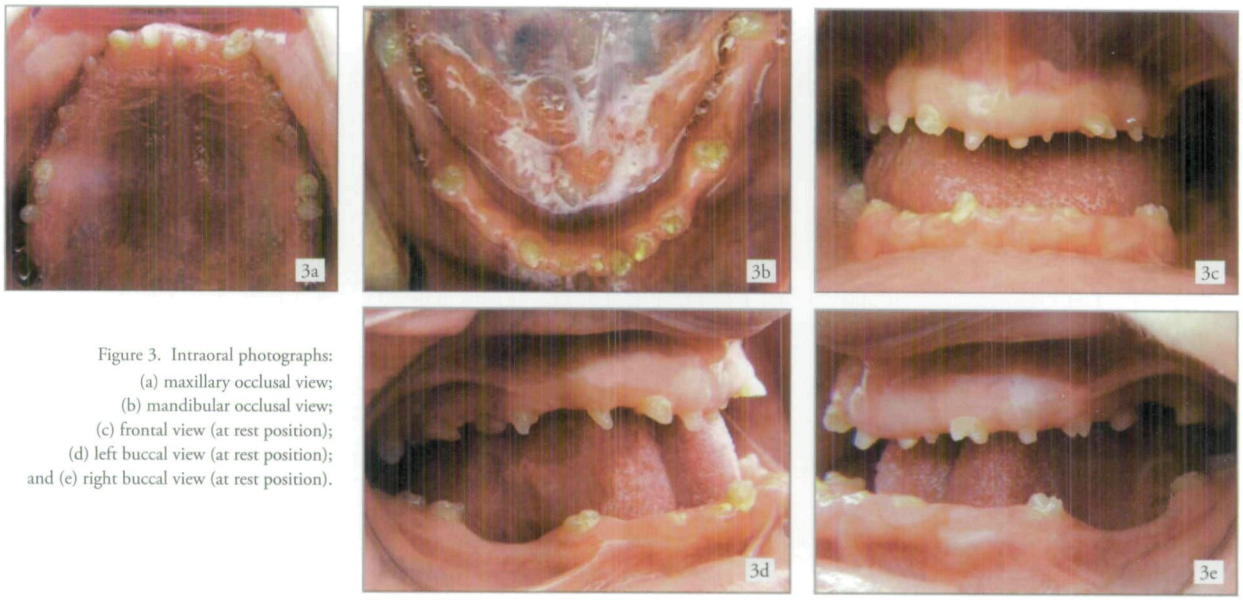


Figure 3. Intraoral photographs: (a) maxillary occlusal view; (b) mandibular occlusal view; (c) frontal view (at rest position); (d) left buccal view (at rest position); and (e) right buccal view (at rest position).

first molars. An impacted supernumerary tooth mesial to the primary mandibular second molars was identified.

A lateral cephalogram taken in the rest position with a horseshoe bite wax in place (Figure 4b) revealed an overall decrease in craniofacial dimensions. Both posterior and anterior facial heights were decreased with a mild maxillary hypoplasia, causing the mandible to appear prominent and giving the patient a slight prognathic appearance. The mandible, however, was normally positioned in relation to the anterior cranial base with forward and upward rotation. The gonial angle was enlarged, resulting in an open bite. The maxillary incisors were slightly proclined, and the mandibular incisors were mildly retroclined (Table 1).

A cone beam computed tomography scan of the maxilla and mandible revealed an atrophic alveolar ridge in the vertical as well as horizontal dimensions (Figure 6a-b), a normal maxillary sinus structure, and a triangular-shaped mandible.

An evaluation of earlier panoramic X rays and dental photos revealed a full primary dentition with the identical characteristics of the present permanent dentition including: small teeth with conical-shaped incisors and very thin and round-shaped molars, short roots, and enlarged interdental spaces. Normal timing was recorded for the permanent dentition eruption process.

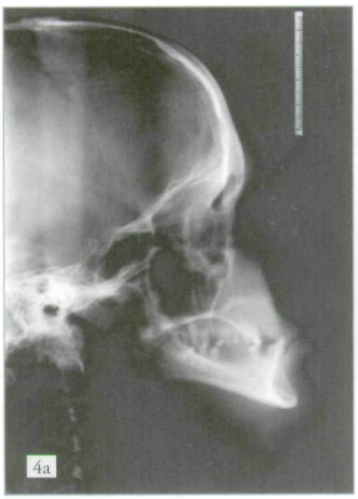
Discussion

ARS is an autosomal dominant condition associated with mutations in transcription factors Pitx2 on chromosome 4q25, FOX-C1 on chromosome 13q14,[13,14] and PAX6 on chromosome 11p13.[15] The patient presented had findings compatible with characteristics common in ARS with the addition of Peter's anomaly, probably due to the common mutation in the PAX6 gene. Family history and pedigree evaluation did not account for autosomal dominant inheritance. According to the literature, this type of inheritance accounts for only 70% of the cases, while 30% arise de novo.[16] We assume that, in the present case, there was a sporadic occurrence of a mutation causing the appearance of this syndrome. It is probable that several other genes (apart from the known ones) are responsible for ARS and, therefore, research in this field must continue.

The list of dental anomalies presented in this case report, as depicted in Table 2, resulted directly from the substantial dental problems summarized in Table 3. Table 4 describes the recommended treatment options. The list of problems pertaining to functional and esthetic issues of the patient resulted from the altered anatomy and morphology of the dentofacial structures which characterize ARS. The patient's basic oral functional disorders, such as chewing, swallowing, and speech from a young age, had severely impaired his quality of life as well as his facial esthetics and emotional well-being.

ARS patients require a modified treatment protocol to overcome their specific difficulties while considering the limitation of their biological ages and stages of growth. All of this should be integrated into an applicable, acceptable treatment plan with which they can cooperate.

Dental rehabilitation issues in young patients. The aim of conservative dental rehabilitation is to improve both esthetics and function. Meticulous oral hygiene and prevention of gingival disease must be emphasized and implemented both in terms of personal and professional care before beginning any treatment. Prefabricated metal/heat-cured resin temporary crowns, functioning as semi-fixed prostheses, can be used at any age for the enlargement of the posterior occlusal dimension and the crown's vertical height. This treatment may partially contribute to bite opening. In the presented case, the small crown size and the large spaces between the teeth precluded installation of temporary crowns. Furthermore, this method of treatment could also worsen the unfavorable crown-root ratio, thus risking the longevity of these posterior teeth in the thin alveolar ridge. Hence, the rehabilitation of the teeth by means of any of the prostheses previously described was not feasible. A partial denture, however, with frenectomy for improved retention, because the frenum in some cases can interfere with the proper fit of the denture and therefore reduce its retention during routine oral function, should always be considered as an alternative.[8] This kind of treatment is reversible and conservative



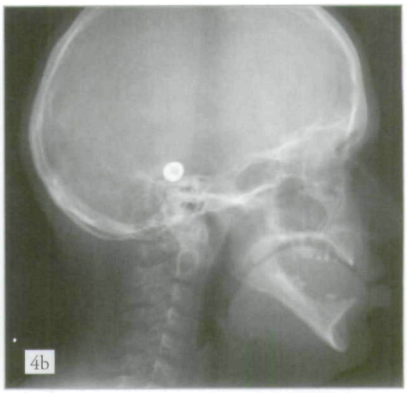


Figure 4. (a) Lateral cephalometric X ray of intercuspal occlusion. (b) Lateral cephalometric X ray in the rest position with horseshoe bite wax.

Table 1. ANGULAR AND LINEAR CEPHALOMETRIC MEASUREMENTS FOR THE PATIENT

Parameters	Mean	Patient's value
SNA angle	82	79
SNB angle	80	81
ANB angle	2	-2
Frankfort mandibular plane (FMA) angle	28	16
Y-axis angle (FH plane to S-Gn)	59	54
Craniomandibular angle (SN-GoGn)	32	18
Gonial angle (Ar-Go-Gn)	130	137
Anterior cranial base length (S-N)	71 mm	67 mm
Effective maxillary length (Co-A)	94.61 mm	88 mm
Maxillary base length (PNS-A)	47.78 mm	51 mm
Effective mandibular length (Co-Gn)	124.30 mm	127 mm
Mandibular base length (Go-Pog)	75.78 mm	69 mm
Upper anterior facial height (N-ANS)	45%	48%
Lower anterior facial height (ANS-Me)	55%	52%
Total anterior facial height (N-Me)	118 mm	100 mm
Total posterior facial height (S-Go)	89 mm	70 mm
UI to SN (angle)	104	108
UI to FH (angle)	100	116
UI to A-pog (mm)	6	3
LI to mand (Go-Gn) angle	90	87
LI to A-pog (mm)	1.5	0

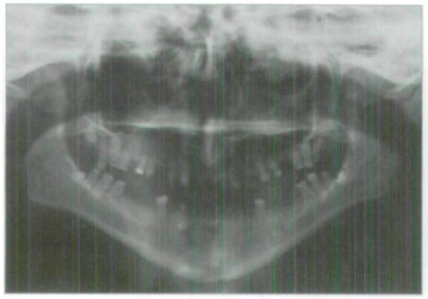


Figure 5. Panoramic X ray.

Figure 6a. Photographs of mandibular alveolar ridge.

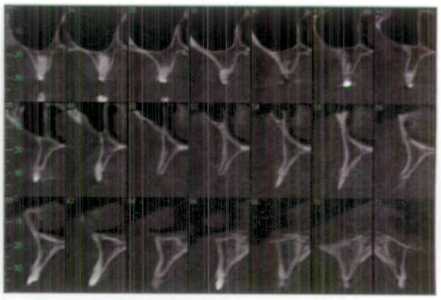


Figure 6b. Photographs of maxillary alveolar ridge.

and, therefore, is the most suitable for these patients' needs and future plans for comprehensive oral rehabilitation post maturation.

As part of the current patient's rehabilitation treatment plan, 2 full overdentures were fabricated. The intent was to improve facial appearance and esthetics by increasing the vertical dimension and allowing the display of teeth at rest and smiling positions, and his original small teeth and gums were used as a retentive unit. Despite the thin alveolar ridge and tongue-thrusting habit resulting from the open bite, the overdentures, were quite retentive and functioned well. The patient, however, could not adapt to their use and preferred not to use them at all as a result of the psychological issue of using a removable prosthetic device.

The anterior teeth can be restored in ARS patients of all ages by the application of resin restorations. These restorations provide an optical illusion so that the incisors and canine crowns no longer appear small. This may boost the patient's self esteem and confidence, especially during adolescent years when physical changes and facial esthetics and attractiveness become significant. We were unable to apply this type of restoration in the present patient due to the small crown size and the enlarged spaces between the anterior teeth, creating large leverage forces on the restoration during oral functioning, which could lead to their failure. The other options of fixed prosthetic rehabilitation were than considered.

Early dental implant insertion issues. At the Consensus Conference on Oral Implants in Young Patients held in Stockholm in 1996, it was agreed that implants should not be placed until growth and skeletal development has completed or nearly completed, except in cases of anodontia and severe oligodontia in which orthodontic treatment and autotransplantation are preferable to prosthetic replacement.[17] Thilander et al.,[18] stated that dental implants are a good treatment option for replacing missing teeth in adolescents, provided the dental and skeletal development has ceased or is almost complete. Due to continuing eruption of adjacent teeth and craniofacial changes following adolescence, the implant-supported crowns become infraoccluded with time.[19,20]

Dental implants can be used only when treatment options other than implant-supported prosthetic replacement of missing teeth as a result of agenesis have been carefully considered. Since 1995, several case reports have been published in which implants were placed in the canine region of the mandibule with anodontia to support an overdenture in patients from 3- to 8-years-old.[19,21-23] Many authors believe that implants should be placed close in time to exfoliation or extraction of persisting primary teeth to preserve the alveolar bone.[17] The most suitable insertion site seems to be the anterior mandible; insertions in the maxilla should be avoided, or at least should not cross the midline.[19] Optimal time for implant insertion, is determined by the status of skeletal growth, the degree of hypodontia, and the extent of psychosocial related stress, in addition to the status of the existing dentition, and dental compliance of the pediatric patient.

In the case presented, the patient's permanent teeth resembled primary ones due to their short clinical crown and roots, especially in the molar region. Therefore thier long term stability and the overall prognosis of these teeth was poor, and extractions with delayed-immediate implant placement were considered. However, the short and narrow alveolar ridge, which is typical of ARS patients,[1] would require a preliminary ridge augmentation with an autografted bone and reconsideration after its consolidation. This would not be the final rehabilitation treatment, as the patient was 13-years-old and major growth of the craniofacial skeleton was still expected; thus the implanted restoration would become infraoccluded with time. With all these factors to consider, we decided to postpone this treatment plan and wait for growth completion.

Early orthodontic intervention issues. Orthodontic treatment in ARS patients is difficult to carry out due to decreased alveolar bone height and abnormal root curvatures that cause significant tooth movement.[1] In addition, abnormal jaw growth

Table 2. THE LIST OF DENTAL ANOMALIES PRESENTED IN THIS CASE REPORT

Anomaly
• Small teeth and small molar occlusal table
• Short clinical crowns
• Short roots
• Enlarged freeway space
• Spaced dentition
• Open bite
• Crossbite
• Short alveolar ridges
• Knife-edge shaped alveolar ridge morphology

Table 3. LIST OF PROBLEMS STEMMING FROM THE DENTAL ANOMALIES PRESENTED IN THIS CASE REPORT

The presented problem
• Mastication and deglutition difficulties
• Occlusal malfunction
• Pronunciation and phonetic difficulties (especially in maxillary teeth to tongue tip articulators)
• Esthetical impairment in rest, smiling, and speaking
• Edentulous and aged appearance
• Thin alveolar ridge morphology prevents implantation

Table 4. LIST OF THE MANAGEMENT CONSIDERATION OPTIONS FOR THE PRESENTED CASE

Management considerations

- Application of anterior resin restorations: Small crown size and enlarged spaces between the anterior teeth create large leverage forces on the restoration during oral functioning, thus risking longevity.
- Provision of temporary/fixed prostheses: The crown-root ratio of the teeth, the large spaces between them, and the periodontal breakdown prevent the fabrication of this kind of prosthesis.
- Orthodontic treatment (fixed or removable appliance): Limited due to the malformed shape of the crowns and short roots. Root resorption and loss of teeth are risks during orthodontic movement.
- Early dental implantation: Limited due to incomplete craniofacial growth, which may result in recurrence of implantation and rehabilitation.
- Early alveolar ridge augmentation: This is an irreversible procedure and, therefore, uncommon in children as a temporary treatment before the final setting of gingival and alveolar architecture definitions. Management can be difficult with such extensive and recurrent procedures.
- Provision of overdentures: These enable improved occlusal, mastication deglutition, and phonetic functions and may result in proper esthetic solution and improved facial appearance and self-esteem. It may, however, involve adaptation difficulties and decrease self-esteem; therefore, it is often rejected by young patients.

prevents the use of orthopedic appliances to modify or to reduce the severity of the developing skeletal abnormalities during the primary dentition or in the mixed dentition. The impaired periodontal apparatus, the short roots and the abnormal-shaped clinical crowns, in the case presented, preclude the use of any kind of removable or fixed orthodontic appliance, since it might directly cause biologic damage resulting in the loss of teeth. Therefore, orthodontic interventions such as a skeletal treatment approach and/or a dental technique for a combined rehabilitation protocol were not feasible in this case.

Dentofacial features may be the first recognizable symptoms of ARS. Ocular complications can be prevented with early intervention; therefore, it is important for dentists to be aware of this autosomal dominant disorder and its pluripotent expressions. Early diagnosis and an interdisciplinary approach is necessary to provide the best short- and long-term treatment plans as well as treatment and follow-up for individuals with the syndrome. The treatment protocol should take into account improvement of the patients' quality of life and emotional state, while still preserving high biological standards. It may be preferable to postpone dental intervention in children who manifest extremely severe dental malformation until the postpubertal growth period.

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