

Case report

A rare clinical presentation of Axenfeld-Rieger syndrome: case report

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ABSTRACT

INTRODUCTION: Axenfeld-Rieger syndrome (ARS) is a rare autosomal dominant disorder. It is characterized mainly by anterior segment abnormalities of the eye, and also comprises non-ocular defects including dental, craniofacial and systemic abnormalities. The purpose of this case report was to present clinic and radiographic findings and treatment approach in a patient with ARS.

CASE REPORT: A 21-year-old woman referred to our clinic with complaints of chewing difficulties, esthetic and speech problems. The medical anamnesis revealed several ocular disorders including glaucoma, cataract and strabismus, and the patient had been using eye-glasses since she was six-months-old. The dental history revealed no tooth extraction. In the extraoral examination, hypertelorism, malar hypoplasia, broad nasal bridge, short philtrum and mandibular retrognathia were observed. Intraoral examination disclosed the presence of an anterior open-bite, an Angle Class II malocclusion and four primary and seventeen permanent teeth. Presence of root anomalies (dilaceration, taurodontism, short roots), caries and a partially-erupted mandibular third molar were observed in radiographic examination. Cephalometric measurements suggested the presence of a variety of craniofacial abnormalities and hypoplasia in the maxilla and the mandible. A multidisciplinary operative approach comprising surgical, endodontic, restorative and prosthetic means were implemented for the oral rehabilitation of the patient.

CONCLUSION: The case reported here was a rare presentation of ARS with unique craniofacial features including mandibular hypoplasia and Angle Class II malocclusion. The oral rehabilitation of these patients necessitates a multidisciplinary clinical work.

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INTRODUCTION

Axenfeld-Rieger syndrome (ARS) is a rare autosomal dominant disorder. It is mainly characterized by anterior segment abnormalities of the eye, and comprises developmental defects involving both ocular and non-ocular structures.¹ ARS contains several conditions with overlapping phenotypes including Rieger anomaly, Axenfeld anomaly and Rieger syndrome.^{1,2} The Rieger anomaly and the Axenfeld anomaly are both disorders of embryological development of the anterior chamber of the eye alone. These are defined as anterior chamber cleavage syndromes.³ Rieger syndrome consists of ocular defects (developmental aberrations of the anterior ocular segment) and non-ocular defects (dental, craniofacial and systemic abnormalities).^{4,5} Because differentiation of the aforementioned disorders is clinically difficult, Shields *et al.*³ proposed the collective term ARS for all variations within this spectrum.

The incidence of ARS is estimated to be 1:200.000 in general population.^{6,7} No gender or racial predilection is indicated.⁸ Inheritance is autosomal dominant in 70% of cases, with 30% sporadic.⁷ The pathogenesis of the syndrome is thought to originate as an ectodermal tissue defect caused by developmental disorders of neural crest cells. Differentiation and migration of neural crest cells are responsible for the formation of normal ocular and craniofacial structures, cardiac valves, the pituitary gland, and the umbilical ring.⁸⁻¹⁰ They are also important in the induction of the enamel organ from the oral epithelium.⁸ Derangement or arrested development of neural crest cells in the anterior chamber of the eye, facial bones, teeth, periumbilical skin, and cardiovascular system is considered the etiological basis for this disorder.^{7,8,10,11}

The purpose of this paper was to present clinic and radiographic findings, and also treatment approaches in a patient with ARS.

CASE REPORT

A 21-year-old woman presented to our clinic with complaints of teeth deficiency in the anterior region of the jaws, difficulty during eating, and esthetic and speech problems. She was the third child of non-consanguineous parents. The patient was mentally normal. Medical history revealed several ocular disorders including glaucoma, cataract and strabismus. There were no similar ocular disorders in parents and siblings. She had undergone bilateral cataract surgery during early childhood and strabismus surgery a year ago. Also, she had undergone an operation for nasal septum deviation two years ago. The patient had been using eye-glasses since she was 6-months-old and was also using some eye drops for glaucoma. She reported a complaint of subtle pain in the right mandible on occasion. The dental history revealed no tooth extraction.

Extraoral examination revealed hypertelorism [increased distance between the orbits (eyes)], malar hypoplasia, broad nasal bridge, short philtrum and mandibular retrognathia (Figures 1 and 2; written informed consent was obtained from the patient to use the photographs). Intraorally, an anterior open-bite and Angle Class II malocclusion was detected. Four primary teeth (73,74,83,84) and 17 permanent teeth (11,12,14,16-18,21,22,26,27,36-38,45-48) were observed and no other abnormality was detected regarding soft tissues (Figure 3). Totally, 15 permanent teeth were missing. There was an approximal caries in tooth number 45, amalgam restorations in teeth 36 and 46, and a peg-shaped lateral incisor (tooth number 22). Panoramic radiograph showed severe hypodontia, dilacerations for 37 and 47, taurodontism for 26 and 37, short roots for 36, partial eruption for 38, and periapical radiolucency for 46 (Figure 4).

Cephalometric measurements were carried out to detect craniofacial abnormalities (Table 1). The cephalo-



Figure 1. Frontal facial appearance of the patient

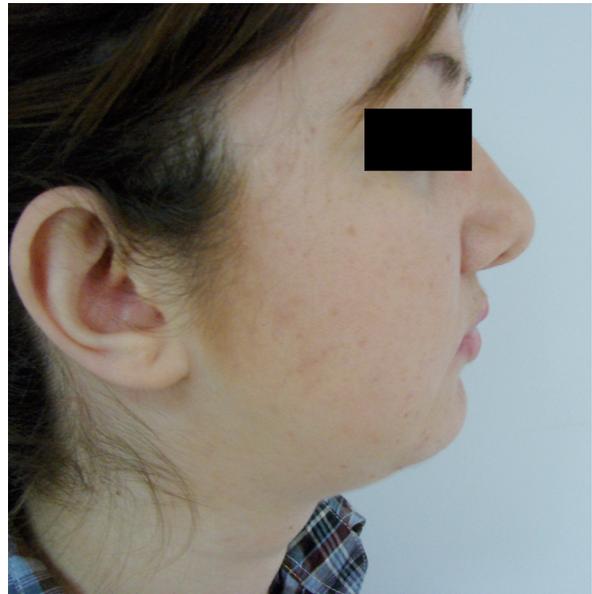


Figure 2. Pre-treatment lateral view of the patient



Figure 3. Intraoral photograph of anterior open-bite and mandibular primary teeth

metric results showed that the patient's anterior (S-N) and posterior (S-Ba) cranial base lengths were below the standards of normal values. In vertical plane, the mandible showed clockwise rotation, so the mandibular plane angle and the gonial angle increased. In addition, the lower face height increased, the ramus length and the posterior face height decreased. The increased anterior face height and the decreased posterior face height concluded as a hyperdivergent case. In sagittal plane, increased ANB angle and Witts appraisal pointed to skeletal Class II malocclusion. The patient had retrognathic maxilla due to reduced SNA angle. Decreased Co-A length demonstrated hypoplastic maxilla. Furthermore, the patient had retrognathic mandible according to the SNB angle. Mandibular length reduced because of hypoplastic mandible. Cephalometrically, the upper



Figure 4. Pre-treatment panoramic radiograph showing the dental anomalies and the pathologies

lip length was less than normative values; this feature indicated to short philtrum. Also, the upper lip was 2 mm retruded from Steiner's S-line and the lower lip protruded 1 mm from this line. Cephalometric measurements of the sella turcica showed that only the depth of the sella turcica increased; the other dimensions were within normal limits.

An ophthalmologist was consulted for the ocular findings. The ocular consultation revealed glaucoma,

microcornea, hypertelorism, corioretinal coloboma, iridocorneal adhesion and visual loss. No other abnormality was found in cardiovascular and internal medicine consultations. Based on ocular, dental and craniofacial findings, the patient was diagnosed as ARS.

Treatment procedures were carried out with multidisciplinary approaches. Orthodontic consultation indicated the requirement of an orthognathic surgery to rehabilitate the skeletal relationship and malocclusion. However, patient declined the surgery; therefore prosthetic treatment was planned. All primary teeth (73,74,83,84) and tooth number 38 were extracted. The teeth number 11-14, 21-24, 31-34 and 41-44 were restored with metal-ceramic crowns and bridges (Figure 5). The crown height for the upper and lower incisors were increased to reduce the anterior open-bite. Restorative and endodontic treatments were performed in teeth number 45 and 46 (Figure 6). Thus, patient's esthetic and functional needs were met (Figure 7).

DISCUSSION

ARS is a very rare condition and there exists little information about ARS in dental literature. Therefore, detailed presentation of the dental and the craniofacial

Table 1. Cephalometric parameters of the patient

| Variables | S (normative values) | M (measurements) | ΔS (difference) |
|----------------------------------|----------------------|------------------|-----------------|
| S-N | 76,9±3,9 | 70 mm | -6,9 mm |
| S-Ba | 45,3±3,1 | 39 mm | -6,3 mm |
| N-S-Ar (Saddle angle) | 123±5° | 116° | -7° |
| Ar-Go-Me (Gonial angle) | 130±7° | 143° | +13° |
| SN/GoGn (Mandibular plane angle) | 32±6° | 44° | +12° |
| N-ANS (Upper face height) | 55,7±2,1 mm | 50 mm | -5,7 mm |
| ANS-Me (Lower face height) | 67,2±4,2 mm | 68 mm | +0,8 mm |
| Herzberg Holic Ratio | 45/55 | + 6,9 mm | +6,9 mm |
| S-Go (Posterior face height) | 79,1±4,3 mm | 67 mm | -12,1 mm |
| Jarabak Ratio | 61±2 | 56,7 | -4,3 |
| SNA | 81,8±3,7° | 78° | -3,8° |
| CoA (Maxillary length) | 93,6±3,2 mm | 83 mm | -10,6 mm |
| SNB | 79,2±2,3° | 72° | -7,2° |
| Ar-Go (Ramus length) | 49,6±3,9 mm | 41 mm | -8,6 mm |
| CoGn (Mandibular length) | 121,6±4,5 mm | 103 mm | -18,6 mm |
| ANB | 2±2° | 6° | +4° |
| Witts | 0±2 mm | 4 mm | +4 mm |
| Upper lip- S line | 0 mm | -2 mm | -2 mm |
| Lower lip- S line | 0 mm | +1 mm | +1 mm |
| Upper lip length | 21,0±1,9 | 17 mm | -4 mm |
| Sella turcica length | 8,4±1,6 | 9 mm | - |
| Sella turcica depth | 7,2±1,2 | 9 mm | +1,8 mm |
| Sella turcica diameter | 11,7±1,1 | 11,2 mm | - |



Figure 5. Post-treatment intraoral photograph

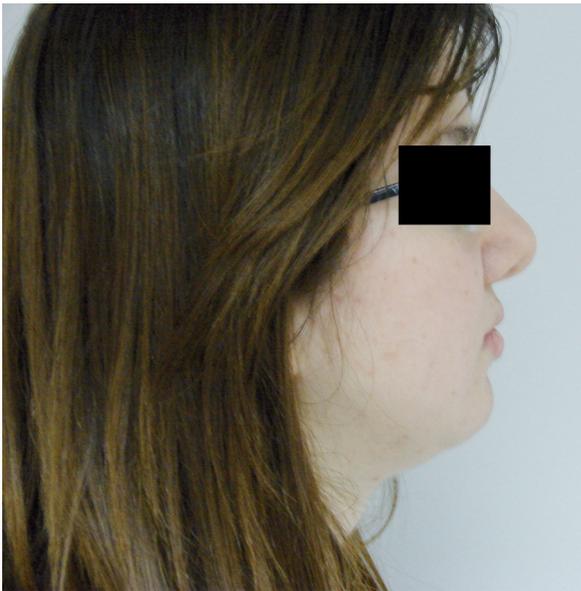


Figure 6. Post-treatment lateral view of the patient

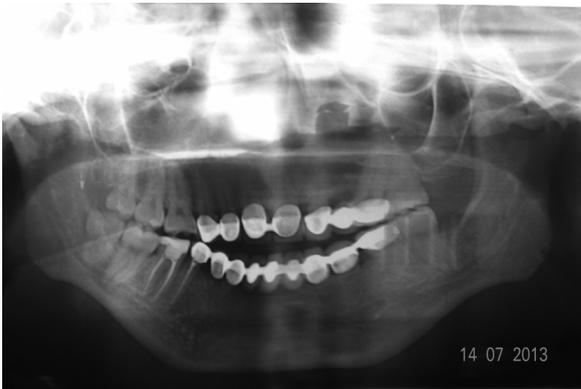


Figure 7. Post-treatment panoramic radiograph

anomalies in this disease is necessary to increase awareness of dentists. The clinical features of ARS can be roughly divided into ocular and non-ocular changes and disease severity shows variation.¹² ARS is genetically heterogeneous and mutations in different genes lead to similar clinical conditions. It has been associated with mutations of two known genes: PITX2 at 4q25 and FOXC1 at 6p25.¹³⁻¹⁵ Although systemic findings are suggestive of a PITX2 mutation, FOXC1 mutations cannot be excluded from patients with systemic symptoms.¹² There is no obvious correlation between the localization of the mutations in the genes and the severity of the phenotype.¹²

A wide variety of ocular manifestations are associated with ARS.^{6,10} The ocular defects of ARS include iris hypoplasia, iridocorneal adhesion, corectopia, posterior embryotoxon, pupil abnormalities, blue sclera, conjunctival xerosis, and other less frequent features such as cataracts, retinal detachment and microcornea.¹⁶⁻¹⁸ Glaucoma and visual loss develops in 50-60% of cases during early childhood or early adulthood.¹⁹ In the present case, glaucoma, microcornea, hypertelorism, corioretinal coloboma, iridocorneal adhesion and visual loss were observed in ocular consultation and the medical history of the patient revealed cataract and strabismus surgery.

Non-ocular defects comprise dental, craniofacial and systemic abnormalities. Systemic changes are occasional findings of ARS and these include cardiovascular, renal and auricular malformations, speech defects, goiter and abnormalities of periumbilical skin, skeleton and skin and/or hair.^{7,8,12,18,20} No systemic involvement was evident in this case. Craniofacial abnormalities consist of midface hypoplasia (due to maxillary hypoplasia), short philtrum, relative mandibular prognathism, skeletal deep-bite, broad nasal bridge, hypertelorism, telecanthus, enlarged sella turcica, protrusive lower lip or recessive upper lip and prominent forehead.^{7,18,20-22} Meyer-Marcotty *et al.*²³ reported that sella turcica anomalies in association with craniofacial and dental aberrations, such as maxillary retrognathia, skeletal Angle Class III relationship, and hypoplasia of teeth, might be important indicators for ARS caused by PITX2 mutation. In the present case, craniofacial abnormalities were hypertelorism, (also cited priorly in the text as an ocular anomaly) broad nasal bridge, short philtrum, retrognathic and hypoplastic maxilla, retrognathic and hypoplastic mandible, skeletal Angle Class II malocclusion and increased lower face height. Also, the depth of sella turcica was found to be increased. In the literature, reported cases of ARS often had skeletal Angle Class III malocclusion, relative mandibular prognathism and mid-face and/or maxillary hypoplasia.^{6,7,23,24} Mandibular hypoplasia and Angle Class II malocclusion are rare

findings for ARS. Although, mandibular hypoplasia was reported previously, Angle Class II malocclusion was not reported in the literature for this syndrome.⁷ In this case, skeletal Angle Class II malocclusion may be associated with concurrent maxillary and mandibular hypoplasia.

Several other oral and dental manifestations have been reported in ARS. These patients may exhibit hypodontia, microdontia, taurodontism, enamel hypoplasia, peg-shaped teeth, hyperplastic maxillary labial frenum and cleft palate.^{7,17,19,25} Central incisors, lateral incisors and second premolars are frequently microdont or missing.^{7,26} In the case presented here, severe hypodontia, with the absence of canines, central and lateral incisors and premolars, a peg-shaped lateral incisor and root abnormalities were observed.

Early diagnosis of ARS and detailed ocular investigations are essential in preventing visual impairment in these patients. Dental and craniofacial features are primary presentations of this syndrome.^{7,24,27} Ophthalmologists, pediatricians and dentists must be aware of the findings and complications of the ARS as multidisciplinary approach can provide satisfactory outcomes for these patients. Dental rehabilitation plays an important role in improving the esthetics and function. In order to follow the facial growth and dental development, and to coordinate appropriate timing for the dental treatment, communication between clinicians such as orthodontist and prosthodontist is necessary. Craniofacial abnormalities can be rehabilitated with orthognathic surgery, and dental implants are frequently the most suitable treatment option for the missing teeth. However, in the present case, alternatively, prosthodontic rehabilitation was carried out to provide esthetics and function.

CONCLUSION

The case discussed here is a rare presentation of ARS, differing from most of the other cases with the findings of mandibular hypoplasia and Angle Class II malocclusion. A multidisciplinary operative approach, including surgical, endodontic, restorative and prosthetic means, was followed for the oral rehabilitation of the patient presented here.

Conflict of interest disclosure: The authors declare no conflict of interest related to this study.

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Nadir görülen Axenfeld-Rieger sendromu: olgu bildirimini

ÖZET

TANITIM: Axenfeld-Rieger sendromu (ARS), otozomal dominant geçişli, nadir görülen bir hastalıktır. Esas olarak gözün ön bölgesini etkileyen anomalilerle karakterizedir, aynı zamanda dental, sistemik ve kafa-yüz anomalilerini kapsayan göz dışında defektler de izlenmektedir. Bu olgu bildiriminin amacı, ARS'li bir hastadaki klinik, radyografik bulguları ve aynı zamanda tedavi yaklaşımlarını sunmaktır.

OLGU BİLDİRİMİ: Yirmibir yaşında kadın hasta estetik problemler, yemek yeme ve konuşma sırasında meydana gelen güçlük şikayetleriyle kliniğimize başvurdu. Medikal anamnezinde hastanın glokom, katarakt ve strabismus gibi bazı göz hastalıkları olduğu ve altı aylıktan itibaren gözlük kullanıldığı öğrenildi. Dental anamnezinde hiç diş çekimi yaptırmadığı anlaşıldı. Ekstraoral muayenede hipertelorizm,

malar hipoplazi, geniş burun köprüsü, kısa filtrum ve mandibular retrognati izlendi. İntraoral muayenede ise ön açık kapanış, Angle Sınıf II maloklüzyon, dört adet süt dişi ve onyededi adet daimi diş mevcuttu. Radyografik incelemede bazı kök anomalileri (dilaserasyon, taurodontizm, kısa kökler) çürük ve yarı sürmüş mandibuler üçüncü molar diş izlendi. Sefalometrik ölçümler hastada çeşitli kafa-yüz anomalileri ile maksilla ve mandibulada hipoplazisi olduğunu gösterdi. Hastaya cerrahi, endodontik, restoratif ve protetik tedaviyi kapsayan multidisipliner tedavi uygulandı.

SONUÇ: Burada bildirilen hasta, mandibula hipoplazisi ve iskeletsel Angle Sınıf II maloklüzyonu içeren farklı yüz özellikleri nedeniyle nadir görülen bir ARS olgusudur. Bu hastaların ağız rehabilitasyonu multidisipliner bir klinik yaklaşım gerektirmektedir.

ANAHTAR KELİMELER: Dişlerin kusurlu kapanması; maksiller hipoplazi; mandibular hipoplazi