Case Report

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ORAL MANIFESTATIONS- AN EARLY DIAGNOSIS FOR AXENFELD RIEGER SYNDROME

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ABSTRACT

Axenfeld Rieger syndrome (ARS) has been recognized for more than hundred years with its rare incidence of 1: 200000 live births. A 10 year old girl and 13 year old boy, siblings, reported to Department of Pedodontics and Preventive Dentistry with chief complaint of missing and irregularly placed teeth. The detailed examination and investigations led to the diagnosis of Axenfeld Rieger syndrome. Early diagnosis of the syndrome from its dental and craniofacial features can be conducted which can prevent further associated malocclusion and ocular complications. This case report gives a detailed description of dental and craniofacial examination that helps in the early diagnosis of this syndrome.

KEYWORDS: Axenfeld Rieger Syndrome; midface hypoplasia; craniofacial Anomalies

INTRODUCTION

Axenfeld-Rieger syndrome (ARS) is a rare autosomal dominant condition characterized by a spectrum of ocular, craniofacial, dental and periumbilical abnormalities.[1] The entity was first described by Karl Axenfeld in 1920.[2] Rieger reported similar cases in 1935.[3] The incidence of Axenfeld Rieger syndrome in general population is 1:200000.[1] No definitive facts exist on gender or racial prevalence. Inheritance is autosomal dominant in 70% of the cases; and sporadic in 30%.[1] Recent advances in molecular genetics have identified two major genes PITX2 and FOXC1; demonstrating a wide spectrum of mutations which aids in the molecular diagnosis of the disease although evidence exists to implicate other loci in this condition.[4] In 1920, Axenfeld described a patient with a white line that he called a *ringlinie* in the peripheral cornea, 1 mm from the limbus. This *ringlinie* had adherent strands of iris that traversed the iridocorneal angle. He called the condition "embryotoxon cornea posterius".[2] Since then many cases have been reported with major involvement of the eye, craniofacial, dental and somatic anomalies. These patients present with a characteristic old appearance with skeletal growth deficiency. Systemic features like cardiovascular defects, middle ear deafness, umbilical anomalies, are diagnosed.[4] The ocular involvement is usually bilateral and is characterized by a triad i.e., hypoplasia of iris, iridocorneal adhesion and prominent anteriorly displaced Schwalbe's line.[5] Midface hypoplasia, a broad flat nasal root, telecanthus, maxillary and occasionally mandibular hypoplasia, short philtrum, receding upper lip and larger everted lower lip are typical facial characteristics although variably expressed.[5] The dental characteristics are microdontia, hypodontia, oligodontia and a thickened frenulum. Other abnormalities are enamel hypoplasia, delayed eruption, taurodontism and shortened roots. The crowns of the anterior mandibular primary teeth can be conical or barrel shaped. These patients usually suffer from hypoplastic growth of the maxilla, leading to prognathic profile and class III malocclusion.[4,5] Dental symptoms are one of the earlier and primary manifestations of this syndrome. This case report aims at describing the orofacial clinical features of ARS syndrome, emphasizing on the importance of early diagnosis.

CASE REPORT

A 13 year old boy and 10 year old girl, siblings,

Fig. 1: Siblings showing ARS: Short stature, retarded physical growth

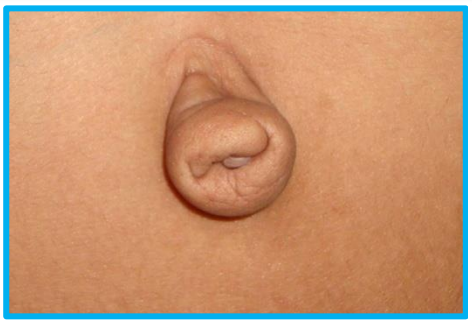

Fig. 2: Protuberant umbilicus

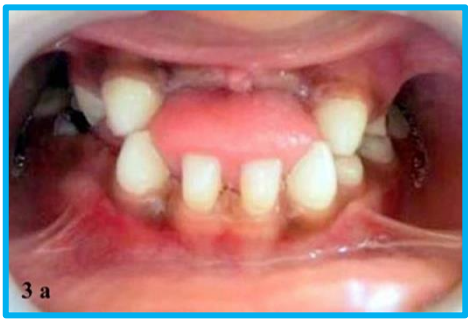

Fig. 3a: An anterior intraoral view of the girl showing hypodontia

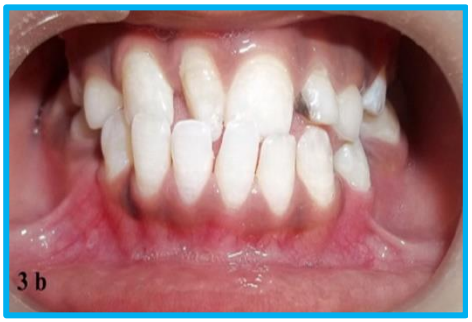

Fig. 3b: An anterior intraoral view of the boy showing mesiodens and hypodontia

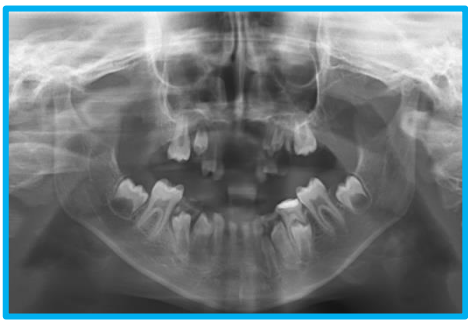

Fig. 4: Orthopantomogram

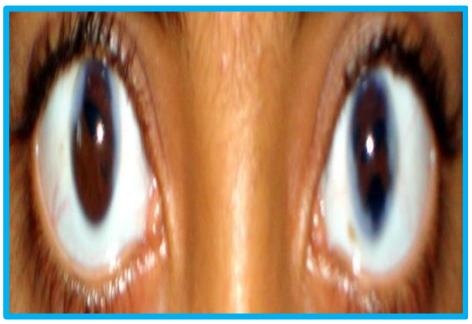

Fig. 5: Eyes of the boy showing typical findings of ARS; Opacification of the cornea

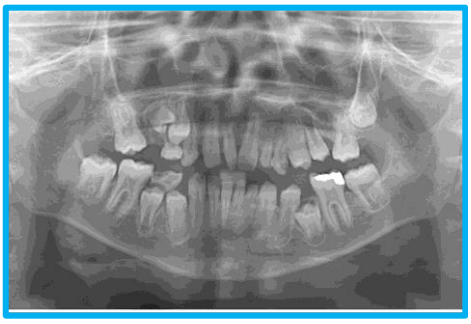

Fig. 4: Orthopantomogram

born from non-consanguineous parents had reported to the Department of Pedodontics and Preventive Dentistry with the chief complaint of missing multiple teeth and irregularly placed teeth. This had been the children's first dental visit. The patients were examined clinically and a thorough family was recorded which did not reveal any significant findings. Both presented with short stature as per age, mild retarded physical development and growth, mild exophthalmoses and abnormal pupils (Fig. 1). A detailed medical history revealed both the patients complaining of blurred vision, increased intraocular pressure and undergoing treatment for the same. The patients were referred for a detailed medical examination which revealed protuberant umbilicus, (Fig. 2) thin upper lip relative to lower lip, broad nasal root and retruded maxilla in both the patients; leading to a diagnosis of Axenfeld Rieger Syndrome for the siblings. No cardiac abnormalities and any other systemic abnormalities were found. In case of the girl, she had slight facial asymmetry. In relation to the child's dental history, her mother confirmed that no primary or permanent teeth had ever erupted in

Table: 1 Angular and linear cephalometric parameters for both patients

Parameters	Normative value	Measurement of [boy]	Measurement of [girl]
SNA Angle	82 (deg)	79 (deg)	75 (deg)
SNB Angle	80 (deg)	81 (deg)	80 (deg)
ANB Angle	02 (deg)	-2 (deg)	-5 (deg)
Frankfort Mandibular Plane Angle (FMA)	25 (deg)	19 (deg)	16 (deg)
Y Axis angle	59.4 (deg)	55 (deg)	50 (deg)
Anterior Cranial Base (S-N)	72.71mm	60mm	62mm
Maxillary Base Length (PNS-A)	47.78mm	40mm	31mm
Mandibular Base Length (Go-Pog)	75.78mm	64mm	62mm
Upper Anterior Facial Height (N-ANS)	53.16mm	40mm	37mm
Lower Anterior Facial Height (ANS-Me)	70.34mm	60mm	57mm
Total Anterior Facial Height (N-Me)	118.48mm	100mm	94mm
Total Posterior Facial Height (S-Go)	89.56mm	66mm	60mm

the premaxillary region. On clinical examination, she presented with severe hypodontia that affected the maxillary and mandibular incisor region. Retained mandibular central incisors were present. The maxillary and mandibular primary molars were grossly destructed. Three of the permanent first molars had erupted. A soft tissue examination revealed a fleshy maxillary midline frenal attachment. Despite having no maxillary anterior incisors at any time, the level of eruption of the primary mandibular central incisors was normal (Fig. 3a). An orthopantomogram revealed severe hypodontia with the absence of maxillary primary and permanent incisors, maxillary permanent canines, and maxillary permanent second molars on right and left sides, mandibular primary lateral incisors, mandibular permanent incisors and canines (Fig. 4). In case of the boy, he had no gross facial asymmetry. Ophthalamic examination revealed opacification of the cornea, iridocorneal adhesions as well as polycoria (Fig. 5). Audiometry test detected sensironeurohearing defect, however the patient did not show any hearing defect clinically. Dental examination showed retained maxillary primary left lateral incisor, maxillary primary canines. All the first permanent molars were erupted with narrow occlusal table. The maxillary left first premolar, mandibular primary right second molar and left permanent first molar were found carious. Also supernumerary tooth (mesiodens) was present showing concomitant hypohyperdontia (Fig. 3b). An orthopantomogram revealed hypodontia with the absence of maxillary permanent lateral incisors, maxillary permanent canines, maxillary permanent right second molar and all third molars. An erupted conical shaped mesiodens was present with incomplete root formation. Most of the teeth had shortened roots (Fig. 6). Orthodontic evaluation of both the patients revealed Class III malocclusion arising from the relative prognathism of the mandible in relation to the hypoplastic premaxilla that lead to anterior crossbite. Cephalometric analysis showed Class III tendency with ANB angle of -2 in the boy and -5 in the girl and retrognathic maxilla with SNA angle of 79 deg in the boy and 75 deg in the girl (Table 1). Diagnosis of Axenfeld Reiger's Syndrome was confirmed for both the patients. Considering the children's and their parent's marked functional and esthetic needs a treatment plan was immediately designed. To ensure the preservation of the existing dentition, preventive dental measures were carried out including oral hygiene instructions, application of pit and fissure sealants to primary and permanent molars and restoration of the carious teeth. To manage the immediate esthetic needs of the girl, a removable partial denture was planned. However, long term management will require a multidisciplinary approach involving orthodontic and advanced restorative care. The boy was referred for orthodontic consultation and immediate fixed appliance therapy was planned for the correction of Class III malocclusion and other abnormalities followed by prosthetic care. The patients are also

reviewed by medical and educational specialists regularly.

DISCUSSION

Axenfeld-Rieger Syndrome is a very rare condition. Thus, the number of patients studied is limited. In addition, this disease shows morphologic variability in terms of frequency and expression of associated anomalies.[4] When only the eyes are affected, the condition has been termed Rieger Anomaly or Axenfeld Anomaly.[6] Extraocular findings, especially dental and craniofacial anomalies, help define the condition. Therefore, a detailed presentation of dental and craniofacial anomalies in patients with ARS is necessary. The syndrome has autosomal inheritance with almost complete penetrance and variable expressivity. According to the literature, this type of inheritance accounts for only 70% of the cases, while 30% arise de novo.[1] In the present cases, there could be either sporadic occurrence of the mutation causing the appearance of the syndrome; or incomplete penetrance that could be considered the probable explanation for clinically normal parents and other family members. Alternatively, the children's condition could have been due to single gene mutation. The pathogenesis of ARS is uncertain.[1] Neural crest cells give rise to most of the mesenchyme related to forebrain and pituitary gland, bones, cartilage of the upper face and dental papillae. Thus, abnormalities of neural crest development, resorption and differentiation during third trimester of pregnancy can be taken into account as the etiological basis of ARS.[7] In this report, both the patients presented with ocular features, failure of the periumbilical skin to involute, which is consistent with findings of Jorsensen *et al*.[8] Little information exists on ARS in dental literature; despite the fact that hypodontia and maxillary hypoplasia are some of the principal features of this syndrome.[1] These patients presented with the classical dental presentation of ARS, hypodontia and midface hypoplasia. Drum *et al*.,[9] concluded that maxillary deficiency existed because of the alveolar hypoplasia resulting from missing teeth. Midface hypoplasia is likely to become more marked as growth continues. In addition, supernumerary tooth (mesiodens) was observed in case of the boy, which is till date reported only once in literature.[10] This association of hypodontia and hyperdontia in the same jaw and quadrant could be considered as transposition (Segura and Jimenez-Rubio, 1998), which is the positional interchange of two adjacent teeth or the development and eruption of a tooth in a position normally occupied by a non-adjacent tooth (Peck and Peck, 1995). The dental practitioner plays a very important role in the management of ARS. Preservation of all dental tissues in optimum health is essential. The patients here have significant dental abnormalities, which will require extensive long-term dento-facial treatment involving a multidisciplinary approach of orthodontics, advanced restorative care with implantology. The severity of ARS varies, and thus treatment is patient dependent. 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. In the present cases, the immediate dental priority was to maintain good dental health along with satisfying patient's functional and esthetic needs. Patients with ARS require regular ophthalmic appointments to monitor intraocular pressure throughout their lives so that glaucoma can be diagnosed.[1] The patients here were undergoing treatment for the same and were regularly reviewed. Thus a regular medical and dental follow up; along with genetic counseling to parents is of utmost importance for the overall development of the child.

CONCLUSION

In clinical practice, it is necessary to differentiate hypodontia from that which is syndrome-related. The knowledge of early diagnosis of the dental, cranio-facial and systemic presentation of ARS to the dental practitioner could prevent the devastating ocular effects of infantile glaucoma. It is important to monitor facial growth and dental development, and to coordinate appropriate timing for dental treatment. The presence of multiple clinical features requires a multidisciplinary management between dentists, pediatricians and geneticists to provide the best treatment and follow up.

CONFLICT OF INTEREST & SOURCE OF FUNDING

The author declares that there is no source of

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