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The Rieger Syndrome: a Case Report with Unusual Dental Findings

SUMMARY

Background/Aim: *The Rieger syndrome is a rare, autosomal dominant and phenotypically variable disorder, characterized by abnormalities of the anterior chamber of the eye, coincident with missing or misshapen teeth.* ***Case report:*** *This report features a case of the Rieger syndrome associated with bilateral cleft lip and palate and a severe open bite, findings not usually reported in association with this condition.* ***Conclusions:*** *The findings described in the present case of Rieger syndrome are unusual and expand the spectrum of manifestations of the condition.*

Key words: Rieger Syndrome, Hypodontia, Iridogoniodysgenesis, Cleft Lip And Palate

Smaragda Kavadia[1], Konstantinos Antoniades[2], Eleni Markovitsi[1], Eleftherios G. Kaklamanos[3]

[1] Department of Orthodontics, School of Dentistry, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessalonki, Greece
[2] Department of Oral and Maxillofacial Surgery, School of Dentistry, Faculty of Health Sciences, Aristotle University of Thessaloniki, Thessalonki, Greece
[3] Hamdan Bin Mohammed College of Dental Medicine, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates

CASE REPORT (CR)
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Introduction

Rieger syndrome is characterized by hypodontia and primary mesodermal dysgenesis of the anterior chamber of the eye[1-4]. The ocular component is usually bilateral and manifests partial or complete hypoplasia of the anterior stromal leaf of the iris, anterior iris synechiae and iridogoniodysgenesis[5-7]. The main oral feature is oligodontia, particularly in the maxillary anterior segment, of the deciduous and/or the permanent dentitions, which varies form a single missing tooth to multiple missing teeth[8-9]. Other dental defects reported are microdontia, barrel or conical crown form, taurodontism, shortened roots and eruption disturbances[5,10,11].

Craniofacial abnormalities represent another constant feature of the syndrome. Deficient maxillary growth and oligodontia result in a mildly prognathic profile, a shortened philtrum, a relatively protruding upper lip and loss of vertical height. Subsequently, the middle part of the face is flattened and broad, flat nasal bridge may be observed[6,10,12]. The cranial base also exhibits defects; an enlargement of the sella turcica has been reported in patients affected by the syndrome, although pituitarity gland function may or may not be disturbed[8,9,13-16]. Dental and craniofacial defects help to distinguish the Rieger syndrome from other anterior chamber malformations (Axenfeld's syndrome, Peters' anomaly) or other syndromes in which goniodysgenesis is a component (goniodysgenesis associated with juvenile glaucoma, anal atresia and goniodysgenesis, arachnodactyly and goniodysgenesis, deafness and goniodysgenesis, myopathy and goniodysgenesis, and short stature and goniodysgenesis)[10,17]. Apart from the aforementioned anomalies, a great variety of other developmental abnormalities have been observed[1-4,6,9]. The only consistent among them is failure of the periumbilical skin to involute[6,8,9,11,17,18,19].

The purpose of this report is to present a case of the Rieger syndrome associated with bilateral cleft lip and palate and severe open bite, features not usually reported in association with this condition.

Case report

A 16-year-old boy was referred to the Department of Oral and Maxillofacial Surgery for closure of alveolar

fistulae due to bilateral cleft lip and palate, evaluation and management of the concomitant dentoskeletal disharmony. He was the only child of unrelated parents with no significant family history. He was born after a 32-week gestation with normal vaginal delivery and his birth weight was 2150 gr. The mother reported having problems during pregnancy and received medication. However, it could not be determined which specific drugs she had taken. At birth the patient was found to have bilateral cleft lip and palate, cryptorchidism, obstruction of left lacrimal duct and congenital glaucoma at the left eye. He also suffered from jaundice of the newborn. Repair of the lip deformity was performed at the age of 6 months and closure of the cleft palate was done at the age of 3 years. At approximately the same period the patient was operated for dilation of the left lacrimal duct and at the age of 5 years for the cryptorchidism.

At clinical examination the proband exhibited microcephaly, pronounced frontal suture and low set ears (Figure 1). The nose was pear-shaped, and hair curly and blonde. In addition, unilateral left micropthalmia with concomitant ptosis, as well as an iris defect were observed. Opthalmologic examination disclosed, in the left eye, microcornea, dyscoria (Figure 2), central opacity and iridiogoniodysgenesis. His visual acuity was 10/10 in the right eye with glasses -6.5-1.0/35º and 1/20 in the left eye with glasses -6.0-0.5/10º. In the abdomen failure of the periumbilical skin to involute was noted.

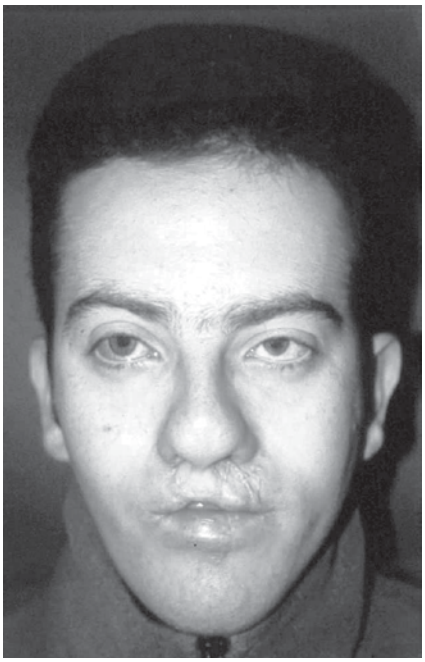

Figure 1. Full facial view revealing a wide nasal bridge, unilateral microphthalmia, with concomitant ptosis and relative mandibular prognathism.

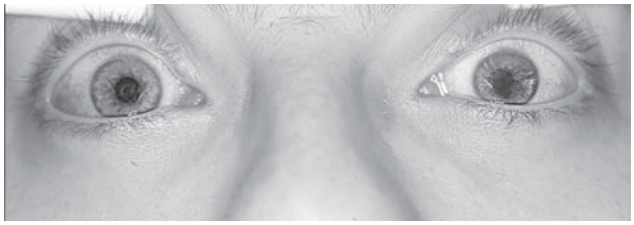

Figure 2. Vertical slit pupil in the left eye, microcornea and dyscoria.

Oral investigation revealed bilateral oronasal fistulae, hypodontia (22, 32, 41, 42, 43 and 47 were missing), rotated and malpositioned teeth, eruption delay of 12 and pronounced microdontia and hypoplasia of the existing incisors. On the orthopantomogram, the roots appeared to be spiked (Figure 3). A severe anterior open bite was evident (Figure 4) (only the last molar teeth on each side were in occlusion), as well as a skeletal Class III relationship.

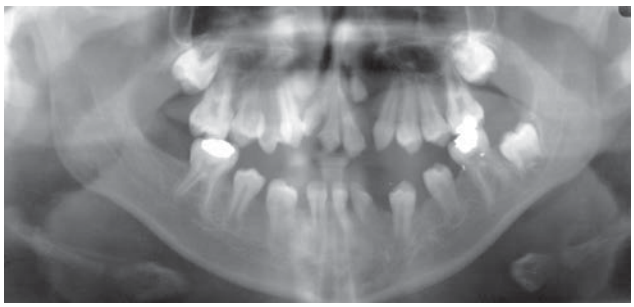

Figure 3. Orthopantomogram radiograph displaying severe hypodontia, rotated and malpositioned teeth.

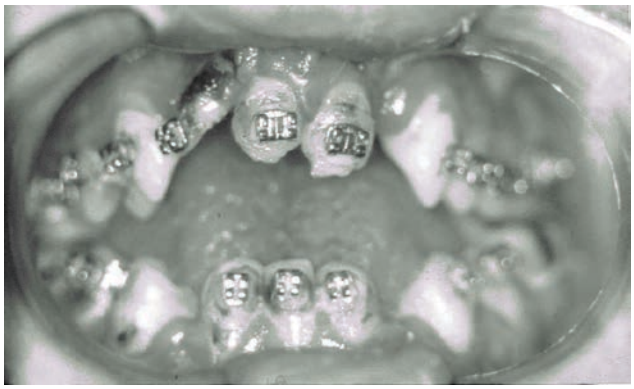

Figure 4. Microdontia and hypoplasia of the existing incisors and a severe anterior open bite, as well as a skeletal class III relationship.

Based on orofacial characteristics, and particularly the dental and ocular findings, the diagnosis of the Rieger syndrome was set. After orthodontic preparation, repair of the alveolar clefts and closure of the orofacial fistulae was made.

Discussion

The Rieger syndrome is a rare, autosomal dominant, phenotypically heterogeneous disorder, characterized by structural defects of the anterior chamber of the eye (iridiogoniodysgenesis) coincident with missing or misshapen teeth[1-5]. The essential ocular findings include hypoplasia of the iris stroma with adhesions to the posterior embryotoxon[6,12,20,21]. Iridocorneal adhesions obstructing the outflow of the aqueous humor cause increased intraocular pressure, resulting in glaucoma, in more than 50% of the patients. As this condition is resistant to therapy, it can lead to optic nerve damage and progressive visual loss[6,7]. Additional ocular manifestations may be microcornea, pupillary anomaly, cataract, glaucoma, corneal opacity, ectopia lentis, aniridia, optic atrophy and ptosis[12,20].

As malformations of the anterior chamber of the eye have been reported in various conditions exhibiting overlapping features, it has been proposed that Rieger anomaly, Axenfeld anomaly and Rieger syndrome represent a single condition termed Axenfeld-Rieger syndrome[22]. On the other hand, other researchers have postulated that Rieger anomaly and Axenfeld anomaly are genetically different from the typical Rieger syndrome[12,23].

Genetic linkage analysis, in spite of opposing evidence[23-25], had previously mapped the locus of the responsible gene to the 4q25-4q26 regions and suggested a tight connection to epidermal growth factor (EGF) supporting its role as a candidate gene[26-27]. In 1996, the EGF was excluded as a candidate gene[28] and a gene causing Rieger syndrome was identified[29]. The researchers observed that in mouse embryos Rieg mRNA, the murine homologue of RIEG, was localized in the periocular mesenchyme, maxillary and mandibular epithelia and umbilicus, all consistent with Rieger syndrome abnormalities[29]. The RIEG gene was also shown to be omologous to the mouse homeobox-containing gene Otlx2 and expressed in the epithelium of the developing teeth. Another study showed that the expression of Otlx2 in branchial arch epithelium starts very early already before tooth initiation is seen morphologically[30]. The RIEG/Otlx2 gene appears to be involved in epithelial-mesenchymal interactions[31]. Later, Saadi and co-workers[32] described the first dominant negative missense mutation, in the PITX2 bicoid-like homeobox gene, causing Rieger syndrome and suggested that such a finding supports a model that may partially explain the phenotypic variation within Rieger syndrome.

Other evidence has suggested genetic heterogeneity of Rieger syndrome. Legius and coworkers[23] failed to find linkage to 4q25 in one pedigree. Deletion of 13q14 was described in 2 cases[33-35]. Phillips and coworkers identified a second locus on 13q14 by linkage analysis of a large four-generation pedigree[35].

The aforementioned data is consistent with the current theory of a developmental arrest in the third trimester of tissues derived from neural crest epithelium[6,20,36]. Differentiation and migration of neural crest cells are responsible for the development of normal orofacial and ocular structures, hence a developmental disturbance of the neural crest may account for the phenotypic characteristics of the Rieger syndrome.

In the case presented, orofacial findings (hypodontia and microdontia), as well as ocular manifestations (congentital glaucoma, iridiogoniodysgenesis, dyscoria) and failure of involution of the periumbilical skin are part of the Rieger syndrome. In addition, the patient exhibits bilateral cleft lip and palate, severe anterior open bite, obstruction of the lacrimal duct and cryptorchidism, features not usually reported in association with this syndrome. From the literature, only one case of cleft palate is reported[12] and another case of obstructed lacrimal duct[37].

Conclusions

Consequently, the Rieger syndrome is a rare condition of particular dental interest as ocular anomalies are coincident with unusual dental and maxillofacial manifestations. Thus, the dentist may have significant contribution in diagnosing and referring such cases so as to minimize ocular complications. Moreover, such cases should always be accompanied by investigation of the relatives of the patient and referral to geneticists for proper and timely genetic counseling.

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Correspondence:

Eleftherios G. Kaklamanos, DDS, Cert, MSc, MA, PhD
Assistant Professor
Hamdan Bin Mohammed College of Dental Medicine (HBMCDM)
Mohammed Bin Rashid University of Medicine and Health Sciences (MBRU) Building 34, Dubai Healthcare City
Dubai, United Arab Emirates
e-mail: eleftherios.kaklamanos@mbru.ac.ae; kaklamanos@yahoo.com