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Review Article

Unlocking dental solutions: strategies for axenfeld rieger syndrome care

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ABSTRACT

Axenfeld-Rieger syndrome encompasses systemic abnormalities such as dental, cardiac, craniofacial, and abdominal-wall defects. As a rare autosomal dominant condition, it presents as a heterogeneous group of features. Managing this syndrome requires a multidisciplinary approach involving dentists, orthodontists, oral surgeons, and geneticists due to the complexity of dental anomalies and the rarity of the condition. Early diagnosis is pivotal not only for addressing dentofacial appearance and function but also for detecting systemic abnormalities that could impact vision. Collaboration among specialists, including ophthalmologists and maxillofacial surgeons, is vital for comprehensive care. Diagnosis is typically based on clinical and ophthalmologic examinations, supplemented by genetic analysis if the syndrome is suspected. Treatment plans are customized by specialized teams to meet the distinct needs of each patient.

1. Introduction

Axenfeld-Rieger Syndrome, a rare genetic disorder, manifests with developmental abnormalities affecting the eyes, teeth, and facial structures. It primarily follows an autosomal dominant inheritance pattern, prevalent in approximately 70% of cases, with an estimated occurrence rate of 1:50,000 to 1:100,000 in newborns.[1] The syndrome is named after Theodor Axenfeld, a German ophthalmologist who described it in 1920. Rieger also described it in 1934.[2] While it's racial or gender prevalence remains uncertain, it is attributed to defects in ectodermal tissue stemming from neural crest disorders. Neural crest cells' differentiation and migration play a crucial role in forming normal ocular and craniofacial structures.[3] It exhibits almost complete penetrance and variable expression, often associated with mutations in the PITX2 and FOXC1 genes, disrupting ocular and craniofacial development.[4] Ocular manifestations include anterior segment dysgenesis, while dental anomalies commonly involve hypodontia, microdontia, enamel hypoplasia, and malocclusion.Mutations in the PITX2 gene, encoding a key transcription factor initiating tooth development, are linked to this syndrome.[5] Patients with this syndrome may experience various dental abnormalities, significantly impacting oral health and quality of life. Malocclusion, including crowding and misalignment, can exacerbate functional and aesthetic concerns. The rarity of the

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syndrome can hinder alveolar process development, leading to disproportionate jaw growth.[6] Genetic counselling is crucial for affected individuals and their families to understand the disorder's inheritance pattern and assess recurrence risks in future generations. Counselling aids informed decision-making regarding family planning and implementing preventive measures to mitigate Axenfeld Rieger Syndrome impact on oral and overall health.[7] It can be classified into three types based on clinical features. Type 1 is mainly characterized by dental abnormalities and mid-face hypoplasia, Type 2 includes auditory and cardiac anomalies, while Type 3 features ocular manifestations with lesser facial and dental abnormalities.[8] Recent advancements in molecular genetics have identified three genetic loci associated with ARS on chromosomes 4q25, 6p25, and 13q14. The PITX2 and FKHL7 genes located on chromosomes 4q25 and 6p25, respectively, have been acknowledged as significant contributors to the syndrome.[9]

2. Discussion

Axenfeld-Rieger syndrome represents a spectrum of disorders characterized by bilateral developmental ocular anomalies, often accompanied by glaucoma. Its inheritance pattern is frequent, but there is no gender predilection, and it is associated with mutations in genes such as PITX2 and FOXC1. In Axenfeld anomaly, one may observe a posterior embryotoxon with attached strands of peripheral iris tissue.[10]

2.1. Ocular features

Rieger anomaly presents with posterior embryotoxon, iris stromal hypoplasia, ectropion uveae, corectopia, full-thickness iris defects, and a range of gonioscopic abnormalities, which can vary from Axenfeld anomaly to broad leaves of iris stroma adherent to the cornea. It presents with systemic manifestations encompassing various ocular abnormalities, including malformations of the eye's anterior segment, iris anomalies such as hypoplasia, corectopia, polycoria, pupillary dyscoria, blepharitis, iridocorneal adhesions, posterior embryotoxon, and increased intraocular pressure leading to glaucoma. Glaucoma is a common complication, occurring in approximately 50% of cases, typically manifesting in childhood or early adulthood.[11]

Additionally, redundant peri-umbilical skin, genitourinary anomalies, kidney abnormalities, hypospadias, cardiovascular outflow tract defects, brain maldevelopment, auditory problems like sensorineural hearing loss, and skeletal anomalies such as flattening of femoral and humeral epiphyses, shortening of the femoral neck, club feet, and other positional joint abnormalities are observed. Patients may also present with short stature, mental retardation and finger malformations.[12]

2.2. Cardiovascular features

Congenital heart defects, particularly ventricular septal defects, are common and may be the clinical manifestations that lead to diagnosis. Neurological abnormalities include white matter abnormalities like leuko encephalopathy and Dandy-Walker malformation, as well as ventriculomegaly/hydrocephalus. Vascular abnormalities may predispose individuals to stroke, both ischemic and hemorrhagic.[13]

2.3. Craniofacial & dental features

This syndrome includes a notable forehead, hypertelorism (wide-set eyes), telecanthus, underdeveloped mid-face (maxillary hypoplasia), flat nasal bridge, and jaw abnormalities.Additionally, patients may exhibit a short philtrum, thin upper lip, and prominent supraorbital ridges. The underdevelopment of the mid-face involves both skeletal and dental factors, often associated with insufficient development of the alveolar bone due to missing teeth (hypodontia, oligodontia) & small teeth (microdonta).[14]

The wide array of abnormalities underscores the complexity of this syndrome and emphasizes the need for a thorough evaluation and management plan involving a team of specialists. Patients typically present with normal height and weight, indicating normal hormonal levels. However, lateral cephalograms often reveal an enlarged sella turcica with decreased anterior and posterior facial height. Skeletal Class III malocclusion, hyperdivergence, and vertical mandibular growth pattern are commonly observed. Some cases may exhibit radiographic signs of ankylosis.[15] Short stature and delayed bone age may be attributed to growth hormone deficiency, as suggested by Shields et al., who noted an "empty" sella turcica in these patients, potentially indicating such deficiency.[16]

Empty sella results from the herniation of the arachnoid membrane through the diaphragma sella, leading to sella enlargement. While empty sella has been observed in these patients, it does not consistently indicate pituitary dysfunction. During the examination, it's essential to measure corneal thickness. Regular and lifelong monitoring of intraocular pressure and performing gonioscopy are critical.[17] Patients face an increased risk of developing glaucoma, making gonioscopy crucial for detecting any angle abnormalities or peripheral anterior adhesions. Disc optical coherence tomography and perimetry aid in evaluating and monitoring optic nerve changes due to glaucoma and associated visual field defects. Electrophysiological tests, including visual evoked potentials and full-field and pattern electroretinogram, are crucial for assessing vision, especially in non-verbal patients.[18,19] Dental anomalies such as unerupted teeth, oligodontia, and microdontia, which are common

in Axenfeld-Rieger syndrome, can be detected on orthopantomogram. Neurological and neurovascular abnormalities linked with Axenfeld-Rieger syndrome can be identified through brain CT or MRI scans.[20] Collaboration between dental and maxillofacial specialists is necessary to address dental and craniofacial anomalies. Referral to a pediatrician for further investigations, including abdominal ultrasound to differentiate redundant periumbilical skin from umbilical hernia, echocardiogram to assess cardiovascular outflow tract defects, and audiology MRI brain imaging for brain abnormalities reported in Axenfeld-Rieger syndrome, is recommended.[21] The list of potential diagnoses includes iridocorneal endothelial syndrome, Peter's anomaly, aniridia, congenital ectropion uveae, ectropia lentis et papillae, and oculodentodigital dysplasia.[22]

2.4. Management

Managing dental abnormalities in Axenfeld-Rieger syndrome requires a personalized approach, considering each patient's individual needs and preferences. The prevalence of infraocclusion falls within the range of 1 to 9%. Orthodontic intervention is vital for rectifying malocclusion and enhancing dental alignment. The objective of treatment is to correct or prevent the deterioration of the skeletal relationship between the upper and lower jaws and to alleviate crowding in the upper arch. The therapeutic approach for malocclusion typically includes employing the Rapid Palatal Expander along with fixed orthodontic treatment. Typically, a profile analysis of patients with this syndrome reveals a more prominent upper third of the face compared to the middle and lower thirds.[23] Additionally, characteristics such as a slightly flattened infraorbital area, prominent cheekbones, and a straight nasolabial angle, superior retrochelia, resting labial seal, inferior normochelia, and a slightly flattened mentolabial angle are observed. Lateral cephalic radiography often shows skeletal Class III due to mild maxillary macrognathism, along with an increased lower facial third. Intraorally, traction of the upper labial frenulum and a lack of vertical development of the superior alveolar process are noted.[24] Asymmetric oval arches and Class III dental malocclusion are common findings. Based on these observations, the orthodontist recommends a treatment protocol involving a facial mask with a Hyrax and a postero inferior bite plane. The Hyrax device is utilized to address cross-sectional discrepancy between the arches, considering the Class III relationship and dental agenesis. Additionally, it helps in disarticulating the circum-pubertal sutures to facilitate the protraction of the maxilla. The postero inferior bite plane is recommended to control verticality. The facial mask aids in protracting the maxilla and guiding mandibular growth. Maxillary and mandibular hypoplasia often necessitates distraction osteogenesis and orthognathic surgery for correction. This treatment approach not only improves dental alignment but also increases space in the dental arch to address dental crowding. Additionally, it can resolve issues like cross-bite and open bite through strategic bracket positioning.[25] Treating hypodontia requires a collaborative effort among specialists to ensure optimal outcomes for the patient and their family. In certain cases, over dentures may be recommended to enhance aesthetics and provide superior lip support compared to standard removable partial dentures.

Prosthetic options, such as removable or implant-supported dentures, offer functional and aesthetic restoration for individuals with multiple congenitally missing teeth.[26] Furthermore, resin-bonded bridges can serve as a fixed alternative, particularly in the mandibular arch, as they are often more manageable for pediatric patients than removable options. The appropriate management of altered pulp pathology may involve pulp therapy and restoration with pre-formed metal crowns. Preserving primary molar teeth in cases of hypodontia is crucial as they help maintain bone integrity for potential future transplantation or implant therapy.[27] Surgical intervention may be necessary in some cases to address complex dental issues in Axenfeld-Rieger syndrome patients. Surgical placement of dental implants can offer stable support for prosthetic teeth, improving chewing efficiency and restoring facial aesthetics. However, the presence of underlying craniofacial abnormalities may present challenges during implant placement, necessitating meticulous preoperative planning and coordination with oral and maxillofacial surgeons.[28] Early orthodontic and restorative interventions are strongly recommended for optimal long-term treatment planning. Pediatric dentists play a crucial role in early diagnosis, as many symptoms involve dental and craniofacial anomalies.[29] Addressing abnormal jaw growth during the mixed dentition period with functional or myofunctional appliances can mitigate occlusal issues severity in adolescence. Timely diagnosis is essential not only for dental health but also for preventing ocular complications like glaucoma.[30] The treatment strategy prioritizes preserving oral health and aesthetics. Therefore, close monitoring of growth and development is vital for timely preventive interventions in patients with Axenfeld-Rieger syndrome. Various non-pharmacological behavior management techniques, such as tell-show-do and positive reinforcement, are employed during preventive care visits to foster a positive dental attitude and long-term commitment to oral health maintenance.[31]

Local anesthesia, a pharmacological behavior management technique, was administered to facilitate the planned comprehensive dental treatment, typically through the infiltration of 2% lignocaine with 1:80,000 epinephrine. Rubber dam isolation may be employed during procedures for better isolation and moisture control.[32] Additionally,

preventive measures, including regular dental check-ups, fluoride applications, and oral hygiene education, are crucial for maintaining oral health and reducing the risk of complications. Encouraging scrupulous oral hygiene habits involves advising patients to brush their teeth twice daily with fluoridated toothpaste containing at least 1,350 ppm fluoride, focusing on brushing before bedtime and in the morning.[33] Dietary guidance may include consuming sweets only at mealtimes as a dessert rather than between meals, limiting sugar intake to no more than four times per day. Fluoride varnish application, typically containing 2.26% fluoride, is also recommended for additional protection against dental caries. Advancements in molecular genetics and regenerative medicine offer promising avenues for novel therapeutic approaches in managing Axenfeld-Rieger syndrome.[34] Targeted gene therapies aimed at correcting underlying genetic mutations hold potential for preventing or ameliorating dental and ocular abnormalities associated with this condition. Moreover, tissue engineering techniques may facilitate the regeneration of damaged dental tissues, providing more sustainable treatment options for affected individuals.[19]

3. Conclusion

Axenfeld-Rieger Syndrome poses intricate dental obstacles, necessitating a holistic and interdisciplinary strategy for successful handling. Through a thorough grasp of the diverse dental presentations, application of suitable diagnostic methods, and utilization of customized treatment approaches, oral health practitioners can maximize outcomes and improve the well-being of individuals affected by this condition. Ongoing research and cooperation among various fields are crucial for furthering our comprehension of this uncommon genetic condition and devising novel treatments to enhance patient welfare.

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5. Conflicts of Interest

There are no conflicts of interest.

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