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General and Oral Aspects in Apert Syndrome: Report of a Case.

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Abstract

Background: The present paper describes the general and oral manifestations in a 32-year-old man previously diagnosed with Apert syndrome.

Clinical examination revealed features of acrocephalosyndactyly. The patient was found to have a flattened occiput with frontal prominence, abnormal contour of head (brachycephaly), shallow and downward slanting orbits with bilateral proptosis, hypertelorism, retruded midface, and prognathic mandible.Dental anormalies were present in a patient. Intraoral evaluation revealed normal mouth opening with anterior severe skeletal open bite and Byzantine-arch palate, maxillary alveolar ridges with crowding of maxillary and mandibular teeth, poor hygiene with heavy dental calculus and periodontal pseudopocket, dental caries, severe anterior open bite and crossbite, macroglosia and smooth tongue.

The high prevalence of dental anomalies and ectopic eruption may suggest a possible etiologic relationship with the Apert syndrome.

Keywords

Acrocephalosyndactylia, Craniosynostosis, Tooth abnormalities, Mouth abnormalities, Apert Syndrome

Introduction

Apert syndrome is a rare congenital type I acrocephalosyndanctyly syndrome, characterized by craniosynostosis (premature fusion of cranial sutures), severe syndactyly of the hands and feet, symphalangism and dysmorphic facial features [1]. Premature fusion of cranial sutures restricts growing in the region of fused sutures and leads to craniofacial abnormalities, including calvarial shape. Various extracranial manifestations are present. The prevalence of this disease is 15.5 per million live births and accounts for 4.5% of all cases of craniosynostosis [2]. Craniosynsostosis syndromes exhibit considerable phenotypic and genetic heterogeneity. Sagittal synostosis is common form of isolated craniosynostosis. The sutures involved, the shape of the skull and associated malformations give a clue to the specific diagnosis. Apert syndrome is one of the most serious of these syndromes. Most syndromic craniosynostosis require multidisciplinary Management [3].

Apert syndrome (acrocephalosyndactylia) is a developmental malformation characterized by craniosynostosis, a cone-shaped calvarium (acrocephaly), hypertelorism, midface hypoplasia, pseudo cleft-palate, a parrot beak shaped nose, pharyngeal attenuation, and syndactyly of the hands and feet [3,4]. The inheritance of Apert's syndrome is autosomal dominant with the locus of a mutation of FGFR2 on chromosome 10q (10q25- 26). Suture progenitor cells with fibroblast growth factor receptors (FGFR2) that have undergone a mutation cannot transduce signals from extracellular fibroblast growth factors (FGFs). Therefore, these cells do not receive the signal to produce the necessary fibrous material essential for a normal calvarial suture [5].

Apert syndrome was first reported by Wheaton in 1894 and French pediatrician Eugene Apert published a series of nine cases in 1906 [3,6]. Most cases are sporadic, with an incidence of 1:160 000; however due to high infant mortality, the incidence in the general population is lower. Advanced male parental age has been consistently noted [7]. During the course of the disease, growth and mental retardation can be observed [4,7].

In Apert cases, the spheno-occipital and spheno-ethmoidal synchondroses and the fronto-ethmoidal suture fuse early, resulting in a severely shortened posterior cranial base and a relatively short anterior cranial base with a resultant hypoplastic midface. Consistent with the observation of midface hypoplasia, the maxilla also exhibits

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a transverse deficiency [5]. The most readily observed malocclusions are a severe maxillary anterior open bite and a severely crowded and retrusive maxillary arch due to the constricted secondary palate [5].

The maxillary alveolar arch is V-shaped [8]. Due to the narrower maxillary arch, bilateral or unilateral posterior crossbite can be observed [9-11]. Cleft of the soft palate is observed in 30% of the cases [12,13]. In mouse models exist data that reveal significantly abnormal cell patterns of proliferation, differentiation and apoptosis local to the inter-premaxillary suture, causing a lack of fusion and maldevelopment of the anterior palate in *Fgfr2+/S252W* mice [9,14-18].

The nose is short and broad with a bulbous tip and nasolabial angle is diminished [19]. The midface hypoplasia contributes to retruded middle third of the face, resulting in relative mandibular prognathism [15,16,19]. The lips frequently assume a trapezoid configuration because the upper lip is lifted in the midline [20,21].

Impactions, severe crowding of developing teeth within the alveolus, delayed eruption, thick gingiva, and sometimes supernumerary teeth or congenitally missing teeth are the hall marks of maxillary dental development in Apert patients [22]. The nasopharyngeal and oropharyngeal attenuation cause Apert's individuals to become mouth breathers with a resultant anterior open bite [22].

The familial pattern, equal number of affected males and females, and increased paternal age in sporadic cases strongly suggest autosomal dominant inheritance [23,24].

Treatment involves multidisciplinary teamwork including craniofacial surgeon, neurosurgeon, neurologist, ENT (ear, nose, and throat), audiologist, pediatrician, speech pathologist, oral surgeon, psychologist, periodontist and an orthodontist [25,26]. Surgical care involves early release of the coronal suture and frontoorbital advancement with reshaping to allow proper brain growth and reduce dysmorphic and unwanted skull growth changes [25]. Craniotomy is often performed during the 1st year of life to treat the craniosynostosis. Frontofacial advancement and midface advancement can be performed later to correct the proptosis and midface hypoplasia. Coordinated orthodontic therapy is often necessary to bring unerupted teeth into place and improve occlusion [27,28].

Case Report

A 32- year- old male presented with the complaints of malaligned teeth, heavy dental calculus, difficulty in chewing food, and craniofacial and limbs deformity.

He was the first child born to nonconsanguineous parents. Pregnancy and labor were uneventful and there was no history of taking any drugs during the entire term of pregnancy. His mother was 45 years old and his father was 52 years old. The family history contained no report of similar cases.

At birth, the child had craniosynostosis, brachycephaly, and syndactyly of hands and feet.

Clinical examination revelaed features of acrocephalosyndactyly. The patient was found to have a flattened occiput with frontal prominence, abnormal contour of head (brachycephaly), shallow and downward slanting orbits with bilateral proptosis, hypertelorism, retruded midface, and prognathic mandible (Figure 1a and Figure 1b).

Intraoral examination showed normal mouth opening with anterior severe skeletal open bite and a high arched (V-shaped) palatal vault or Byzantine-arch palate associated with lateral swellings of the palatine processes, one on either side of the middle miming a pseudocleft in the midline (Figure 2). Maxillary alveolar ridges were thick with crowding of maxillary and mandibular teeth. Heavy dental calculus, congestion and swelling of the gingiva and periodontal pseudopockets associated with anterior and posterior teeth. Dental caries on anterior and posterior teeth were present. Severe maxillary and mandibular dental crowding, with the rotation of maxillary central incisors and the palatal position of second bicuspids and lateral incisors were observed. At the occlusal examination, severe anterior open bite and crossbite were observed, only the first and second molars being involved in centric occlusion and macroglosia and smooth tongue were observed too (Figure 2, Figure 3 and Figure 4).

On investigation, panoramic view radiograph showed deformity

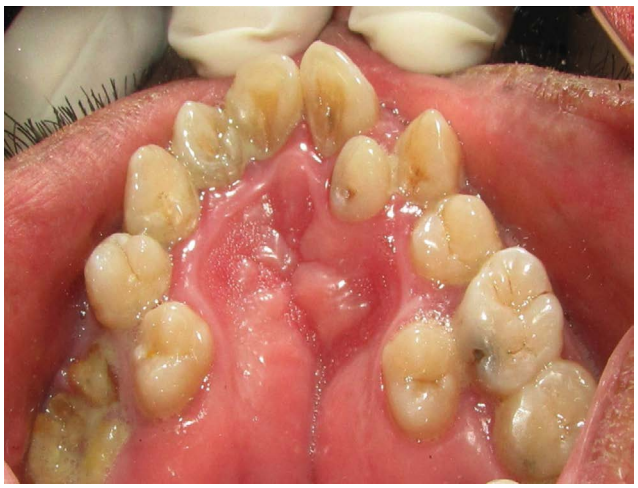
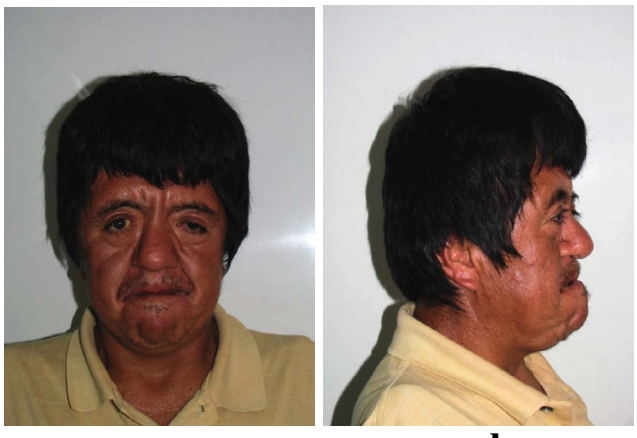


Figure 2: Intraoral maxillary view showing Byzantine-arch palate, pseudocleft in the midline, crowding of teeth, caries and root fragment.



Figures 1: (a) Extraoral front view of patient showing hypertelorism, parrot beak nose, depressed nasal bridge, and downward alanting outer canthus of eyes. (b) Maxillary hypoplasia results in psudoprognatism.

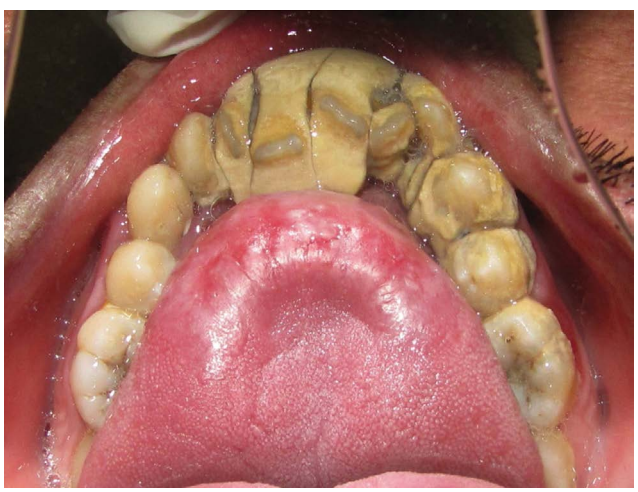
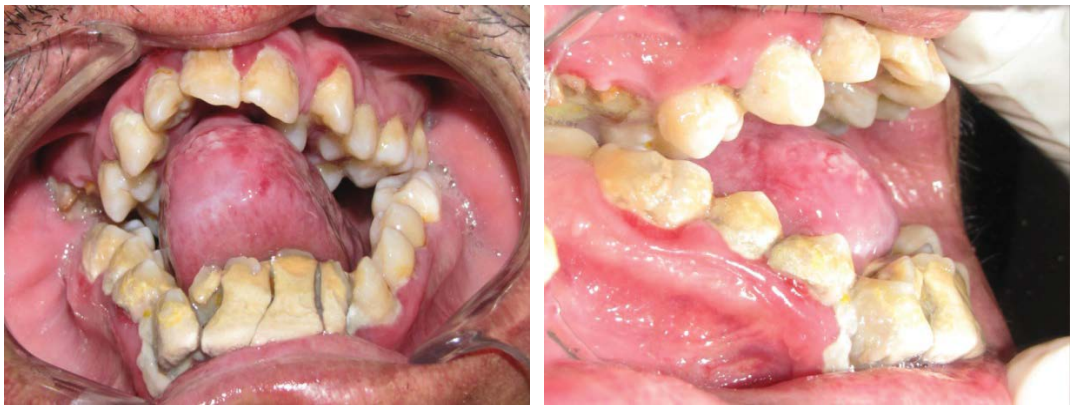


Figure 3: Intraoral maxillary view showing crowding of teeth, macroglosia and heavy dental calculus.



Figures 4 (a and b): Intraoral front and lateral views showing swelling of gingiva, crowding of teeth, macroglosia heavy dental calculus. severe anterior open bite and crossbite.

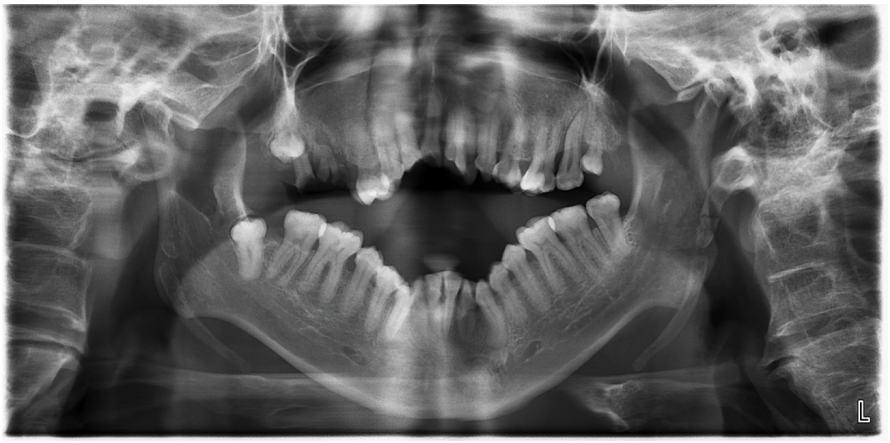


Figure 5: Panoramic view showing non- erupted third molar, open skeletal bite and root frgaments.

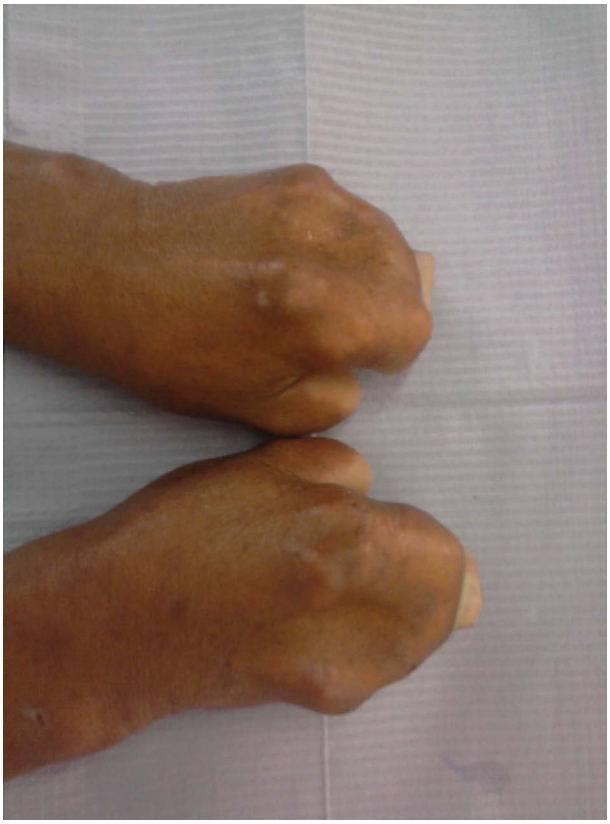


Figure 6: Photographs showing syndactyly in hands.

of jaws with severe skeletal open bite, partially erupted lower right wisdom molar , and presence and root fragments of first and second upper right molars (Figure 5).

He had symmetrical syndactyly with complete fusion of all digits of hands (except thumb) and feet (Figure 6). The systemic examination revealed that patient has some ophthalmologic, ear, and central nervous system abnormalities and mild degree of mental deficiency have been observed.

Discussion

This patient demonstrated the clinical triad that characterizes Apert syndrome: Brachycephalic skull, midface hypoplasia and syndactyly of hands and feet [12].

Craniosynostosys refers to a premature fusion of the calvarial sutures. Historically, the clinical description of craniosynostosys date back to Hippocrates and Galen, but first historical reference to craniosynostosys was made by Mestrius Plutarchus (46–127 AD) [29]. The identification of two pre-Columbian skulls with sagittal synostosys (dated at 6000 and 250 BC) confirms that craniosynostosys is an ancient disorders of humans [30]. Wheaton SW, in 1894, described the first two cases of Apert syndrome revealing craniofacial, skull base and limbs findings, but unfortunately he attributed the calvarial phenotype and respiratory deficiencies to con- genital syphilis and the syndactyly to fetal inflammation [31]. Twelve years later, the Dr. Eugene Charles Apert described nine cases of syndactyly associated with acrocephaly [32].

The clinical features of Apert syndrome are distinctive. The coronal suture fuses prematurely, at least three month leading, as we described earlier, to an acrocephalic (cone-shaped) head

with a flattened occiput, shortened anterior-posterior diameter, a high prominent forehead, a characteristic form of the nose and of the mouth. The midface of these patients is hypoplastic. Occular anomalies as hypertelorism, proptosis, strabismus and down slanting palpebral fissures are often present and are due to shortening of the bony orbit [33,34]. Our patient presented some of the above mentioned features [1]. Commonly associated systemic features include cardiac anomalies, visual and hearing defects [13]. This is in accordance with the present case.

A pseudocleft due to the accumulation of the proliferated lateral palatal tissue mass was recorded for our patient. In Apert syndrome cases, the swellings are usually present in infancy and increase in mass as the child growth older. The cumulative tissues can proliferate to such an extent as to lead sometimes to a mis- taken diagnosis of cleft palate. The prevalence of a real cleft palate was reported between 25 to 75% of Apert subjects [34].

Failure in the anteroposterior and downward growth of the maxilla causes the maxillary hypoplasia and a resultant contraction of nasopharyngeal airway [22].

In patients with Apert syndrome, severe skeletal Class III open bite malocclusion can be observed due to the maxillary deficiency and the inclination of the upper jaw. Therefore, it is usually necessary to add ortognathic surgery to the treatment plan. The infant is likely to suffer from oral hygiene problems during treatment [22].

The maxillary dental arch is v-shaped and there can be some compensatory growth of the alveolar base. Most probably, the alveolus thickens to accommodate the teeth that are impacted and crowded to an extreme degree in a small maxilla. The maxilla slants down posteriorly. As a result, open bite is common, if untreated, the maxilla-mandibular discrepancy and class III malocclusion worsens with age [35].

The appearance of a patient with Apert syndrome is prognathic. The "pseudoprognathic" appearance is basically due to maxillary retroposition. Impactions, severe crowding of developing teeth within the alveolus, delayed eruption, thick gingival and sometimes supernumerary teeth or congenitally missing teeth are the hallmarks of the maxillary dental development in the Apert patient. There is severe arch length deficiency to accommodate the tooth material. There is a mean dental developmental delay of 0.96 years, with a range of 0.5 to 2.9 years. It is postulated that mutation in the FGFR2 gene has an effect on the mesenchymal development, which has an effect on tooth morphogenesis [35].

For the patient with Apert syndrome, oral hygiene is as important as it is difficult. Hand deformities make it difficult to brush the teeth. The new generation of electric tooth brushes and fluoride mouth rinses may make the task easier. Professional care including frequent dental examination, oral hygiene prophylaxis, fluoride treat- ments, and dental sealants are very important [6].

The fact that the therapeutic management of patients with Apert syndrome should be multidisciplinary is a logical consequence of the previously exposed facts. These patients generally require lifelong management by a multidisciplinary team of health care specialists [1].

Conclusion

The rarity of the AS, the typical craniofacial and dental features, remains a major medical condition with considerable morbidity. In the treatment plan, the odontological aspect plays an important role for the management of preventable oral diseases such as dental caries and periodontal disease.

The information and the motivation of the parents regarding the necessity of the treatment and the extensive use of home prevention methods are essential.This case report attempts to throw some light on this rare syndrome.

Competing Interests

The authors declare that they do not have any competing or financial interests.

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