CASE REPORT

Oral manifestations in Apert syndrome: case presentation and a brief review of the literature

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Abstract

Background: The present paper describes the oral manifestations in a 16-year-old boy previously diagnosed with Apert syndrome. *Patient and Methods*: The extraoral and intraoral pathological findings were recorded. The following intraoral parameters were recorded: plaque and calculus deposits, dental caries, periodontal status, malpositions, and occlusion. For the upper anterior teeth, dental shade was recorded, using a dental spectrophotometer. The corresponding diagnostics were established. A treatment plan was established and discussed with the child's parents. *Results*: The dysmorphic characters were obvious, including acrocephaly, prominent forehead, hypoplastic midface, hypertelorism, short nose. The intraoral features revealed a bifid uvula and Byzantine-arch palate associated with lateral swellings of the palatine processes, one on either side of the middle miming a pseudocleft in the midline. Heavy dental plaque, dental calculus, congestion and swelling of the gingiva and periodontal pseudopockets associated with anterior teeth were recorded. Dental caries on anterior and posterior teeth were present. Severe maxillary dental crowding associated with the rotation of central incisors and the palatal position of second bicuspids and the malposition of the mandibular anterior teeth were observed. No intrinsic discoloration of the dental structure was recorded. Severe anterior and posterior open bite and crossbite were observed. Other signs were represented by syndactyly involving partial fusion of the fingers and toes. Also, mild mental deficiency was recorded. *Conclusions*: The information and the strong motivation of the parents regarding the necessity of the treatment and the extensive use of home prevention methods are essential to control oral conditions in these patients.

***Keywords*:** acrocephalosyndactylia, craniosynostosis, malocclusion–periodontal attachment loss.

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].

Mutation of human fibroblast growth factor receptor genes have been identified as etiologic agent of some craniosynostosis syndromes, including Apert syndrome. These receptors have a high affinity for fibroblast growth factors that, when bond to their specific receptors, play a role in signaling pathways with multiple biologic effects as cranial development and growth [3].

Patient and Methods

We present the case of a 16-year-old boy from a special school, in Cluj-Napoca, Romania, in which a preventive programme was planned. The extra-oral pathological findings were recorded. The oral examination was performed under natural daylight, using a dental mirror, a dental and a periodontal probe. The following intra-oral parameters were recorded: plaque and calculus deposits, dental caries, gingival status, periodontal probing depth, malpositions and occlusion. For the upper anterior teeth, dental shade was recorded, using a dental spectrophotometer, VITA Easyshade® (VITA Zahnfabrik H. Rauter GmbH & Co. KG, Bad Sackingen, Germany), in global mode. Digital images were taken in order to sustain the clinical data. The corresponding diagnostics were established. A treatment plan was previewed and discussed with the parents. A written consensus of the parents was obtained in order to use the photos.

Results

The child was previously diagnosed as having Apert syndrome and is currently medically monitored by the Pediatric Psychiatric Department of our University. The dysmorphic characters were obvious, including acrocephaly, prominent forehead, hypoplastic midface, hyper-

telorism, and short nose associated with a wide depression of the nasal bridge, a characteristic trapezoidal mouth-shape and mouth breathing.

The intraoral features revealed a bifid uvula and Byzantine-arch palate associated with lateral swellings of the palatine processes, one on either side of the middle miming a pseudocleft in the midline. Heavy dental plaque, dental calculus, congestion and swelling of the gingiva and periodontal pseudopockets associated with anterior teeth were recorded. Dental caries on anterior and posterior teeth were present. Severe maxillary dental crowding, with the rotation of central incisors and the palatal position of second bicuspids and of a right molar and the malposition of the mandibular anterior teeth were observed. No intrinsic discoloration of the dental structure was recorded; however, the critical oral hygiene resulted in a grayish shade mainly in the cervical third; the spectrophotometric values ranged between A3–A4.

At the occlusal examination, severe anterior and posterior open bite and crossbite were observed, only the second molars being involved in centric occlusion (Figure 1).

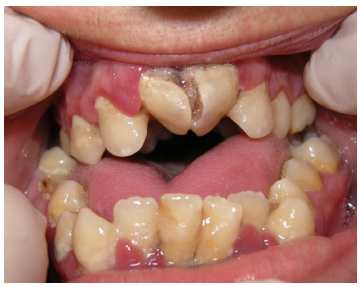

Figure 1 – ***Clinical presentation of the anterior and posterior region at baseline.***

Other symptoms were represented by syndactyly involving partial fusion of the fingers and toes. Also, mild mental deficiency was recorded.

A complex treatment plan was in view for our patient. An aggressive prophylactic approach including regular mechanical and chemical professional plaque control, with fluoride and chlorhexidine applications is essential in order to control the intense carioactivity and periodontal inflammation. The treatment of dental caries is previewed in sedation. The aim of the orthodontic treatment would be to improve lips position, occlusion and breathing [4]. For the present case, the professional plaque control including supra-gingival debridement and the treatment of the caries in anterior teeth were performed by the general dentist (Figure 2). No other therapeutic approaches are unrolling now.

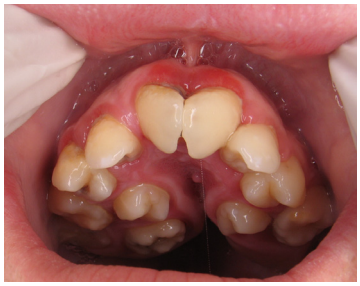

Figure 2 – ***Maxillary anterior region after dental treatment.***

Discussion

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) [5]. 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 [6]. 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 congenital syphilis and the syndactyly to fetal inflammation [7]. Twelve years later, the Dr. Eugene Charles Apert described nine cases of syndactyly associated with acrocephaly [8].

This condition is a hereditary form of craniosynostosis, that can be inherited in an autosomal dominant fashion; most mutations are new and of paternal origin, being associated with advanced paternal age. The risk of a second child being affected is 1% [9].

Most of the molecularly characterized cases of Apert syndrome result form two specific mutations of a gene located on chromosome 10q26, encoding fibroblast growth factor receptor 2 (FGFR2). The two mutations involve C-to-G transversions at adjacent codons in exon IIIa of the gene. The first mutation is C934G transversion, leading to a change of codon TCG to TGG, producing a serine-to-tryptophan substitution at amino acid 252 (S252W or Ser252Trp). The second mutation is a C937G transversion, changing codon CCT to CGT, resulting in proline-to-arginine substitution at amino acid 253 (P253R or Pro253Arg) [10]. The former (S252W) is the most common mutation, occurring in 67% of patients and has been proposed to be associated with more severe craniofacial anomalies, whereas the later (P253R) may be associated with more severe syndactyly [11]. These mutations affect the region linking the immunoglobulin-like domains II and III of FGFR2 and result to increased affinity and altered specificity of ligand binding [12]. This in turn leads to deregulation of cell migration, proliferation and differentiation and ultimately to premature osteogenesis and skeletal abnormalities that characterized the syndrome.

In the same category of major craniosynostosys syndromes associated with a mutation of the fibroblast growth factor receptor family as Apert syndrome, belong others well defined clinical entities: Crouzon syndrome, Jackson–Weiss syndrome and Pfeiffer syndrome [5].

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 [13, 14]. Our patient presented some of the above mentioned features.

Regarding the intraoral characteristics, a normal teeth form was recorded for our patient; however, some studies reported shovel-shaped incisors [1]. The maxillary lateral incisors agenesis observed in the present case is not a rare condition, since this feature was reported in 41% Apert syndrome cases [4].

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 mistaken diagnosis of cleft palate. The prevalence of a real cleft palate was reported between 25 to 75% of Apert subjects [4].

In the present case, periodontal examination revealed the presence of pseudopockets in anterior region. Due to difficulties in communication with the patient, we could not perform a radiographic examination and more precise periodontal measurements. Having in view the heavy debris, the presence of attachment loss is not excluded, but the comparison with the results of other studies is not possible. However, the reported periodontal status in individuals with different syndromic craniosynostosis was similar, the posterior region being more affected than the anterior region regarding the plaque deposits, probing depth and attachment level [15].

Mouth breathing observed in most cases with Apert syndrome is related to an alteration in facial growth. The absence of maxillary growth will lead to a reduction in size of the nasal cavity and the formation of the trapezoidal-shaped mouth, symptoms which could be improved with the orthodontic treatment.

As a common condition for Apert syndrome patients, in this clinical case, orthodontic anomalies and malocclusion were recorded, directly related to the maxillary hypoplasia. Dental crowding was so severe that the malpositioned teeth generated a parallel row with the normal erupted teeth.

Apart mental deficiency, no other systemic abnormalities were diagnosed for our patient, but general signs are usually described in Apert syndrome cases. Abnormalities of the lower respiratory tract include choanal stenosis, anomaly of the tracheal cartilage, and sometimes, in 40% of cases, some degree of air obstruction [16]. Cardiovascular, genitourinary and gastrointestinal anomalies have been also recorded [1]. Cardiovascular and genitourinary defects occur in 10% and 9.6% of patients with Apert syndrome, respectively [17]. The literature reports also skin manifestations in Apert syndrome, such as acne, hyperhydrosis, hypopigmentation and hyperkeratosis of plantar surfaces [1].

Only some part of the previewed therapeutic approaches was performed in our case, because of the difficulties in cooperation with the child and his parents.

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.

Management of children with Apert syndrome includes surgical correction of the craniosynostosys, midfacial hypoplasia and syndactyly [1]. Prenatal sonographic detection of structural abnormalities associated with Apert syndrome is usually possible, even if the differential diagnosis with other craniosynostosis syndromes may be difficult. The specialist should inform the parents that prognosis is not optimal (increased risk of mental retardations and multiple postnatal operations) so that the parents could opt for termination of pregnancy, before the stage of fetal viability [18].

Non-surgical manipulation of Apert syndrome may be a possibility in the future, for example by using selective inhibitors of the FGFR-kinase domain [19]. Also, in rate craniosynostosis model, premature suture fusion was prevented by topical application of recombinant Noggin, which production is suppressed by FGF increased signaling from craniosynostosis syndromes [20].

Conclusions

Craniosynostosys, which occurs in sporadic and hereditary forms, remains a major medical condition with considerable morbidity. In the complex treatment plan, the aggressive oral prophylactic plan plays an important role for the management of preventable oral diseases such as dental caries and periodontal disease, contributing to the wellbeing of the patients with Apert syndrome.

The information and the strong motivation of the parents regarding the necessity of the treatment and the extensive use of home prevention methods are essential.

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