



Orofacial Manifestations in Apert Syndrome: A Case Report and a Review of the Literature

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ABSTRACT

Introduction: Apert syndrome (AS) is a craniosynostosis syndrome caused by mutations in the gene coding for the fibroblast growth factor receptor 2 (FGFR2). It is a rare autosomal dominant disorder characterized by a triad of clinical manifestations: craniosynostosis, facial dysmorphisms and syndactyly of the fingers and toes. Facial and oral abnormalities are common.

Case Report: We reported a 5-year-old boy with genetically confirmed Apert syndrome. Clinical examination showed characteristic facial dysmorphism and oral manifestations. We performed a review of literature of orofacial findings in Apert syndrome. We focused on facial and oral manifestations.

Results: Ten articles were reviewed. **Facial findings** reviewed were classified into four categories: Cranial features such as: frontal prominence, Flattened occiput, brachycephaly. Ophthalmologic abnormalities: Proptosis, Exorbitism, Hypertelorism. Nasal and earing abnormalities: Depressed nasal bridge, Bulbous nose, Low set ears.. and Front and profile view: Midface hypoplasia, Concave profile, Cross bow-shaped lips. **Syndactyly** is a constant finding. **Oral findings** were classified into 3 categories: Maxilla features: high arched palatal vault, Pseudo-cleft. Malocclusion: teeth crowding, Retruded maxilla, Prognathic mandible, Anterior open bite, anterior and Posterior crossbite and other features, the most common of which are: delayed eruption and Poor oral hygiene.

Conclusion: Typical dental and skeletal findings of Apert syndrome were observed upon extraoral and intraoral examination. Early dental check-up and management of AS is very important as a preventive option.

Key Words: Apert syndrome, Acrocephalosyndactyly, Craniosynostosis, Oral manifestations, Dentofacial features, Abnormalities, Craniofacial

INTRODUCTION

Apert syndrome (AS) or acrocephalosyndactyly type 1 is a rare genetic disease that is present from birth. It is one of the most severe craniofacial synostosis, it has a triad of clinical manifestations: in addition to this craniosynostosis (early closure of the cranial sutures), there are craniofacial dysmorphisms and malformations of the fingers and toes.^{1,2}

This syndrome was first described by Baumgartner in 1842 and by Wheaton in 1894; later it was extensively reviewed by French pediatrician Eugène Apert in 1906, hence its name.³

Transmission occurs in an autosomal dominant mode, however, most cases are sporadic (neomutation) or can be associated with advanced paternal age, maternal infections, drug use during pregnancy as well as a cranial inflammatory process.⁴

With a prevalence of 1/50,000 to 1/65,000 cases, this syndrome affects both sexes equally.²

The aim of this paper is to describe and highlight the specific facial and intraoral features of Apert syndrome throughout a clinical case and a review of literature.

We performed a review of literature to define the orofacial manifestations of Apert syndrome. PubMed and Science direct were databases used, with restrictions on the publication date from 2012 to 2023. The keywords combinations were used mixed with the Boolean operator “AND”, “OR”: “Apert syndrome”, “acrocephalosyndactyly”, “craniosynostosis”, “oral manifestations”, “dentofacial features”, “abnormalities, craniofacial”.

Among the 63 included articles, only 10 have been retained in our review. We reported a clinical case of a young boy with a genetically confirmed AS.

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CASE REPORT

Youssef Dridi, 5-year-old boy, youngest of two siblings, with notion of 1st degree parental consanguinity. No other family members were affected by the same features.

The mother reported that the pregnancy was carried to term, but not followed up with gestational diabetes also not followed up. She was 35 years old at the time of delivery and the father was 42 years old.

The child presents with a delay in psychomotor development, mental retardation, language disorders and academic delay. Extraoral examination revealed that he had abnormal facies evidenced by brachycephaly, flattening of the occiput, anterior frontal bulge, bilateral proptosis with exorbitism, hypertelorism, strabism, depressed nasal bridge with a small bulbous nose and open mouth with Trapezoidal-shaped lips. The ears were wide and displaced downwards. He had a mid-facial deficiency with a concave profile [Figure 1].

This is associated with syndactyly of the hands affecting the 3rd and 4th fingers bilaterally and symmetrically, a short and broad thumb at its tip with clinodactyly, and syndactyly of the 5 toes of the feet [Figure 2].

He had undergone suturotomy surgery for relieving craniosynostosis at 6 months of age and plastic surgery for relieving syndactyly 2 years ago.

Intraorally, there was a V-shaped maxillary arch and a pseudo cleft palate. Severe maxillary and mandibular teeth crowding were noticed. The terminal plane was a mesial-step type on both sides with an anterior open-bite and unilateral posterior cross-bite, poor oral hygiene and dental caries [Figure 3 A, B, C].

Functional examination was in favor of mouth breathing with absence of lip closure, infantile deglutition with tongue thrusting.

Radiological explorations have proved that there have been abnormalities in number: missing of the second mandibular premolar and also proved overcrowded premolars germs [Figure 4].

Results of cephalometric analysis revealed a skeletal Class III jaw-base relationship due to severe maxillary deficiency [Figure 5].

RESULTS

Ten articles were reviewed. **Facial findings** reviewed were classified into four categories: Cranial features such as: frontal prominence(N=10)(83,33%), Flattened occiput(N=9)(75%), brachycephaly(N=6)(50%), acrocephaly(N=4)(33,33%) ,Ophthalmologic abnormalities: Proptosis(N=9)

(75%) , Exorbitism(N=9)(75%), Hypertelorism(N=9)(75%), Down sliding lateral palpebral fissures(N=5)(41,66%), Strabism(N=2)(16,66%), lagophthalmos(N=1)(8,33%). Nasal and earing abnormalities: Depressed nasal bridge(N=8)(66,66%), Bulbous nose(N=8)(66,66%), Small retro displaced(N=1)(8,33%), short nose(N=1)(8,33%), Low set ears(N=3)(25%), Overfolded helix(N=2)(16,66%) and Dysplasia of the auricle(N=1)(8,33%) and Front and profile view: Midface hypoplasia(N=9)(75%) ,Concave profile(N=1)(8,33%), Cross bow-shaped lips(N=4)(33,33%), Trapezoidal mouth-shape(N=4)(33,33%), open mouth(N=2)(16,66%).

Syndactyly (N=12) (100%).

Oral findings were classified into 3 categories: Maxilla features: high arched palatal vault(N=7)(58,33%), Pseudo-cleft(N=7)(58,33%), Reduced maxillary width(N=1)(8,33%), Malocclusion: maxillary crowding(N=6)(50%), mandibular crowding(N=6)(50%), Retruded maxillar(N=5)(41,66%), Anterior open bite(N=4)(33,33%), Posterior crossbite(N=4)(33,33%), Anterior crossbite(N=2)(16,66%) Prognathic mandible(N=2)(16,66%), Skeletal Class III(N=2)(16,66%), Aligned mandibular teeth(N=1)(8,33%), Angle class III (N=1)(8,33%), Deep-bite(N=1)(8,33%) and other features, the most common of which are: delayed eruption(N=3)(25%) and poor oral hygiene(N=3)(25%).

Table 1 summarizes the key characteristics of the included studies.

DISCUSSION

Our review included studies that focused on orofacial abnormalities associated with Apert syndrome. This syndrome has been shown to be the result of mutation of the FGFR2 gene, which is located on chromosome 10, involved in cell signaling during embryonic development. This leads to deregulation of cell migration, proliferation, and differentiation and ultimately to premature osteogenesis and skeletal abnormalities that characterize the syndrome.⁵

According to these literature review findings, AS patients present distinctive clinical features, with usual orofacial anomalies.

Suture fusion is not limited to the skull but may also involve facial sutures in patients with Apert syndrome.⁶ Thus, it results in a particular facies⁷ seen in all of the cases including our case, marked by a cone-shaped head due to bilateral coronal suture fusion (acrocephaly) with a shortened anteroposterior diameter, flattened occiput, with a high and broad forehead.^{8-12,14-16}

The underdevelopment of the midface caused by severe maxillary hypoplasia, contributes to the development of shallow orbits, exorbitism and down slanting palpebral fis-

tures, which are constant signs. Hypertelorism is also seen in almost all of the patients with AS.

Depressed nasal bridge, bulbous nose^{9,10,11,12,15,16} and low set ears^{9,16} were also observed upon these patients and are responsible of this particular facies.

Oral examination revealed a high arched and narrow palate seen with lateral palatal swellings that can give the appearance of pseudo cleft, seen in our case.^{8,9,10,11,14,15,16}

Teeth crowding,^{8,9,12,13,15} anterior open bite,^{8,10,13} and posterior crossbite^{9,10,12} due to the underdeveloped maxillary structures are the most common malocclusions, seen also in our patient.

This maxillary deficiency contributes also to the appearance of relative mandibular prognathism^{8,11} and a concave profile.

Mouth breathing and tongue thrusting was detected in only one case other than our case 10, which are the consequence of this maxillary constriction.⁵

Moreover, difficulty in brushing the teeth because of hand anomalies, malocclusion, and palatal pseudo cleft in addition to the lack of motivation partly due to the mental condition of the patient,⁶ makes it difficult to maintain adequate oral hygiene thus leads to high risk of caries like our patient.^{9,11}

Some oral signs such as delayed eruption^{9,6,11} and agenesis⁶ were suspected in some cases.

CONCLUSION

The pediatric dentist is capable of recognizing the genetic disorders pertaining to orofacial structures. Typical dental and skeletal findings of Apert syndrome were observed upon extra oral and intraoral examination.

The treatment of these patients begins at birth and a multi-disciplinary approach is required to arrive at a collaborative corrective plan for the deficiencies.

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Authors' Contribution:

Mariem Nefzaoui: wrote the manuscript, conducted the patient interviews and the review of the literature.

Imene Jazi: Conducted the review of the literature and reviewed the final manuscript.

Jihene Zaroui: Reviewed the final manuscript.

Mohamed Ali Chemli: revised the article critically for important intellectual content and approved the version to be published.

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Table 1: Review of literature about orofacial findings in Apert Syndrome patients.

Author's name	Age	Facial findings				Syn-dacti-ly	Oral findings		
		Cranial features	ophthalmo-logic abnormalities	Nasal and earing abnormalities	Front and profil view		Maxilla features	Malocclusion	Other
P. V. Bhatia, P. S. Patel, Y. V. Jani and N. C. Soni [8]	14 YO	-Flattened occiput -Frontal prominence -Brachycephaly	-Proptosis -Exorbitism -Hypertelorism	-	-Midface hypoplasia	x	-High arched palatal vault	-Anterior open bite -Prognathic mandible -Aligned mandibular teeth -Maxillary crowding	-
B. Jose, T. B. Emmatty, J. J. Methippara, K. Kumar and N. M. Thampi [9]	12 YO	-Flattened occiput -Frontal prominence -Brachycephaly -Acrocephaly	-Proptosis -Exorbitism -Hypertelorism -Down sliding lateral palpebral fissures	-Depressed nasal bridge -Bulbous nose -Low set ears	-Midface hypoplasia	x	-High arched palatal vault -Pseudo-cleft	-Anterior crossbite -Posterior crossbite -Deep-bite -Retruded maxilla -Maxillary and mandibular crowding	-Delayed eruption -Poor oral hygiene -Decreased mouth opening
H. Kakutani, Y. Sato, Y. Tsukamoto-Takakusagi, F. Saito, A. Oyama and J. Iida [10]	5 YO and 2 MO to 9 YO and 10 MO	-	-Proptosis -Exorbitism	-Small retro-displaced nose	-Midface hypoplasia -Concave profil	x	-High arched palatal vault -Reduced maxillary width	-Anterior open bite -Anterior crossbite -Posterior crossbite -Retruded maxillar -Skeletal Class III	-Delayed eruption -Tongue thrusting -Tooth agenesis
S. Khan, L. Chatra, P. Shenai and K. Veena [11]	9 MO	-Flattened occiput -Frontal prominence -Brachycephaly	-Proptosis -Exorbitism -Hypertelorism -Strabism -Down sliding lateral palpebral fissures	-Depressed Nasal bridge -Bulbous nose	-Midface hypoplasia -Cross bow shaped lips -Trapezoidal mouthshape	x	-High arched palatal vault -Pseudo-cleft	-Retruded maxilla	-
Tuba Tulay Koca [12]	19 YO	-Flattened occiput -Frontal prominence -Acrocephaly	-Proptosis -Exorbitism -Hypertelorism	-Depressed Nasal bridge -Bulbous nose	-	x	-	-Prognathic mandible -Mandibular crowding	-
G. R. Kumar, M. Jyothsna, S. B. Ahmed and K. R. Sree Lakshmi [13]	14 YO	-Frontal prominence -Brachycephaly	-Proptosis -Exorbitism	-Depressed Nasal bridge -Bulbous nose	-Midface hypoplasia -Cross bow shaped lips -Trapezoidal mouthshape	x	-High arched palatal vault -Pseudo-cleft	-Anterior open bite -Posterior crossbite -Angle class III -Maxillary and mandibular crowding	-Delayed eruption -Poor oral hygiene
F.Kunwar, S.Tewari and S.R.Bakshi [14]	13 YO	-	-Proptosis -Exorbitism -Down sliding lateral palpebral fissures	-	-	x	-	-Maxillary and mandibular crowding	-
M. A. Siminel, C. O. Neamtu, D. DiTescu, M. C. ForTofoiu, A. C. Comănescu, M. B. Novac, et al. [15]	New born	-Flattened occiput -Frontal prominence	-Exorbitism -Hypertelorism	-Short nose	-Midface hypoplasia -Trapezoidal-shaped lips	x	-Pseudo-cleft	-	-

Table 1: (Continued)

Author's name	Age	Facial findings				Syn-dacti-ly	Oral findings		
		Cranial features	ophthalmo-logic abnormalities	Nasal and earing abnormalities	Front and profil view		Maxilla features	Malocclusion	Other
S. Benmi-loud, S. Chaouki, S. Atmani and M. Hida [16]	10 YO	-Flattened occiput -Frontal prominence -Brachycephaly	-Exorbitism -Lagophthalmos -Hypertelorism	-Depressed nasal bridge -Bulbous nose -Overfolded helix	-	x	-Pseudo-cleft	-Retruded maxilla -Maxillary and mandibular crowding	-
F. Cammarata-Scalisi, E. Yilmaz, M. Callea, A. Avendaño, E. Mihçi and O. M. Alper [17]	3 Days old	-Flattened occiput -Frontal prominence -Acrocephaly	-Proptosis -Exorbitism -Hypertelorism -Down sliding lateral palpebral fissures	-Depressed nasal bridge -Bulbous nose -Low set ears -Overfolded helix -Dysplasia of the auricle	-Midface hypoplasia -Open mouth -Cross bow-shaped lips	x	-Pseudo-cleft	-	-
	2 MO	-Flattened occiput -Frontal prominence -Acrocephaly	-Proptosis -Hypertelorism -Down sliding lateral palpebral fissures	-Depressed nasal bridge -Bulbous nose	-Midface hypoplasia -Open mouth -Cross bow-shaped lips	x	-High arched palatal vault	-	-
Our case	5 YO	-Flattening occiput -Frontal prominence -Brachycephaly	-Proptosis -Exorbitism -Hypertelorism -Strabism	-Depressed nasal bridge -Bulbous nose -Low set ears	-Midface hypoplasia -Open mouth -Trapezoidal-shaped lips -Concave profil	x	-V-shaped maxillary arch -Pseudo-cleft	-Anterior open bite -Severe teeth crowding -Skeletal class III -Severe maxillary deficiency -Posterior cross-bite	-Poor oral hygiene -Dental caries -35, 45 agenesis -Mouth breathing -Tongue thrusting



Figure 1: Extraoral features in the patient: front and profile view



Figure 2: Syndactyly of the hands and feet.



Figure 3: Intraoral view: A: Maxillary intraoral view showing poor oral hygiene, carious lesions, and the palate was extremely deep with pseudo-cleft. B: Mandibular intraoral view showing narrow dental arch and carious lesions. C: Occlusion view showing anterior open-bite, unilateral posterior cross bite.



Figure 4: PANORAMIC RADIOGRAPH shows dental caries; crowding teeth and second mandibular premolar agenesis.



Figure 5: LATERAL CEPHALOMETRIC RADIOGRAPH shows shortened anteroposterior diameter, midface hypoplasia, retruded maxilla, prognathic mandible and anterior open-bite.