

## Apert Syndrome: Report of a Case with Emphasis on Oral Manifestations

B. Vadiati Saberi <sup>1</sup>✉, A. Shakoopour <sup>1</sup>

<sup>1</sup>Postgraduate Student, Department of Periodontology, School of Dentistry, Babol University of Medical Sciences, Babol, Iran

### Abstract:

To report the oral findings, including dental anomalies, ectopic eruption of the maxillary permanent first molars and periodontal disease and soft tissue alterations, in a subject with Apert syndrome. Clinical and radiographic examination of a patient with Apert syndrome, aged 21 years old, not previously submitted for orthodontic or orthognathic treatment.

Dental anomalies were present in a patient. Intraoral evaluation revealed poor oral hygiene with varying degrees of periodontal involvement, an arched swelling (pseudo cleft configuration), class III malocclusion, anterior open bite, posterior crossbite, supernumerary teeth, ectopic eruption and creamy white enamel opacities, an excessively large appearing tongue and a v-shaped maxillary arch. The occurrence of typical lateral palatal swellings agrees with the literature. The high prevalence of dental anomalies and ectopic eruption may suggest a possible etiologic relationship with the syndrome.

**Key Words:** Tooth Abnormalities; Mouth Abnormalities; Tooth Eruption, Ectopic; Craniosynostoses; Acrocephalosyndactylia

*Journal of Dentistry, Tehran University of Medical Sciences, Tehran, Iran (2011; Vol. 8, No.2)*

✉ Corresponding author:  
B. Vadiati Saberi, Department of  
Periodontology, School of  
Dentistry, Babol University of  
Medical Sciences, Babol, Iran.  
dr.bardia\_vad@yahoo.com

Received: 7 November 2010  
Accepted: 16 February 2011

### INTRODUCTION

Apert syndrome (mendelian inheritance in man #101200) represents approximately 5% of all craniosynostosis syndromes showing a prevalence of 1 in 65,000 to 160,000 live births [1,2]. Apert syndrome was first described by Whearon in 1894 and reviewed extensively by Apere in 1906 [3].

This disorder is characterized by severe craniosynostosis, craniofacial abnormalities and symmetric syndactyly of the hands and feet [4]. Among the craniofacial alterations are brachycephaly, midface hypoplasia, flat occiput, hypertelorism, proptosis and a short, broad nose with a bulbous tip [5]. The syndrome's oral manifestations have also been described in a few studies [5-10]. The configuration of the palate is characterized by an arched palate with bilateral swellings of the

palatine processes, resulting in a pseudocleft in the midline [5,7,8]. Other frequent oral findings include hypotonic lips, bifid uvula, delayed or ectopic eruption and malocclusion [5,9,10].

Apert syndrome demonstrates an autosomal dominant mode of inheritance and is associated with advanced paternal age, although most cases are sporadic possibly representing new mutations [11]. It is one of the five craniosynostosis syndromes associated with allelic mutations of the fibroblast growth factor receptor 2 (FGFR2) genes, along with Crouzon, Pfeiffer, Jackson-Weiss and Beare-Stevenson syndromes. Besides the genetic similarity, these three syndromes share similar clinical features that make the differential diagnosis sometimes difficult. The missense mutations S252W and P253R in the FGFR2 gene ac-



**Fig 1.** Clinical view of Apert syndrome: face (A) hands (B) and feet (C).

count for more than 99% of Apert syndrome cases [12]. The oral cavity is characterized by impaction, severe crowding, delayed eruption, thick gingiva, sometimes supernumerary teeth, or genetically missing teeth. Other frequent oral cavity findings include class III malocclusion, anterior open bite [13,14], bilateral posterior cross-bite and unilateral posterior cross-bite but to a lesser degree and a midline deviation. The aim of this study was to describe one sporadic case of Apert syndrome and discuss its craniofacial and dental features.

### CASE REPORT

A 21-year-old woman with the presumptive diagnosis of Apert syndrome was referred to the department of periodontology, school of dentistry, Babol University of medical sciences for regular dental treatment. She was born of a nonconsanguineous marriage. Her parents were clinically normal and at birth her mother was 22 years old and her father was 29 years old. There were no complications during pregnancy, and no other family member showed a similar condition. At birth, she had craniosynostosis, brachycephaly and syndactyly of the hands and feet. The patient has mild mental retardation, but her social development and bonding skills are satisfactory. She has never experienced seizures.

Extraoral examination revealed a brachycephalic skull with midface hypoplasia, a flat forehead, depression of the temporal bones, proptosis, hypertelorism, short nose with a

bulbous tip and septal deviation and trapezoidal shape of the mouth. In the lateral cephalogram, hypoplasia of the maxilla gave the appearance of a class III skeletal relationship (Fig 1-A). Syndactylies of the right hand's third, fourth and fifth digits and the left hand's second, third and fourth digits were present (Fig 1-B). Both feet showed a fusion of all toes (Fig 1-C). Intraoral evaluation revealed poor oral hygiene with varying degrees of periodontal involvement, an arched swelling (pseudo cleft configuration), class III malocclusion, anterior open bite (Fig 2), posterior cross-bite, supernumerary teeth, ectopic eruption and creamy white enamel opacities, the tongue appeared excessively large and the maxillary arch was v-shaped (Fig 3).

The CT scan revealed palatal cleft and maxillary hypoplasia and nasal septum deviation. The patient's medical history showed recurrent media otitis.

Initial dental treatment consisted of oral hygiene orientation for both patient and mother by means of disclosing tablets to be more familiar with plaque concepts and electrically powered toothbrushes (Oral-B®) and chlorhexidine mouth rinse 0.2% (Donyaye Behesht Co®) two times per day for two weeks, followed by plaque control via monthly professional prophylaxis. After an adaptation period, restorations and primary tooth extractions were performed. Orthodontic therapy is under consideration. The therapy consisted of supernumerary teeth extraction and orthodontic mi-

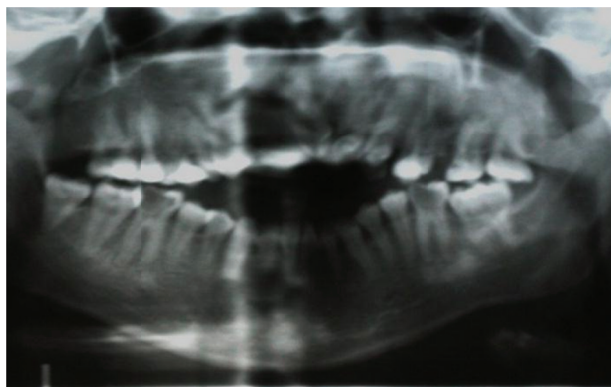


Fig 2. Panoramic view.



Fig 3. Occlusal view and v-shaped maxillary arch.

nor tooth movements to correct the crowding and achieving a stable occlusion. Preventive treatments included topical fluoride therapy. The patient was referred to a plastic and reconstructive surgeon for her extremities as she also complained of inability to brush her teeth because her fingers were malformed.

## DISCUSSION

Our patient demonstrated the clinical triad that characterizes Apert syndrome: brachycephalic skull, hypoplastic middle third of the face and syndactyly of the hands and feet. Other typical facial characteristics of Apert syndrome in our patient included flat forehead, depression of the temporal areas, shallow orbits with ocular proptosis and hypertelorism. Her nose was short and wide with a depressed nasal bridge and the nasolabial angle was diminished. All these craniofacial features are common in Apert syndrome patients due to the premature fusion of the cranial sutures [5].

Our patient had all typical oral manifestations of an Apert patient together, for example an arched swelling (pseudo cleft configuration), class III malocclusion, anterior open bite, posterior crossbite, supernumerary teeth, ectopic eruption and creamy white enamel opacities, tongue appeared excessively large and maxillary arch was v-shaped. In addition, it was very interesting for us that our patient had not been detected till this age and her family thought her situation was because of her laziness

and she did not use her hands and feet in childhood.

Although there are several different surgical techniques involved in craniosynostosis treatment, the key element is the timing of treatment with early intervention, before the first year of life, giving better results [15,16].

Early cranioplasty corrects both functional and esthetic consequences of craniosynostosis. Mental retardation is considered usual for Apert syndrome patients and in most cases is due to high intracranial pressure [15].

Central nervous system malformations have also been reported in Apert syndrome patients [17]. But our patient showed no evident alterations in the central nervous system.

Apert syndrome's oral features have been reported in a few studies [5-10]. The oral cavity is reduced in size, especially the anteroposterior dimension of the maxilla. The mandible is within normal size and shape, producing a relative prognathism. The unusual palate of Apert syndrome patients is diagnostically important. The high arched palate shows lateral swellings that induce a midline pseudocleft of soft tissue. Kreiborg and Cohen [7], in the largest clinical study of Apert syndrome's oral manifestations, found pseudocleft soft palate or bifid uvula in approximately 75% of the cases. Other studies have described a lower occurrence, such as 44% [6] and 4% [10] of the cases. The lateral palatine swellings are described as present in infancy and increase in

mass with aging, and histological studies have revealed acid mucopolysaccharide deposits consisting predominantly of hyaluronic acid [1]. According to Kreiborg and Cohen [7], Apert syndrome patients may present several dental abnormalities, including delayed eruption, ectopic eruption and shovel-shaped incisors.

In a recent study, Letra et al [10] detected a high incidence of tooth agenesis in Apert syndrome patients. Malocclusions are frequent in Apert syndrome patients mostly relating to maxillary hypoplasia [5,7]. These include mesial molar occlusion, mandibular overjet, anterior open bite, posterior cross-bite, midline deviation and dental crowding [5,7,8,10]. FGFR2 mutations have been identified as causing Apert syndrome [18]. To date, there are five identified mutations in FGFR2 in Apert syndrome patients [12,13,19]. In almost all cases (99%), two specific mis-sense substitutions have been described involving adjacent amino acids (S232W and P253R) in the linker between the second and third extracellular immunoglobulin domains of FGFR2 [12]. Although the variability in Apert syndromes clinical presentation is well established, Park et al [1] did not find any correlation between the type of FGFR2 mutation (S252W and P253R) and the affected patients' clinical features [2]. According to those authors, the lack of phenotypic differences in the two genotypic subgroups of Apert syndrome patients is not un-

expected, considering that the mutations themselves are adjacent and are in the same functional domain. In spite of the reported clinical characteristics, Apert syndrome may be confused with other craniosynostosis syndromes, whereas the presence of broad thumbs and halluces in association with cutaneous syndactyly differentiate Pfeiffer syndrome from Apert syndrome [20]. In Jackson-Weiss syndrome, the phenotype is extremely variable and the most consistent manifestation is abnormality in the clinical or radiographic appearance of the feet [21]. The presence of cutaneous disorders, cutis gyrate and acanthosis nigricans are the key elements for the correct diagnosis of Beare-Stevenson syndrome [22]. When the clinical features and uncharacteristic syndrome overlap, mutation analysis is helpful in distinguishing Apert syndrome from other clinically similar craniosynostosis syndromes [18]. Proper evaluation and characterization of the clinical features (Table 1) are important for the correct diagnosis and treatment of affected patients [23]. Affected individuals generally require lifelong management by a multidisciplinary team of health care specialists.

## CONCLUSION

The occurrence of dental anomalies, ectopic eruption and soft tissue alterations observed in our patient with Apert syndrome suggests a possible relationship between these disturbances and the syndrome.

**Table 1.** Oral characteristics of craniosynostosis syndromes.

Craniosynostosis Syndrome	Oral Characteristics
<b>Apert</b>	Maxillary hypoplasia, lateral palatal swellings, gingival hypertrophy, multiple tooth agenesis, shovel-shaped incisors, high caries prevalence, early tooth loss, difficult oral hygiene control due to hand malformations
<b>Crouzon</b>	Maxillary hypoplasia, lateral palatal swellings, reduced maxillary length, maxillary hypoplasia, counterclockwise mandibular rotation, mandibular prognathism due to positional changes with normal mandibular growth, ectopic eruption, tongue thrusting, partial tooth agenesis
<b>Pfeiffer</b>	Maxillary hypoplasia, lateral palatal swellings, mandibular prognathism, high-arched palate, tooth crowding
<b>Saethre-Chotzen</b>	Maxillary hypoplasia, lateral palatal swellings, narrow palate, cleft palate, Class III malocclusion, teeth with large crowns and thin and long roots, multiple pulp stones



**ACKNOWLEDGMENTS**

The authors thank Department of Periodontology, School of Dentistry, Babol University of Medical Sciences; also Department of Orthodontics, School of Dentistry, Guilan University of Medical Sciences for their assistants. Special thanks also go to Dr. Babak Amoian for his kind consultation.

**REFERENCES**

- 1-Park WJ, Theda C, Maestri NE, Meyers GA, Fryburg JS, Dufresne C, et al. Analysis of phenotypic features and FGFR2 mutations in Apert syndrome. *Am J Hum Genet* 1995 Aug;57(2):321-8.
- 2-Cohen MM Jr, Kreiborg S, Lammer EJ, Cordero JF, Mastroiacovo P, Erikson JD, et al. Birth prevalence study of Apert syndrome. *Am J Med Genet* 1992 Mar 1;42(5):655-9.
- 3-Apert M. De l'acrocephalosyndactylie. *Bull Mem Soc Med Hop Paris* 1906;23:1310-3.
- 4-Cohen MM Jr, Kreiborg S. A clinical study of the craniofacial features in Apert syndrome. *Int J Oral Maxillofac Surg* 1996 Feb;25(1):45-53.
- 5-Cunningham ML, Seto ML, Ratisoontorn C, Heike CL, Hing AV. Syndromic craniosynostosis: from history to hydrogen bonds. *Orthod Craniofac Res* 2007 May;10(2):67-81.
- 6-Peterson Sj, Pruzansky S. Palatal anomalies in the syndromes of Apert and Crouzon. *Cleft Palate J* 1974 Oct;11:394-403.
- 7-Kreiborg S, Cohen MM Jr. The oral manifestations of Apert syndrome. *J Craniofac Genet Dev Biol* 1992 Jan-Mar;12(1):41-8.
- 8-Paravatty RP, Ahsan A, Sebastian BT, Pai KM, Dayal PK. Apert syndrome: a case report with discussion of craniofacial features. *Quintessence Int* 1999 Jun;30(6):423-6.
- 9-Tosun G, Sener Y. Apert syndrome with glucose-6-phosphate dehydrogenase deficiency: a case report. *Int J Paediatr Dent* 2006 May;16(3):218-21.
- 10-Letra A, de Almeida AL, Kaizet R, Esper LA, Sgarbosa S, Granjeiro JM. Intraoral features of Apert's syndrome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007 May;103(5):e38-41.
- 11-Chang CC, Tsai FJ, Tsai HD, Tsai CH, Hseih YY, Lee CC, et al. Prenatal diagnosis of Apert syndrome. *Prenat Diagn* 1998 Jun;18(6):621-5.
- 12-Kan SH, Elanko N, Johnson D, Cornejo-Roldan L, Cook J, Reich EW, et al. Genomic screening of fibroblast growth-factor receptor 2 reveals a wide spectrum of mutations in patients with syndromic craniosynostosis. *Am J Hum Genet* 2002 Feb;70(2):472-86.
- 13-Goodman RM, Gorlin RJ. *Atlas of the Face in Genetic Disorders*. St Louis: Mosby Company; 1977. p. 80-1.
- 14-Ferraro NF. Dental, orthodontic and oral/maxillofacial evaluation and treatment in Apert syndrome. *Clin in Plast Surg* 1991 Apr;18(2):291-307.
- 15-Renier D, Lajeunie E, Arnaud E, Marchac D. Management of craniosynostoses. *Childs Nerv Syst* 2000 Nov;16(10-11):645-58.
- 16-McCarthy JG, Glasbetg SB, Cutting CB, Epstein FJ, Grayson BH, Ruff G, et al. Twenty year experience with early surgery for craniosynostosis: II. The craniofacial synostosis syndromes and pansynostosis—results and unsolved problems. *Plast Reconstr Surg* 1995 Aug;96(2):284-95.
- 17-Avantaggiato A, Carjnci F, Curioni C. Apert's syndrome: cephalometric evaluation and considerations on pathogenesis. *J Craniofac Surg* 1996 Jan;7(1):23-31.
- 18-Wilkie AO, Bochukova EG, Hansen RM, Taylor IB, Rannan-Eliya SV, Byren JC, et al. Clinical dividends from the molecular genetics diagnosis of craniosynostosis. *Am J Med Genet A* 2007 Aug;143A(16):1941-9.
- 19-Passos-Bueno MR, Sertie AL, Zatz M, Richieri-Costa A. Pfeiffer mutation in an Apert patient: how wide is the spectrum of variability due to mutations in the FGFR2 gene. *Am J Med Genet* 1997 Aug;71(2):243-5.
- 20-Vogels A, Fryns JP. Pfeiffer syndrome. *Orphanet J Rare Dis* 2006 Jun 1;1:19.
- 21-Cohen MM Jr. Jackson-Weiss syndrome. *Am J Med Genet* 2001 May 15;100(4):325-9.
- 22-Izakovic J, Leitner S, Schachner LA. What syndrome is this? Beare-Stevenson cutis gyrata syndrome. *Pediatr Dermatol* 2003 Jul-Aug;20(4):358-60.

23-Mufalo P, Kaizer R, Dalben G. Comparison of periodontal parameters in individuals with syndromic craniosynostosis. J Appl Oral Sci 2009 Jan-Feb;17(1):13-20.