Apert Syndrome: A Case Report with Review
Madhuri Gawande, Minal Chaudhary, Mimansha Patel

Abstract
There are several developmental malformations affecting human population, Apert syndrome or acrocephalo-syndactyly is one of the rare autosomal dominant malformation syndromes characterized by craniosynostosis, severe symmetric syndactyly and a variety of abnormalities of the skin, skeleton, brain, other visceral organs and oro-facial anomalies. These craniofacial characteristics predispose the affected individual to maxillary transverse and sagittal hypoplasia with concomitant dental crowding, a pseudo cleft palate and a skeletal and dental anterior open bite. Most cases of Apert syndrome are sporadic. However a few examples of genetic transmission of the disease have been observed and an autosomal dominant mode of inheritance has been considered. Generally, clinical signs and symptoms are sufficient to confirm the diagnosis of ‘Apert Syndrome’. Characteristic radiographic finding of hand, foot and AP view of skull further confirms clinical diagnosis. We report a case of Apert syndrome in an 11 year old male patient with brief literature review.

Keywords: Apert syndrome; Craniosynostosis; Syndactyly; Oro-facial; Autosomal dominant; Hypoplasia.

Introduction
Apert syndrome is a rare congenital type I acrocephalo-syndactyly syndrome, characterized by craniosynostosis showing premature fusion of one or more sutures, severe syndactyly of the hands and feet, symphalangism and dysmorphic facial features. Reduced or asymmetrical skull growth ensues, causing deformity of the skull vault or the base. Virchow in 1851 noted that there is a cessation of growth in a direction perpendicular to that of the affected suture while growth proceeds in a parallel direction. There are also distinct craniofacial synostosis syndromes that share common features such as suture synostosis, midfacial hypoplasia and facial and limb abnormalities.

Apert's syndrome is one such syndrome, and was first reported by Baumgartner in 1842. Eugene Apert in 1906 reported the systemic presentation of the syndrome and so the eponym credit is given to him. According to Cohen incidence of Apert Syndrome is about 15 per 1,000,000 live birth. Morbidity is of 4.7% and male and female being equally affected. Here, we report a case of Apert Syndrome in an 11 year old male patient, along with brief literature review.

Case Report
An 11 year old male patient reported with a chief complaint of pain and bleeding of gums since 2 months. Extra oral examination of the face showed the sunken and hypoplastic maxillae. The nose was of parrot beak type. Examination of the hands showed that thumbs were separate but all other fingers were fused. In the feet there was fusion of all the toes. The clinical appearance of the deformed extremities of the patient was typical of the so called “Mitten hand” and “sock foot” type (Fig 1a & 1b). Family history and past history was not contributory. The patient’s siblings and relatives exhibited no similar disorder.

Examination of the oral cavity revealed that lips were normal in appearance except for a small and clear protrusion of the middle portion of the upper lip. In the upper jaw teeth present were #16, 55 (Root stump), 54, 53 (Root stump), 13, 11, 61 (Root stump), 21, 23, 63 (Root stump), 64, 65 (Root stump), and 26. In the lower jaw teeth #46, 45, 44, 83 (Root Piece), 42, 41, 31, 32, 33, 73, 34, 35, and 36 were present. The oral hygiene was poor and generalized chronic gingivitis and gingival enlargement was present with a high arched palate. There was a mild prognathism of mandible (Fig 1c).
Investigations included frontal and lateral X-rays of the skull, hands and feet. Radiographs of both hands showed soft tissue syndactyly of second, third, fourth and fifth digits and synostosis involving phalanges of second, third and fourth digits with deformed phalanges of first digit. Radiographs of both feet showed soft tissue syndactyly of all the toes with syndactyly of all the toes with synostosis involving metatarsals of first, second and third digits. Skull radiographs revealed fused coronal sutures, turri brachycephalic skull contour, elongated flat forehead with bitemporal widening and hypertelorism. Multiple impacted teeth were also seen. On the basis of radiographic examination diagnosis of Apert syndrome was confirmed (Fig 2).

Treatment of these patients was done by a multidisciplinary team. Initial dental treatment consisted of oral hygiene orientation for both patient and mother by means of demonstration of tooth brushing technique & plaque control with electrically powered toothbrushes and chlorhexidine mouth rinse 0.2% 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 minor 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 his extremities.

Figure 1: The Clinical Picture showing Turricephaly, prominent head, flat face, nasal bridge, shallow orbit, hypertelorism (a) and syndactyly of hands and foot (b) with intraoral picture showing narrow and V shaped palate (c).

Figure 2: Radiograph showing Turricephaly and syndactyly.

Discussion
The hallmarks of the syndrome include craniosynostosis (abnormal development and premature fusion of the cranial sutures), symmetric severe syndactyly (Cutaneous and bony fusion of the digits), dental abnormality (high arch palate, generalized gingival enlargement, multiple impacted teeth and multiple caries teeth) and a variety of abnormalities of the skin, skeleton, brain, and visceral organs. The condition results from a specific missense mutation in the gene encoding fibroblast growth factor receptor-2 (FGFR-2), mapped to 10q26 chromosome. This pleiotropic gene is involved in the complex intercellular signalling network that controls cell proliferation, differentiation, migration, and survival in many different contexts, including embryonic development, angiogenesis, and
malignancy. Mutations of the FGFR-2 gene have also been associated with several other craniosynostosis malformation syndromes, including Crouzon, Jackson–Weiss, Pfeiffer and Beare–Stevenson cutis gyrata syndromes.\textsuperscript{3,4}

Oral characteristics of craniosynostosis syndromes are summarized in Table 1. Several etiological hypotheses are put forward for the same.

<table>
<thead>
<tr>
<th>Craniosynostosis Syndrome</th>
<th>Oral Characteristics</th>
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<tr>
<td>Apert</td>
<td>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.</td>
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<tr>
<td>Crouzon</td>
<td>Maxillary hypoplasia, lateral palatal swellings, reduced maxillary length, maxillary hypoplasia, counterclockwise mandibular rotation, and mandibular prognathism due to positional changes with normal mandibular growth, ectopic eruption, tongue thrusting and partial tooth agenesis.</td>
</tr>
<tr>
<td>Pfeiffer</td>
<td>Maxillary hypoplasia, lateral palatal swellings, mandibular prognathism, high-arched palate, tooth crowding.</td>
</tr>
<tr>
<td>Saethre-Chotzen</td>
<td>Maxillary hypoplasia, lateral palatal swellings, narrow palate, cleft palate, Class III malocclusion, teeth with large crowns and thin and long roots, multiple pulp stones.</td>
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**Table 1:** Oral characteristics of craniosynostosis syndromes

Premature fusion of cranial sutures, most commonly of the coronal suture, is observed in all patients with Apert syndrome. Antero–posterior shortening of the cranial base leads to acrocephaly or brachycephaly. Other characteristic craniofacial abnormalities include prominent forehead with skin wrinkling, broad cranium, and a flat occiput. Hypertelorism, proptosis, and strabismus are often present due to shortening of the bony orbit. Additional craniofacial features include a short, broad nose with a bulbous tip, micrognathia, and a cleft palate.\textsuperscript{5} Symmetric syndactyly of the hands and feet is another universal finding in patients with Apert syndrome. All these features were documented in our patient. Wilkie et al, scored severity of syndactyly in Apert Syndrome according to modified version of classification of Upton (1991):

**Type I:** Thumb and part of fifth finger are separated from syndactylous mass.

**Type II:** Little fingers are not separated.

**Type III:** Thumb and all fingers are included.

Syndactyly in foot may involve three digits (type I), digits two–five with separate toes (type II) or be continuous.\textsuperscript{5} Central nervous system abnormalities include defects of the corpus callosum and limbic structures, ventriculomegaly and progressive hydrocephalus. A significant number of patients function at an intellectual level two standard deviations below the mean. Cardiovascular and genitourinary defects occur in 10% and 9.6% of patients with the syndrome, respectively.\textsuperscript{3,4,6} As a result of progressive osseous fusion of the tarsal and metatarsal bones, transfer of weight bearing to the mid and lateral plantar regions occurs in most patients, leading to lateral plantar hyperkeratosis which was also seen in our case. Moreover, patients may show cutaneous and ocular hypopigmentation as a result of the failure of melanoblast migration in utero.\textsuperscript{6,7}

**Medical Care:** Medical management of Apert syndrome includes the following:\textsuperscript{11,12}

- Protection of the cornea
  - Instil lubricating bland ointments in the eyes at bedtime to protect corneas from desiccation
  - Artificial teardrops during the day
- Upper airway obstruction during the neonatal period
  - Remove excessive nasal secretions
  - Treat upper airway infection
  - Humidification with added oxygen
  - Judicious use of topical nasal decongestants
- Sleep apnea
  - Polysomography (a sleep recording of multiple physiologic variables), currently the most reliable method for determining the presence of sleep apnea
  - Continuous positive pressure
- Chronic middle ear effusion associated with bilateral conductive hearing deficit
  - Antimicrobial therapy
- Psychological and social challenges confronted by individuals with Apert syndrome
  - Emotional adjustment
  - Body image development
  - Impact of surgery and hospitalization on children with Apert syndrome.

Surgical Care: Surgical management of Apert syndrome includes the following:
- Protection of the cornea: Lateral or medial tarsorrhaphy is performed in severe cases to narrow the palpebral fissure cosmetically and to protect the corneas and the vision.
- Upper airway obstruction during the neonatal period: This rarely requires orotracheal intubation.
- Sleep apnea: Tracheostomy is indicated in severely affected children.
- Chronic middle ear effusion associated with bilateral conductive hearing deficit: Bilateral myringotomy and placement of ventilation tubes are the most effective treatment.
- Cranial surgery
  - Removes synostotic sutures
  - Reshapes the calvaria
  - Allows more normal cranial development to proceed with respect to shape, volume, and bone quality.
  - Relieves increased intracranial pressure
- Orbital surgery
  - Correction of ocular proptosis
  - Reduction of increased interorbital distance (hypertelorism)
  - Correction of increased interior malrotation
- Nasal surgery
  - Infants and children: Nasal reconstruction focuses on correction of the excessively obtuse nasofrontal angle, flat nasal dorsum, and ptotic nasal tip.
  - Teenagers and adults: Reduction of the nasal tip bulk is indicated.
- Midfacial surgery
  - Normalization of midfacial appearance
  - Expansion of the inferior orbit
  - Volumetric expansion of the nasal and nasopharyngeal airways
  - Establishment of a normal dentoskeletal relationship
- Mandibular surgery: Mandibular osteotomies are performed to improve dentoskeletal relations for masticatory and aesthetic benefit.

- Other surgical approaches
  - Surgical care involves early release of the coronal suture and fronto-orbital advancement and reshaping to reduce dysmorphic and unwanted skull growth changes. Craniosynostosis requires multistaged operative procedures. A significant cosmetic improvement is possible. Initial surgery is often performed as early as age 3 months.
  - Facial cosmetic reconstruction for dysmorphisms is indicated.
  - A new technique of craniofacial disjunction, followed by gradual bone distraction (Ilizarov procedure), has been reported to produce complete correction of exophthalmos and improvement in the functional and aesthetic aspects of the middle third of the face without the need for bone graft in patients aged 6-11 years.
  - Surgical separation of digits (mitten-glove syndactyly) provides relatively little functional improvement
  - Shunting procedure reduces intracranial pressure.
  - For orthodontic treatment, most patients require 2-jaw surgery (bilateral sagittal split osteotomy with mandibular setback and distraction in the maxilla). During the period of distraction, the orthodontist guides the maxilla into final position using bite planes and intermaxillary elastics.

Non-surgical manipulation of Apert syndrome may be a possibility in the future, for example by using selective inhibitors of the FGFR-kinase domain. 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.

Conclusion
The occurrence of dental anomalies, ectopic eruptions, soft tissue alterations and craniosynostosis are observed in these patients with Apert syndrome. It occurs in sporadic and hereditary forms and 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 wellbeing of the patient. The information and 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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