Apert’s Syndrome: A Rare Case Report

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INTRODUCTION AND REVIEW
Apert’s syndrome is a form of acrocephalosyndactyly, a rare congenital disorder characterized by craniosynostosis, midface hypoplasia, syndactyly of hands and feet with a tendency of fusion of bony structures. Craniosynostosis syndrome is defined as premature closure of the cranial sutures producing deformity of skull. Craniosynostosis syndromes are a human skeletal disease, which includes Apert’s syndrome, Crouzon’s syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome.

Apert’s syndrome was first mentioned in as early as 1842 by Baumgartner and 1894 by Wheaton. In 1906, Eugene Apert, first described nine people with a similar disorder. Since he was the first to do so, his name is associated with the syndrome.

Apert’s syndrome is classified as branchial arch syndrome, affecting the first branchial arch. Males and females are equally affected. It has an autosomal dominant trait with the locus of a mutation of FGFR2 on chromosome 10q26. Two activating mutations, Ser-252 to Trp and Pro-253 to Arg, in fibroblast growth factor receptor 2 (FGFR2) account for nearly all known cases of Apert’s syndrome.

In 1998, Chang et al. was the first to do genetic analysis of the mutation responsible for the syndrome. Apert’s syndrome presents with various clinical features like craniosynostosis with brachycephaly, high prominent forehead with a flat posterior skull and flat or concave face. Other features include low-set ears, orbital proptosis, down slanting of palpebral fissures, down-turned nose with depressed nasal bridge. Facial features consist of hypoplastic maxilla, prominent mandible, high arched palate, crowded teeth and occasionally cleft palate.

The major attribute of the syndrome is syndactyly of the hands and feet. It is typical for the middle three fingers to be fused together with complete fusion of the distal soft tissues, and occasionally of the bones. The syndactyly resembles a ‘Mitten hand’ or ‘Sock foot’. Other features include CNS abnormalities (megalencephaly, gyral abnormalities, encephalocele, pyramidal tract abnormalities, etc.), skeletal abnormalities (limited mobility at glenohumeral joint and elbow joint, multiple epiphyseal dysplasia, very short or absent neck of scapula, etc.) and other features like cardiac anomalies, mental retardation, and visual and hearing defects, etc.

Investigations in the form of radiographs of hands and feet, and skull are taken to see syndactyly of hands and feet and malformation of midfacial bones and craniosynostosis of skull. CT scan images give better view of the deformity of skull and facial bones in various planes.

The ideal treatment of Apert’s syndrome begins at birth with proper prenatal diagnosis. Various multidisciplinary surgical approaches to Apert’s syndrome include surgical repair of craniosynostosis by release of coronal suture and fronto-orbital advancement, correction of syndactyly by corrective plastic surgery, treatment of facial dysmorphisms by cosmetic reconstruction, orthodontics and orthognathic surgery.

CASE REPORT
A 14-years-old girl presented with the complaints of malaligned teeth, difficulty in chewing food, and facial deformity. Her past medical history revealed that she had undergone palatal fistula closure and fronto-orbital advancement 7 years ago. Her family history revealed that no other family members were affected by same features.

On examination, the girl was found to have flattened occiput with frontal prominenence, abnormal contour of head (brachycephaly), shallow orbits with bilateral proptosis, hypertelorism, and parrot beaked like nose, retruded midface, incompetent everted lips and prognathic mandible (Figs 1A to C). She had symmetrical syndactyly with complete fusion of all digits of hands (except thumb) and feet (Figs 2A and B). Palm was deeply concave and nail beds were contiguous (Synonymia). Intraoral examination showed normal mouth opening with anterior open bite and high arched (V-shaped) palatal vault. Maxillary alveolar ridges were thick with crowding of maxillary teeth. Mandibular teeth were normally aligned (Fig. 3). The systemic examination revealed no other abnormality.

On investigation, orthopantomogram showed deformity of maxilla with malaligned maxillary teeth and high arched palate,
Apert’s Syndrome: A Rare Case Report

Fig. 1A: Patient at 14 years of age (Front view)

Fig. 1B: Patient at 16 years of age (Front view)

Fig. 1C: Patient’s profile view showing midface hypoplasia with exophthalmos

Fig. 2A: Shows complete fusion of all digits of hands

Fig. 2B: Shows complete fusion of all digits and toe of feet

Fig. 3: Intraoral view showing crowded maxillary teeth and normal aligned mandibular teeth
and lateral cephalogram showed concave profile with retruded and deformed midfacial bone (Fig. 4). X-ray of hand-wrist showed that there was bony fusion of the phalanges of 3rd and 4th digits (Fig. 5). X-ray of spine, abdominal ultrasonography, and echocardiography were normal. Later CT scan of the face was done, which revealed that there was obvious abnormal growth of middle-third of the face with bilateral proptosis, deviation of nasal septum and turriccephalic skull (Fig. 6).

Due to the typical features and presence of the triad of craniosynostosis, syndactyly of hands and feet with maxillary hypoplasia, patient was diagnosed as Apert’s syndrome. Due to presence of syndactyly of hands and feet, Crouzon’s syndrome was ruled out.

Patient was advised orthodontic treatment with orthognathic surgery for correction of the facial dysmorphisms, and corrective plastic surgery for the syndactyly of hands and feet. As patient was not ready for any interventional procedures, only oral prophylactic measures were taken and kept under regular follow-up.

**DISCUSSION**

Apert’s syndrome is an autosomal dominant, but in many cases, the inheritance is sporadic. A localized mutation of the gene FGFR2 with chromosomal localization at 10q26 is responsible. The incidence of Apert’s syndrome is approximately one in 50,000 births. Some state that 4.5% of all craniosynostosis represent Apert’s syndrome.

Unique fibroblast growth factor receptor 2 (FGFR2) mutations lead to an increase in the number of precursor cells that enter the osteogenic pathway. Ultimately, this leads to increased subperiosteal bone matrix formation and premature calvaria ossification during fetal development. Once a suture becomes fused, growth perpendicular to that suture becomes restricted, and the fused bones act as a single bony structure. Compensatory growth occurs at the remaining open sutures to allow continued brain growth. However, complex, multiple sutural synostosis frequently extends to premature fusion of the sutures at the base of the skull causing brachycephaly, midfacial hypoplasia, shallow orbits, hypertelorism, foreshortened nasal dorsum, maxillary hypoplasia and mandibular prognathism as seen in our case.

Radiographs of hands and feet, and skull show syndactyly of hands and feet and malformation of midfacial bones and craniosynostosis of skull, which is in accordance to our case.

According to the literature, Apert’s and Crouzon’s syndrome has similar clinical presentation with the exception of syndactyly of hands and feet in Apert’s syndrome, which is seen in our case. Cleft or pseudocleft palate is a frequent finding in Apert’s syndrome, which is absent in Crouzon’s syndrome (Table 1).

Various complications arising due to late diagnosis, include defective brain development, mental retardation, increase in facial deformity, prognathic mandible, etc. It is very important to diagnose and treat this syndrome at an early age to prevent the late diagnosis effects.

The treatment of patients presenting complex facial deformities is one of the most challenging multidisciplinary tasks. Due to advances in medical technology and surgical techniques in the last 20 years, correction of severe malformations has become possible and is performed by highly specialized teams, frequently in a single operation. Craniotomy is often performed during the first year of life to treat the craniosynostosis. Frontofacial advancement and midface-advancement can be performed later to correct the proptosis and mid-face hypoplasia. Coordinated orthodontic therapy is often necessary to bring unerupted teeth into place and improve occlusion. Surgery can also be used to separate the fused fingers.

**SUMMARY AND CONCLUSION**

The rarity of the Apert’s syndrome, its spectra heterogeneity, craniofacial anomalies and being a multifactor digenetic syndrome,
Apert’s Syndrome: A Rare Case Report

Table 1: Comparison of typical features of Apert’s syndrome and Crouzon’s syndrome with the present case

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Apert’s syndrome</th>
<th>Crouzon’s syndrome</th>
<th>Present case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milestones</td>
<td>Severely delayed</td>
<td>Normal or delayed</td>
<td>Delayed</td>
</tr>
<tr>
<td>Mental development</td>
<td>Severe mental retardation</td>
<td>Normal or mild</td>
<td>Mild mental retardation</td>
</tr>
<tr>
<td>Stature</td>
<td>Short</td>
<td>Normal</td>
<td>Short</td>
</tr>
<tr>
<td>Head</td>
<td>Acrocephaly, supraorbital depression</td>
<td>Cephalocele</td>
<td>Acrocephaly, frontal bossing, flat occiput</td>
</tr>
<tr>
<td>Palate</td>
<td>High arched with furrow in midline, cleft palate</td>
<td>High palate, no furrow</td>
<td>High arched palate, treated for cleft palate</td>
</tr>
<tr>
<td>Ears/Hearing</td>
<td>Deafness later in life</td>
<td>Low set, deafness early in life</td>
<td>Normal</td>
</tr>
<tr>
<td>Hands and feet</td>
<td>Syndactyly present</td>
<td>Normal</td>
<td>Syndactyly present</td>
</tr>
<tr>
<td>X-ray skull</td>
<td>Synostosis</td>
<td>Raised ICT, premature closure of sagittal and coronal sutures, proptosis</td>
<td>Synostosis with concave profile and pseudo-mandibular proptosis</td>
</tr>
<tr>
<td>CT scan</td>
<td>Hydrocephalus absent, corpus callosum abnormal, ventricular and septum pellucidum</td>
<td>No hydrocephalus, raised ICT</td>
<td>Craniosynostosis, turricephalic skull, nasal septum deformed, maxillary hypoplasia</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>Antimongoloid slant, shallow orbit, proptosis, hypertelorism, ectopic lens, etc</td>
<td>Exophthalmos, spontaneous luxation, hypertelorism, nystagmus, cataract, blue sclera</td>
<td>Hypertelorism, proptosis, exposure keratopathy, downward slanting palpebral fissures</td>
</tr>
</tbody>
</table>

it is necessary to carry out the genetic advising and detailed study in each individual affected by this syndrome.

Therefore, the study has to be continuous to promote prenatal diagnosis and early multidisciplinary treatment approach to prevent the late diagnosis effects.

So, our case is an addition to the literature of the clinical and radiographic features and treatment modalities of this rare syndrome.

REFERENCES