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Apert Syndrome: A Rare Craniosynostosis

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Abstract: *Apert syndrome is one of the rarest of the craniosynostosis syndrome. It was named for the French physician Eugene Apert in 1906. It is an autosomal dominant genetic disorder characterized by premature fusion of certain skull bones (craniosynostosis), craniofacial anomalies and severe symmetrical syndactyly of hands and feets. Most of the cases are sporadic, may result from new mutations in FGFR2 (fibroblast growth factor receptor 2) gene. Incidence is 15 per 1,000,000 live births with no sex predilection. The case report describes a 12 year old boy clinically and genetically diagnosed with apert syndrome displaying all the classic features of the syndrome.*

Keywords*: Apert syndrome; Craniosynostosis; Syndactyly; Fibroblast growth factor receptor 2 gene.*

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I. Introduction

Apert syndrome is a rare genetic form of Acrocephalosyndactyly(type I). It was first mentioned in 1842 by Baumgartner and 1894 by Wheaton[1,2,3] and tilted after Eugene Apert a French Pediatrician in 1906 described the syndrome in nine people[4]. According to cohen ,the incidence of apert syndrome is about 15 per 1,000,000 live births.[5] And it is rarley reported from india[6]. It is an uncommon congenital disorder with an autosomal dominant inheritance pattern which demonstrate itself with craniosynostosis, midface hypoplasia, and symmetric syndactyly of hands and feets.[7]

It is classified as a branchial arch syndrome specifically affecting the first branchial (Pharyngeal)arch which is the Forerunner of maxilla and mandible. The gene involved with AS is FGFR2 (fibroblast growth factor receptor 2) located on chromosome 10q25, 10q26. The syndrome has no sexual predilection and are more frequent in certain races, highest in the Asians and lowest in the Hispanics.[8]

Apert syndrome has both craniosynostosis and syndactyly. In syndromic patients because of the mutations in FGFR2 gene, alters the protein and prolonged signaling can promote the premature fusion of bones in hands and feets. The FEFR2 gene is also responsible for the early fusion of several sutures of the skull. These two reasons explains why both the symptoms like craniosynostosis and syndactyly are found in apert syndrome[8].

Craniofacial deformities specific to Apert syndrome (AS) include acrocephaly (cone- shaped calvarium), prominent forehead, proptosis, hyperteleorism, and flattened nose with a low bridge. Oral signs include pseudocleft, high- arched palate, transverse and sagittal maxillary hypoplasia, dental crowding, delay in dentition, ectopic teeth and disarrayed teeth. Mandible is generally normal in size, and pseudoprognatism can be seen. Rarely symptoms related to central nervous system, cardiac, gastrointestinal, and urogenital system, and vertebral anomalies have been reported[9].

II. Case Report

A 12 year old boy was referred to the Department of Pediatric and Preventive Dentistry with complaint of malaligned teeth and dental caries on lower molars. A general assessment showed evidence of malformations in other areas. On general physical examination, patient was moderately built and moderately nourished with short stature and normal gait with shorter humerus and femur bones. All the vital signs were within normal limits .The hands and feet showed partial syndactyly. So a detailed medical and dental history was obtained from his mother.

The child's medical report showed that the child had Apert syndrome diagnosed at birth. He was born to a healthy mother via C- section. The child had a premature birth at 32weeks of gestation with a birth weight of 2.5kg. There was no family history of any congenital abnormalities, consanguinity or increased parental age. He has a normal younger brother.

On extraoral examination, patient has Acrocephaly with leptoprosopic face with prominent head, hypertelorism, proptosis, psittichorhina (parrot beak like nose) , and flattened nose with a low bridge. Lateral profile of the patient showed low set ears and midface deficiency. Bilateral synchronous movements of the mandible were evident . No abnormality was detected with respect to the muscles of mastication and lymph node.

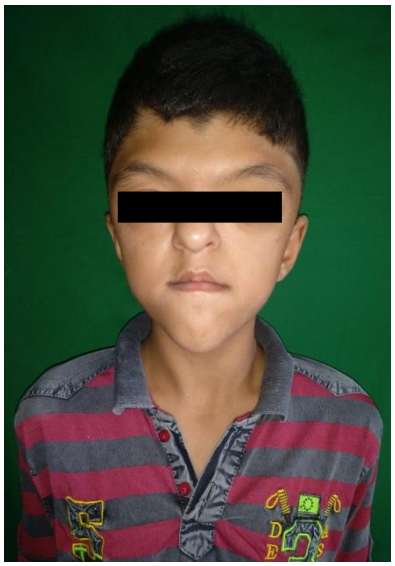


Figure 1: Frontal view

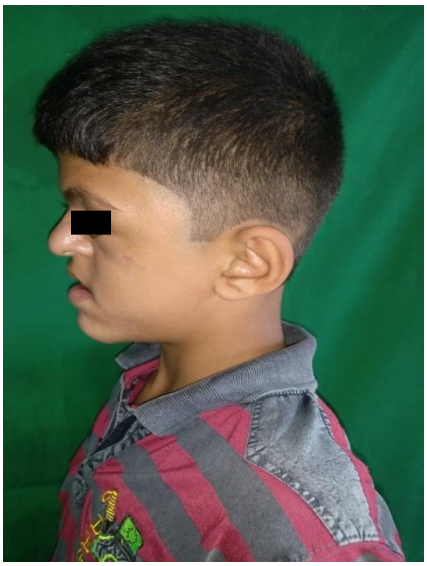
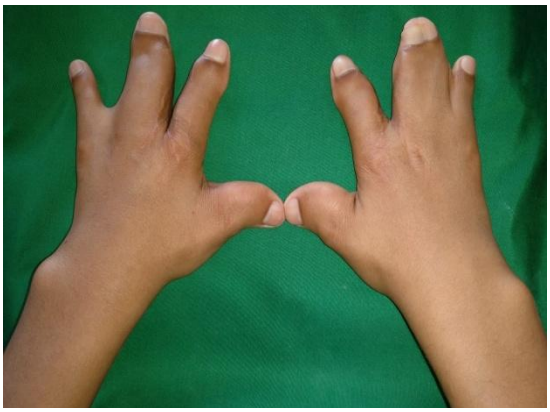


Figure 2: Lateral view



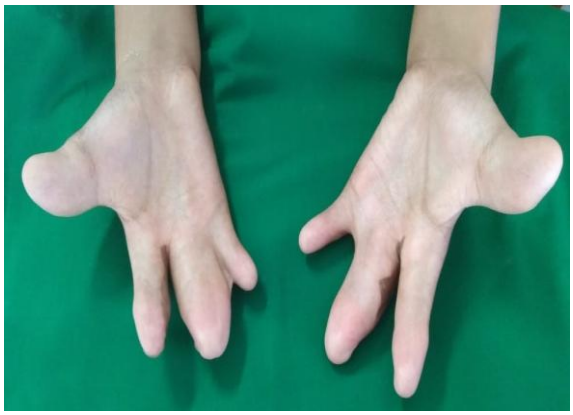


Figure 3 & 4: Syndactyly of hands

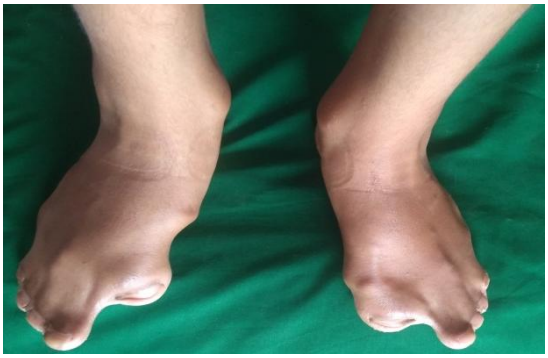


Figure 5: Syndactyly of feet

On intra oral examination , dental caries was noted on 36 and 46. Grossly decayed 85 was also noted. Other signs include pseudocleft, high-arched palate, transverse and sagittal maxillary hypoplasia, bilateral anterior and posterior crossbite, severe anterior deep bite, dental crowding, delay in eruption and malaligned teeth. OPG revealed supernumerary teeth in maxillary anterior region. There is no other associated systemic condition and the boy was intellectually normal.

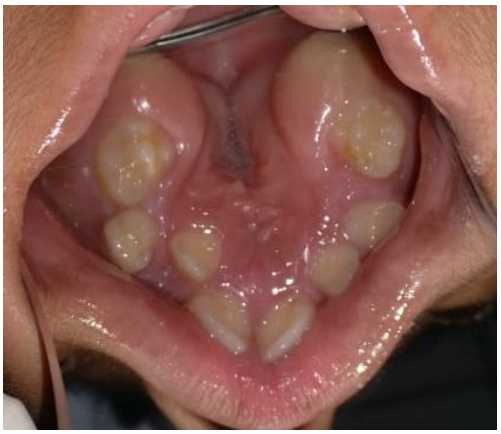


Figure 6: Intra oral view - Maxilla arch

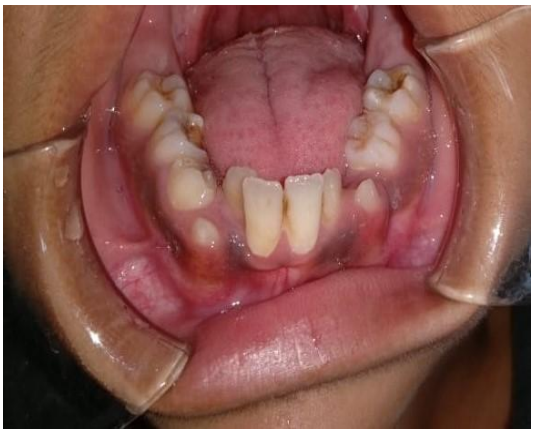


Figure 7: Mandibular arch

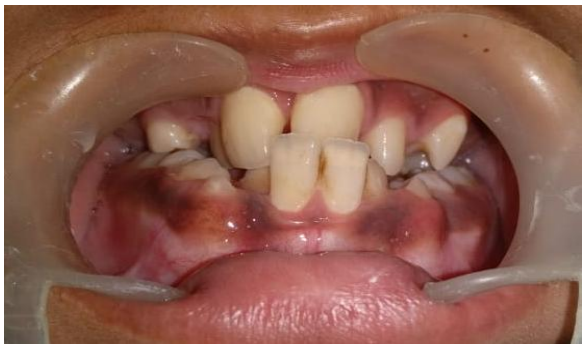
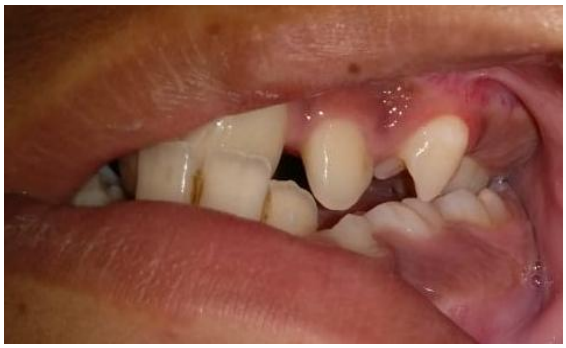


Figure 8: Occlusion- anteriorly



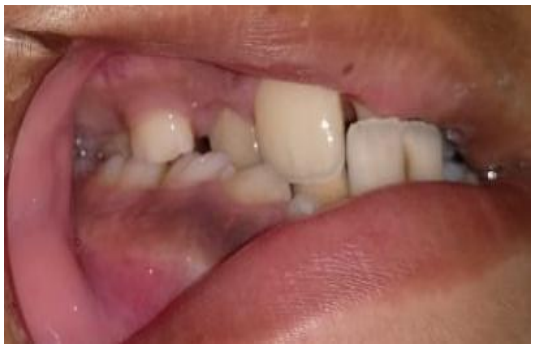


Figure 9& 10: Occlusion Posteriorly

Radiological investigations were carried out. Intraoral periapical radiograph revealed dentinal caries on 36 and 46 with grossly decayed 85. Panoramic view showed supernumerary teeth in maxillary anterior region (Figure 10) and lateral cephalogram showed hypoplasia of the zygomatic and maxillary bones (Figure 11).

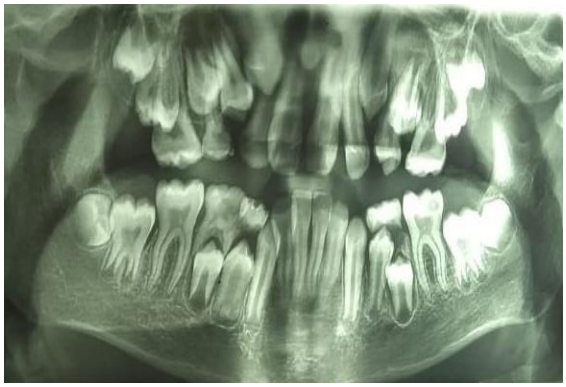


Figure 10: Panoramic view

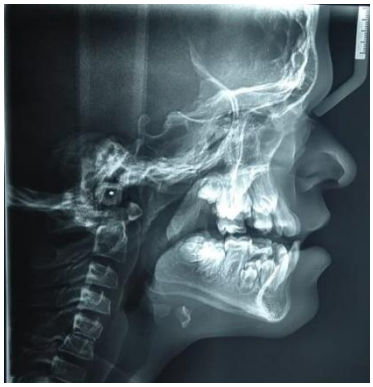


Figure 11: Lateral cephalogaram

Treatment was started with patient and parent counseling, education and motivation were given priority during treatment. Oral prophylaxis and brushing technique were demonstrated. Restoration of carious 36 and 46 done, extraction of grossly decayed 85 were also done. Patient is currently under follow up and development of occlusion is being monitored.

III. Discussion

Apert's syndrome is a rare type I acrocephalosyndactyly syndrome characterized by craniosynostosis, severe syndactyly of the hands and feet, and dysmorphic facial features. The skull is prematurely fused and unable to grow normally therefore the midface appears sunken. The fingers and toes showed fusion in varying degrees.

The molecular basis of this syndrome appears remarkably specific: Two adjacent amino acid substitutions (either S252W or P253R) occurring in the linking region between the second and third immunoglobulin domains of the fibroblast growth factor (FGR) 2 gene, which is responsible for early synostosis[10]. Also studies have shown that FGFR2 gene has an effect on mesenchymal development of tooth morphogenesis and many of the oral manifestations can be a result of this. The offspring of a parent with AS has a 50% chance of inheriting the condition or occur from fresh mutation[8]. This mutations usually occurs in a sperm and AS is one of the few genetic conditions linked to older fathers particularly men over the age of 50[11]. The present case was sporadic because both the parents had normal karyotype and age below 30 years.

The clinical and oral features of Apert's syndrome are well established in the present case report. It is clinically characterized by premature fusion of the coronal suture and hypoplastic midface , ocular anomalies and short nose with depression of the nasal bridge and Syndactyly. The oral cavity characteristics included reduction in the size of the maxilla, which may result in tooth crowding .

The cause of mental retardation in AS is unclear. The only possibility is that premature closure of cranial sutures, increased cranial pressure closure can limit the growth of the brain and hence the intelligence[8]. These present case discussed here has no mental retardation.

Additional signs and symptoms of AS include hearing loss, unusually heavy sweating (hyperhidrosis), oily skin with severe acne, patches of missing hair in the eyebrows, fusion of spinal bones in the neck (cervical vertebrae), and recurrent ear infections, sleep apnea, and malnutrition. Some affected individuals have anomalies of the viscera, skeleton, and central nervous system, or abnormalities of the upper and lower respiratory tracts[8]. However, the case reported here did not present any related signs and symptoms during clinical examination.

For the patient with Apert's syndrome, oral hygiene is as important as it is difficult. Hand deformities made for child difficult to brush the teeth. The new generation of electric tooth brushes and fluoride mouth rinses may make the task easier. Professional care, including frequent dental examinations, oral hygiene prophylaxis, fluoride treatments, and dental sealants, are very important in preventing the caries related issues.

Tosun and Sener's study showed that Apert's syndrome was in parallel with G6PD deficiency. Therefore dental surgeons must avoid drugs that may potentially induce hemolysis as a result of G6PD deficiency[12].

IV. Conclusion

Apert's syndrome still a rare and unsolved area of investigation in congenital diseases, affects many parts of the body. Many of the molecular features exhibited in this syndrome are still unexplainable and requires intensive research. The evolution of prenatal diagnostic modalities has made early detection and timely multidisciplinary intervention a reality, hence offering a better quality of life to affected individuals. The integral healthcare delivery should include a multidisciplinary approach provided by dentists, neurosurgeons, plastic surgeons, ophthalmologists, and geneticists for the effective planning the treatment of such patients.

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