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Case report:

Apert syndrome (A rare human malformation syndrome): A Case report

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Abstract:

Apert syndrome is named for the French physician,'Eugene Apert' who has described the syndrome acrocephalosyndactylia in 1906. It is a rare autosomal dominant disorder characterized by craniosynostosis, craniofacial anomalies, and severe symmetrical syndactyly of the hands and feet. Apert syndrome is characterized by the premature fusion of certain skull bones (craniosynostosis). This early fusion prevents the skull from growing normally and affects the shape of the head and face. In addition, a varied number of fingers and toes are fused together (syndactyly). Most cases of Apert syndrome are sporadic, may result from new mutations in the gene. It is generally accepted that management of Apert syndrome is multidisciplinary in approach.Early diagnosis and treatment is important because Apert syndrome when treated early has good prognosis in adult life. Here,we are presenting a case report a of Apert syndrome and review of literature of presented case with clinical interest.

Key words: Acrocephalosyndactylia ,Craniosynostosis, Syndactyly

Introduction:

Apert syndrome (Acrocephalosyndactylia) is a rarely seen congenital disorder characterized by an autosomal dominant inheritance which manifests itselt with craniosynostosis, midface hypoplasia, and symmetric syndactyly of hands, and feet . [1,3]It was first described by Wheaton' in 1894 and subsequently further cases were reported by Apert. Apert syndrome, named after this French physician "Eugene Apert" who first described it in 1906.[1]

Linguistically "acro" is a Greek word for "peak" referring to a "peaked" head that is common in the syndrome. "Cephalo", also a Greek, is a combining form meaning "head". "Syndactyly" refers to webbing of fingers and toes . Embryologically, the hands and feet have selective cell that die, called selective cell death or apoptosis, causing separation of digits, however, in acrocephalosyndactyly selective cell death fail to occur and the skin and rarely bone between the fingers and toes fuses .[2]

Major Features of Apert Syndrome

1. Prematurely fused cranial sutures.
2. A retruded midface i.e. abnormal shaped head and face.
3.Abnormalities of eyes, including down slanting palpebral fissures, hypertelorism, exophthalmoses.
4. Low-set ear sand hearing loss.

5. Malformations of the brain. Hydrocephalus and learning disability.

6. Cleft palate.

7. The skin and bones of the hands and feet are also fused. This is called syndactyly and is usually obvious at birth.

Other related features are

1. Congenital heart defects, Dextrorotation, Pulmonary Artesia and Patent Ductus ateriosus.

2. Tracheoesophageal Fistula and Pyloric stenosis.

3. Polycystic kidneys and bicornuate uterus.

4. Excessive sweating and severe acne. [1]

Prenatal diagnosis can be made by demonstration of craniosynostosis, and syndactyly on prenatal ultrasound, and detection of FNGR gene mutation at 16 gestational week.[3] For sporadic Apert syndrome a three dimensional computed tomography and molecular biology is preferred.[1]It is generally accepted that management of Apert syndrome is multidisciplinary in approach, which should compose of neonatologists, neurosurgeons, craniofacial surgeons, plastic surgeons, otolaryngologists, orthodontists, orthopaedic surgeons, ophthalmologists, radiologists, geneticists, clinical psychologists and speech and language pathologists for the effective management of this condition.[4] In the light of the current literature, this article reviews and presents a case of Apert syndrome.

Case Report:

A 3 year old child male patient presented to department of oral medicine and radiology with the complain fo cleft palate. Patient's parent were informed during sonography at 5th month of pregnancy that the featus was having some defect in the head. Pregnancy and labour were uneventful and was not on medicines during the entire term of pregnanacy .The family history was non contributory. He was the first child born to nonconsanguineous parents. Since birth ,the child has craniosynostosis,achrocephaly,and syndactyly of hands and feet.At birth patient has complaint of cleft palate so advised platal plate but patient didn't go for the same. As patient was having complaint of vomiting, diarrhea,cough and cold, they visited civil hospital for the same complaint. Where all the investigation were carried out. He weighed 9.9 kg, his length was 88 cm, was conscious with good activity,normal hearing ability, normally presents primitive reflexes ,delayed in speech developmentand physical and mental activities. 2D echo and Dopler study was within normal limit with heart rate of 140 BPM. Then the patient was referred to dental hospital for cleft palate So he visited to Oral medicine and radiology department.

Clinical examination revealed features of acrocephalosyndactyly. The patient was found to have a flattened occiput with frontal prominence ,abnormal contour of head(Acrocephaly), shallow and downward slanting orbits with bilateral proptosis,hypertelorism,depressed nasal bridge, low set ears,retruded midface hypoplasic maxilla,and prognathic mandible with normal mouth opening,anterior skeletal open bite macroglossia with protruded tongue.(Figure 1 A,B) Bilateral fingers and toes presented cutaneous syndactyly,all digits of hands and feet are fused ,with the palm deeply concave and cup shaped and the sole supinated.(Figure 2 A,B,C) Intraoral clinical examination revealed that cleft palate, primary developing dentition shows mal-alignment of maxillary teeth ,rotated maxillary central incisors (Figure 3).

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Computerized tomography (CT) scan of maxillofacial region shows fusion of bilateral coronal and sagital suture with resultant brachycephaly with prominent forehead and resultant tower shaped skull,hypoplastic frontal sinus, with skeletal open bite ,spina bifida at C1 vertebra ,normal NCCT of brain(Figure 4).Molecular genetic testing (Karyotyping) was carried out but was non informative.

On the basis of all above findings clinical diagnosis Apert syndrome, (Acrocephalosyndactyly type 1) was considered. Crouzon, Carpenter, Apert- Crouzon syndrome (Acrocephalosyndactyly Type II),and Pfeifer syndrome were considered as differential diagnosis.Patient was advised to visit pedodontia,orthodontia and oral maxillofacial surgery department for correction of cleft palate and further treatment plan and being monitored in colloboration with plastic and reconstructive surgery,neurosurgery,and psychiatry specialists.

Discussion:

Apert syndrome is known as acrocephalosyndactyly type I which is a form of craniosynostosis. The inheritance of Apert syndrome is usually autosomal dominant, but sporadic cases have been reported and probably represent new mutations.It develops as a mutation of fibroblast growth factor receptor -2 gene (FGFR2) on 10q26 gene locus. FGFRs responsible for the formation of blood vessels, wound healing, embryonic evolution, and regulation of cellular division, growth, and maturation and plays an important role in signal pathways which function in the fusion process of skull bones.[3] Mutation in the FRFR2 gene has an effect on the mesenchymal development,which has an effect on tooth morphogenesis.Many oral manifestations can be attributed to the presence of this mutation.[5] Sporadic transmission indicates that a family may have a child with Apert syndrome when no other member of the family is affected. The recurrence risk of having another child with Apert syndrome for two unaffected parents is negligible. However, there is a higher mutation rate in males because the germ-cell divisions in males are greater than those in females. Hence the mutation rates increase with advanced paternal age.[1-4] The present case was sporadic as parents' age was below 30 years of age. In our case karyotyping is non informative.

According to Cohen, the incidence of Apert's syndrome is about 15 per 1,000,000 live births. Apert's syndrome has been rarely reported from India.More prevalent in certain races, highest in the Asians and lowest in the Hispanics. Males and females are affected equally.[1]

Phenotypic manifestations of the disease are explained by premature fusion of cranial sutures Premature closure of coronal sutures before 3 months of age causes shorter anteroposterior diameter, high, and prominent forehead associated with acrocephalic (cone-shaped) head.[3] Eye manifestations include hypertelorism, proptosis, and down slanting palpebral fissures. Nose, and nasal root is short, and widened,low set ears .[3] Our patient carries all specific facial characteristics.

The most prominent symptoms of this syndrome are syndactyly of hands, and feet,which is distinguish from other craniosynostosis. The hands of Apert's three types i.e. type I (spade), type II (mitten) and type III (rose bud). The present case has type II, mitten variety in which presence of fusion of fingertops that forms a concave palm.[1] Our patient also had the most marked symptoms namely acrocephaly, syndactyly of fingers, and toes. According to Dr. Trisha Macnair other associated abnormalities of the heart and blood vessels, gastrointestinal tract, kidneys and genital-urinary organs can also occur in Apert syndrome. [1-4,6] In present case patient has normal 2D echo , no any other related systemic abnormality detected till now.

Intraoral examination revealed a reduction in the size of the maxilla, particularly in the antero- posterior direction. This reduction may result in tooth crowding and an anterior open-bite of the maxilla. The mandible is

within normal size and shape, and simulates a pseudoprognathism. Dental anomalies such as impacted teeth, delayed eruption, ectopic eruption, supernumerary teeth, and thick gingiva are also common . Abnormalities of the upper and lower respiratory tracts include cleft palate, bifid uvula,mouth breathing, observed in most cases of Apert's syndrome, is related to alteration in facial growth.[6] In present case hypoplasic maxilla,anterior open bite ,crowding of maxillary teeth and cleft palate, macroglossia, mouth breathing were found.

Diagnosis of Apert syndrome is mainly dependent upon the clinical and radiological findings, molecular analysis. Computerized tomography (CT) scan with 3-dimensional reconstruction analysis of the calvaria and cranial bases has become the most useful radiological examination in identifying skull shape and presence or absence of involved sutures. CT scan precisely reveals the pathological anatomy and permits specific operative planning. Magnetic resonance imaging (MRI) is the imaging modality of choice for detecting intracranial abnormalities.[2] In our case CT finding shows fusion of bilateral coronal and sagital suture with resultant brachycephaly with prominent forehead and resultant tower shaped skull,hypoplastic frontal sinus and molecular genetic testing (Karyotyping) was non informative.

Differential diagnoses should include evaluation of other genetic disorders associated with craniosynostosis. The most common genetic disorders accompanying craniosynostosis include Crouzon, Carpenter, Apert- Crouzon syndrome (Acrocephalosyndactyly Type II),and Pfeifer syndrome. Apert syndrome can be differentiated by genetic analysis and various craniofacial appearance.[3]

Apert syndrome requires a multidisciplinary treatment approach, involving follow-up therapies provided by plastic and reconstructive surgery, neurosurgery, and psychiatry specialists,cardio-respiratory problems and interventions against brain compression should be prioritized during neonatal period. Multiple surgeries are required.[4] Majority of patients with Apert syndrome have mental retardation and only a small minority have normal intelligence. Mental status of these patients is influenced by surgical therapies, accompanying brain abnormalities, family and environmental factors. Therefore, the patients' psychological condition should also be regularly evaluated and psychological consultation should be provided. Our patient is currently being followed-up in collaboration with orthodontic,pedodontic and oral maxillofacial surgery, plastic and reconstructive surgery,neurosurgery,and psychiatry departments.

Conclusion

The rarity of the AS, the typical craniofacial and dental features, remains a major medical condition with considerable morbidity. The information and the motivation of the parents regarding the necessity of the treatment and the extensive use of home prevention methods are essential. Early daignosis of AS is important to provide correct management of preventable oral diseases such as dental caries,periodontal disease and provide management of cleft palate, guiding proper eruption pattern of teeth.

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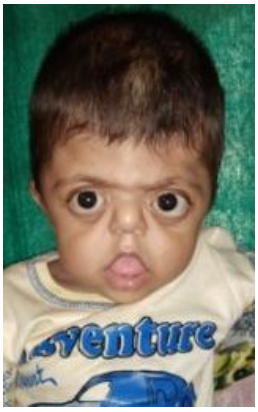
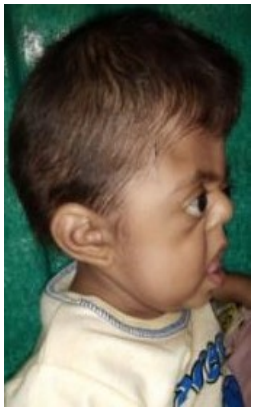

Figure -1 A **Figure 1 B**

Figure 1 (A) Frontal view and (B)Side view. Note the frontal prominence ,acrocephaly, short and wide nose with depression of the nasal bridge,Hypertelorism, proptosis hypoplasic maxilla,anterior skeletal open bite macroglossia with protruded tongue.

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