

CASE REPORT

Apert's syndrome: Report of a rare case

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ABSTRACT

Apert's syndrome (AS), a form of acrocephalosyndactyly, is a rare congenital disorder with autosomal dominant mode of transmission; characterized by craniosynostosis, midface hypoplasia, and syndactyly of hands and feet. The rarity of the syndrome and similarity of features with other craniosynostosis syndromes makes it a diagnostic dilemma. Genetic counseling and early intervention form an essential part of treatment. Because of the paucity of reported cases in Indian literature and typical features in oral cavity, a dentist should be competent to diagnose and form a part of the multidisciplinary management team. Here, we report a case of a 14-year-old boy with AS.

Key words: Apert's syndrome, craniosynostosis, syndactyly

INTRODUCTION

Apert's Syndrome (AS), a form of acrocephalosyndactyly, is a rare congenital disorder characterized by craniosynostosis, midface hypoplasia, and syndactyly of hands and feet.^[1-6] AS was first mentioned as early as 1842 by Baumgartner and 1894 by Wheaton. In 1906, French pediatrician 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.^[1,4,6-11] According to Cohen, the prevalence of the syndrome is estimated to be approximately one in 65,000 newborns^[4,5,12] and accounts for about 4.5% of all cases of craniosynostosis.^[4,10] More than 98% of cases with AS are caused by specific missense substitution mutations, involving adjacent amino acids (i.e., Ser252Trp, Ser252Phe, Pro253Arg) in the linker between the second and third extracellular immunoglobulin domains of fibroblast growth factor receptor 2 (FGFR2), which maps to chromosome bands 10q25-q26.^[2,4,7,9,13] The familial pattern, equal number of affected males and females, and increased paternal age in sporadic cases strongly suggest autosomal dominant inheritance.^[2,4,6,8-10,13] The newborn infant presenting AS shows a fused coronal suture and agenesis of the sagittal and metopic sutures, which results in a wide defect extending from the glabella to the posterior fontanelle.^[9,12] Additionally, the sphenoccipital, sphenothmoidal, and frontoethmoidal sutures fuse early; resulting in a turribrachycephalic skull.^[5,9,11,12] The typical appearance includes a flat, elongated forehead

with bitemporal widening and occipital flattening.^[1-3,7,8,11-13] Cloverleaf skull appearance depends on the degree to which the temporal bones are obliquely placed.^[1,3] The nose is short and broad with a bulbous tip and nasolabial angle is diminished.^[1,3,7,11] The midface hypoplasia contributes to retruded middle third of the face, resulting in relative mandibular prognathism.^[1,2,5-8,10,12-15] The lips frequently assume a trapezoid configuration because the upper lip is lifted in the midline. The configuration of the hard palate seems unique and is characterized by an arched palate with bilateral swellings of the palatine processes, resulting in a pseudocleft in the midline.^[3,5,6,11,12,14] Cleft of the soft palate is observed in 30% of the cases.^[1-3,5-8,15] It becomes readily apparent that individuals become mouth breathers out of necessity due to reduced airway patency with subsequent anterior open bite.^[5,14] The most readily observed dental mal-relationships are severe maxillary anterior open bite and a severely crowded and retrusive maxillary arch due to the constricted secondary palate. Therefore, the skeletal class III is not the result of a prognathic mandible, but is due to the sagittal maxillary hypoplasia.^[1,5,6,11,12,14,15] Dental anomalies include delayed and ectopic eruption, shovel-shaped incisors, crowding of teeth, especially in the maxilla, anterior open bite, bilateral crossbite, mandibular overjet, and midline deviation.^[1,3,5,6,8,11] There is syndactyly or webbing involving second, third, and fourth fingers with the expression ranging from partial fusion of the skin to a true osseous syndactyly of fingers and toes. When the fingers are completely fused, there is often a common nail.^[1,2,6,7,11] There can be a similar deformity involving the foot and hence described as 'mitten hand' and 'sock foot'.^[2,6-8] Radiographs of hands, feet, and skull show syndactyly of hands and feet, malformation of midfacial bones, and craniosynostosis of skull.^[6] Prenatal detection of specific FGFR mutations now allows definitive antenatal diagnosis of AS, other craniosynostosis syndromes, and skeletal dysplasias. Prenatal detection of the syndrome became feasible only in recent years

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after the advent of routine prenatal ultrasound screening for fetal anomalies.^[4] Plain skull radiographs including anteroposterior, lateral, and Towne's projection are usually done. Radiographs of hands and feet are taken to see syndactyly of hands and feet.^[6] Now, three-dimensional computed tomography (CT) scans have added a further dimension in planning surgery of these patients and for objective assessment of operative outcome. Ideally, treatment of AS begins at birth with proper diagnosis, identification of the child's individual needs, and a proper facility to administer what is needed.^[5,6] Treatment involves multidisciplinary teamwork including craniofacial surgeon, neurosurgeon, neurologist, ENT (ear, nose, and throat), audiologist, pediatrician, speech pathologist, oral surgeon, psychologist, and an orthodontist.^[2,5,6,10] Surgical care involves early release of the coronal suture and frontoorbital advancement with reshaping to allow proper brain growth and reduce dysmorphic and unwanted skull growth changes.^[2,13] Craniotomy is often performed during the 1st year of life to treat the craniosynostosis. Frontofacial advancement and midface advancement can be performed later to correct the proptosis and midface hypoplasia. Coordinated orthodontic therapy is often necessary to bring unerupted teeth into place and improve occlusion.^[6,9]

CASE REPORT

A 14-year-old boy presented with the complaints of malaligned teeth, difficulty in chewing food, and facial deformity. His past medical history revealed that he had undergone suturotomy surgery for relieving craniosynostosis 11 years ago and plastic surgery for relieving syndactyly 5 years ago. His chest radiograph revealed no abnormality. He had hypochromic microcytic anemia since 11 years and experienced seizures occasionally since 1 year. He had bilateral optic disc edema since birth, for which the treatment was still ongoing. He also suffered from severe acne last year for which treatment lasted for 7-8 months. Prenatal history revealed that he had premature

birth by 40 days. His parents were nonconsanguineously married in their 3rd decade. No other family members were affected by same features.

On examination, the boy was found to have a flattened occiput with frontal prominence, abnormal contour of head (brachycephaly), shallow and downward slanting orbits with bilateral proptosis, hypertelorism, retruded midface, and prognathic mandible [Figures 1 and 2]. Intraoral examination showed normal mouth opening with anterior open bite and a high arched (V-shaped) palatal vault. Maxillary alveolar ridges were thick with crowding of maxillary teeth. Mandibular teeth were normally aligned [Figure 3]. He had symmetrical syndactyly with complete fusion of all digits of hands (except thumb) and feet [Figure 4]. The systemic examination revealed that patient has some ophthalmologic, ear, and central nervous system abnormalities.

On investigation, Water's view radiograph showed deformity of maxilla with malaligned maxillary teeth and deviated nasal septum [Figure 5]. Lateral cephalogram showed concave profile with retruded midfacial bone and fusion between cervical vertebra C5, C6, and C7 [Figure 6]. CT scan of the brain revealed premature fusion of coronal and lamdoid sutures with bilateral proptosis, deviation of nasal septum, and turriccephalic skull. It also revealed a bone defect in the vault of skull due to previous operative procedures [Figure 7]. Magnetic resonance imaging (MRI) of brain also revealed abnormal skull shape with similar changes. Due to these typical features and presence of the triad of craniosynostosis, syndactyly of hands and feet with maxillary hypoplasia, patient was diagnosed with AS. Patient was advised orthodontic treatment with orthognathic surgery for correction of the facial dysmorphisms. As patient was not ready for any interventional procedures, only oral prophylactic measures were taken and he was kept under regular follow-up.

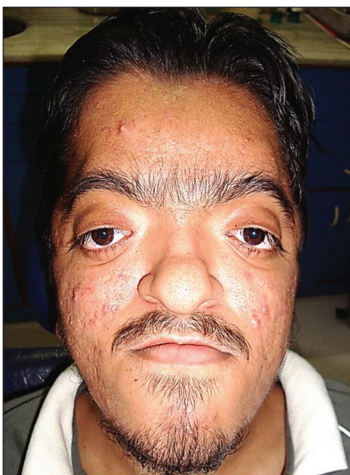


Figure 1: Extraoral front view of patient showing parrot beak nose, hypertelorism, downward slanting outer canthus of eyes, and depressed nasal bridge



Figure 2: Extraoral lateral view of patient showing concave facial profile with mandibular prognathism and large, low set ears

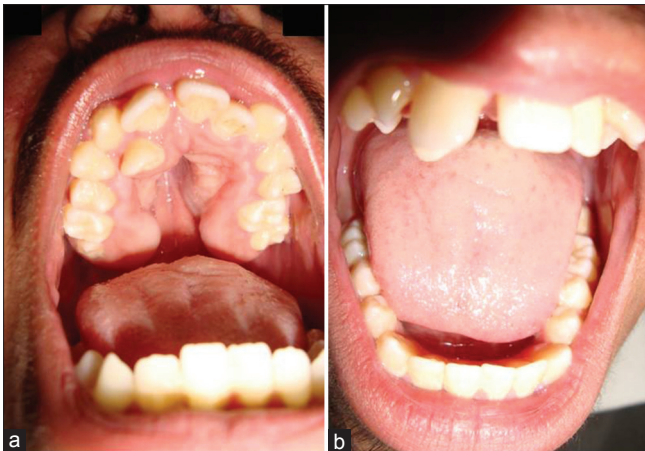


Figure 3: (a and b) Intraoral views showing crowded maxillary arch with deep pseudocleft in midline and normally aligned mandibular teeth



Figure 4: (a and b) Photographs showing surgically operated syndactyly in hands and syndactyly of feet

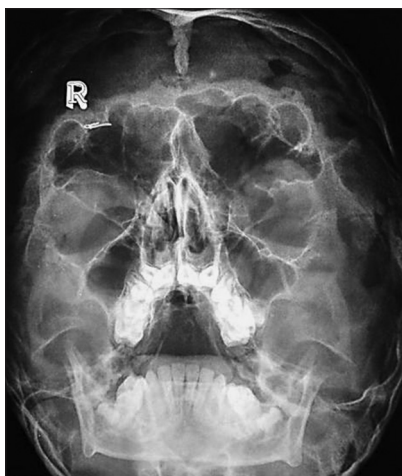


Figure 5: Water's view showing abnormal skull shape, facial asymmetry, and deviated nasal septum



Figure 6: Lateral cephalograph showing midface hypoplasia and fusion of cervical vertebra C5, C6, and C7

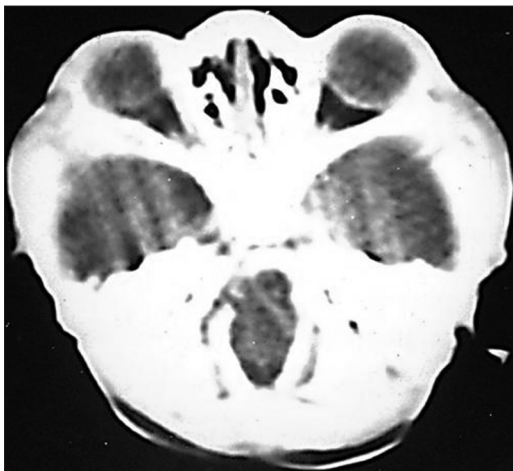


Figure 7: Axial section of computed tomography scan showing bilateral proptosis, fused lambdoid, and coronal sutures

DISCUSSION

Craniosynostosis are a heterogenous group of syndromes characterized by a premature sutural fusion that may occur

alone or together with other anomalies.^[3,6,7,13,15] More than 70 craniosynostosis syndromes are described, which amongst many others, include AS, Crouzon syndrome, Pfeiffer syndrome, and Jackson-Weiss syndrome.^[2,6,15] AS is classified as branchial arch syndrome, affecting the first branchial arch.^[6] The following etiological hypotheses have been proposed: Virus embryopathy following maternal infection; antenatal drug consumption by mothers; an inflammatory process at the base of the skull and maldevelopment of the skull; high paternal age.^[9] Apert fibroblasts synthesized greater quantities of glycosaminoglycans (GAGs). The amount of hyaluronic acid (HA) secreted by Apert fibroblasts was much higher than that secreted by normal fibroblasts, but because the absolute values of heparan sulfate, chondroitin sulfate, and dermatan sulfate also rose in Apert media, the HA-sulfated GAG ratio was similar in the media obtained from both populations.^[15] Cohen (2005) states that sutural agenesis in the midline region is characteristic of AS. This midline defect normally obliterates during 2nd-4th year of life.^[10] Once a suture becomes fused, growth perpendicular to that suture becomes restricted, and the fused bones act as a single bony structure while compensatory growth occurs at the remaining open sutures to allow continued brain growth.^[6] In AS, there is often no suture in the metopic or sagittal regions, but there are sutures in the coronal, lamdoid, squamosal, and sphenotemporal regions.^[10] The anterior cranial fossa is very short with consequent shallow orbits, ocular proptosis, orbital hypertelorism, downslanting palpebral fissures, and interruption of the eyebrows.^[1,3,6,8,12,15]

The nasal bridge is depressed.^[2,3,5-7,11,14,15] There is an overall tendency for the ears to be large and low set.^[1,3,5,6] These findings are in accordance with the current case. The most common cervical spine abnormality is intervertebral fusion.^[5] Dental anomalies include crowding of teeth, especially in the maxilla, is in accordance with the current case.^[1,3,5,6,8,11] Other skeletal abnormalities include limited mobility at glenohumeral joint and elbow joint, multiple epiphyseal dysplasia, very short or absent neck of scapula, small capitulum, and flat radial head.^[2,6,7]

Besides skeletal anomalies, AS can be associated with a variety of visceral malformations, particularly of the central nervous system, and it is often accompanied by mental retardation.^[4,8] Many other anomalies are associated with AS, such as central nervous system, cardiovascular, urogenital, and dermatologic abnormalities.^[13] Central nervous system abnormalities include malformations of the corpus callosum, the limbic structures, or both, megalencephaly, gyral abnormalities, encephalocele, pyramidal tract abnormalities, hypoplasia of cerebral white matter, and heterotopic gray matter. There is also an increased incidence of delayed mental development in these children, but many of them develop normal intelligence.^[2,6,7,11,14] The patient reported hereby had normal intelligence for his age. Commonly associated systemic features include cardiac anomalies, visual and hearing defects, and varying degrees of acne.^[2] This is in accordance with the present case.

Apert's and Crouzon syndrome seem to be the same syndrome, with the exception of syndactyly of hands and feet in AS.^[6,8,9] When fusions are present, C5–C6 involvement in the Apert's syndrome and C2–C3 involvement in Crouzon syndrome separate the two conditions in most cases.^[15] Also, cleft or pseudocleft palate is a frequent finding in AS; whereas these traits are extremely rare in Crouzon syndrome.^[6,9] These features favor the diagnosis of Apert's syndrome over Crouzon syndrome in the current case. The presence of broad thumbs and halluces in association with cutaneous syndactyly differentiate Pfeiffer syndrome from Apert's syndrome.^[3]

It is important to evaluate the entire length of each suture as a small segment only may be involved (not seen on plain radiography) resulting in a functional synostosis of the whole suture. This is only effectively done with axial CT images on bone window settings.^[7] The CT findings of the case under consideration revealed the fused coronal and sagittal sutures, which is in accordance with literature.

Various complications arising due to late diagnosis, include defective brain development, mental retardation, increase in facial deformity, prognathic mandible, etc.^[6] Surgical separation of digits (mitten glove syndactyly) provides cosmetic results, but relatively little functional improvement.^[2,5,6] The operation should be planned to define the digits and allow unimpeded skeletal growth. If surgery is postponed, incongruities of length and growth between fingers usually produce additional deformities in an already deformed hand.^[11]

CONCLUSION

The rarity of the AS, the typical craniofacial and dental features, the genetic transmission makes it necessary to carry out genotyping and genetic counseling of each diagnosed case. 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. This case report attempts to throw some light on this rare syndrome.

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