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Case Report

CROUZON SYNDROME - A RARE GENETIC DISORDER. A CASE REPORT AND A DETAILED REVIEW OF LITERATURE

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ABSTRACT

Crouzon's syndrome is an autosomal dominant disorder with complete penetrance and variable expressivity. Described by a French neurosurgeon in 1912, it is a rare genetic disorder. Crouzon's syndrome is caused by mutation in the *fibroblast growth factor receptor 2* (FGFR2) gene. Normally, the sutures in the human skull fuse after the complete growth of the brain, but if any of these sutures close early then it may interfere with the growth of the brain. The disease is characterized by premature synostosis of coronal and sagittal sutures which begins in the first year of life. Here is a Case report of a 6 year old boy is presented with characteristic features of Crouzon's syndrome clinically and radiographically.

Key words: Crouzon Syndrome; Rare Case; Premature Synostosis, Mutation.

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INTRODUCTION

Crouzon Syndrome is otherwise called as craniofacial dysostosis [1,2]. Crouzon syndrome is an autosomal dominant disorder [3,4]. But there is an equal incidence of sporadic cases which probably represent new mutations [5]. The sporadic cases are postulated to be associated with advanced paternal age and some investigators have found that this mutation is more common in the sperm of older men. Crouzon is characterized with pre-mature closure of cranial sutures, midfacial hypoplasia and orbital deformities [4,6,7]. Crouzon syndrome is the most common craniofacial dysostosis occurring without syndactyly [8,9]. This condition was first reported by a French Neurosurgeon, Octave Crouzon in 1912 in a mother and daughter [8,9]. Facial abnormalities typically include proptosis owing to shallow orbits: divergent strabismus or exotropia,ocular hypertelorism, and a small, underdeveloped upper jaw(hypo plastic maxilla), with protrusion of the lower jaw (relative mandibular prognathism).multiple staged surgeries are the general treatment plan for children with crouzon syndrome. With proper treatment, children can be productive and active members of mainstream society [10]. The diagnosis is based on clinical findings and radiological examination. Both genders are equally affected. The condition is thought to arise due to a mutation in the Fibroblast Growth Factor Receptor-2 (FGFR-2) gene in both the sporadic and the inherited Cases [3,4,11]. The genetic defect from mutation in the fibroblast growth factor receptor 2 (FGFR) on chromosome locus 10q25q26 which results in the early fusion of the skull bones during the development of the foetus. Cranial malformation in Crouzon syndrome depends on the order and rate or progression of sutural

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Synostosis [2,12]. Here we present a case of crouzon syndrome in 6 year old boy with review of literature.

Definition/ meaning:

Crouzon syndrome, also called craniofacial dysostosis, is one of a large group of facial birth defects in which there is abnormal craniofacial fusion (joining between some of the bones of the skull and of the face). This fusion does not allow the bones to grow normally, affecting the shape of the head, appearance of the face and the relationship of the teeth [10].

CASE REPORT:

A 6 year old male child reported to the dental op with his parents with the complaint of decayed tooth in his right upper back teeth region for past 1 week. he had undergone craniectomy before 5 years for relieving the sutures. On family history, Patient, is of first birth order, born to a non-consanguineous couple aged 27 and 28 years. Patient has a younger sibling, who is apparently normal and all other family members are also apparently normal. On extra oral examination, Head appears to be dolycocephalic, flat face with concave profile and increased interocular distance(hypertelorism), strabismus, depressed nasal bridge. Upward slanting of lower palpebral fissures. Small everted ears. Hypoplastic maxilla, Increased skull ratio which means the upper part of the skull is large. Hands were normal and feet showed sandal gap deformity. On intra oral examination, the patient's palate is high arched. Based on this a provisional diagnosis of Dental caries with pulpitis of 55 other findings Generalized marginal Gingivitis, crouzon syndrome. Patient was subjected for further investigations, the patient was subjected for opg. Opg revealed number of teeth present:19, missing: 74,64. Lateral ceph reveals thickening of cortex in the frontal region causing frontal bossing, absence of frontal sinus, depth is increased in the pituitary fossa. Anteroposterior view and true latera skull radiograph reveals hazy radiopaque mass interspersed throughout the skull, hypoplastic maxilla, mandible and zygomatic arch with beaten copper appearance of the skull. Chest x ray appears to be normal. Hand wrist radiograph Right and Left reveals absence of few carpals. Based on this a FINAL DIAGNOSIS of Crouzon syndrome was given.

Table 1. Abnormalities associated with Crouzon syndrome.

Cranium	Craniosynostosis Brachycephaly and acrocephaly Palpable ridge Flat occiput Frontal bossing
Facial Features	Maxillary retrusion Malar deficiency Relative mandibular prognathism
Ear	Low set ear Conductive hearing loss Bilateral atresia of auditory meatus
Eye	Downslanting palpebral fissure Exophthalmos Iris-coloboma Ptosis Exposure keratitis Hypertelorism Divergent strabismus Nystagmus
Nose	Beaked nose (psittichorhina)Deviated nasal septum
Mouth	Short upper lip Class III malocclusion with maxillary crowding High arched and narrow palate Pseudocleft(bilateral palatal swelling) Cleft palate and bifid uvula
Neurological	Headache Mild to moderate mental retardation Seizures
Musculoskeletal	Cervical spine abnormalities (scoliosis) Calcification of stylohyoid ligament

	Meniere'disease: (vertigo, dizziness, and/or ringing in the ear).
Respiratory system	Breathing difficultySleep apnoea
Cutaneous	Acanthosis nigricans

FIG.A(PROFILE)

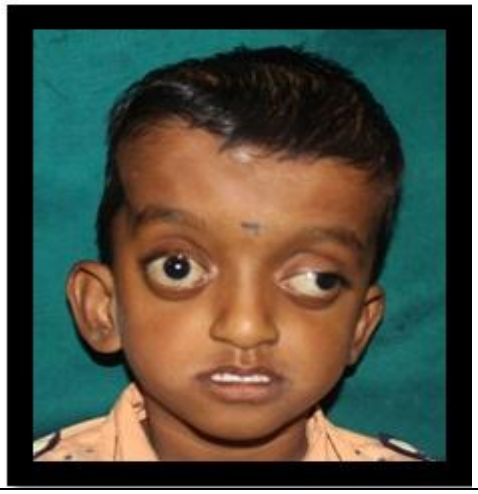


FIG.B(OPG)

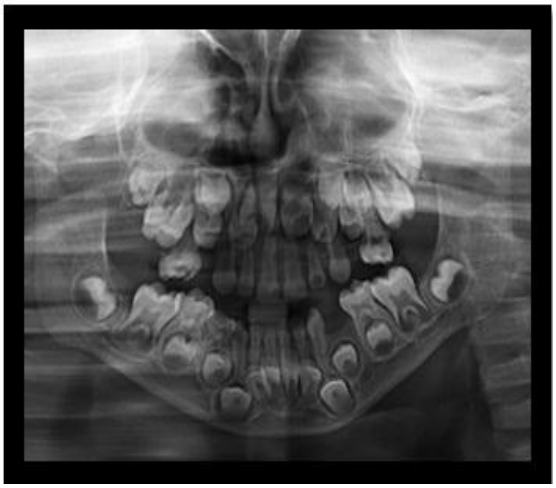


FIG.C

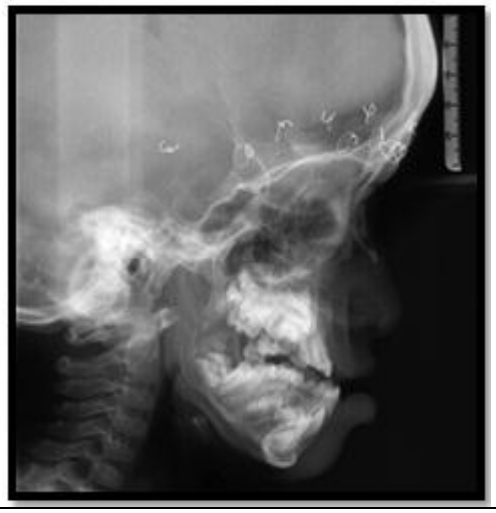


FIG.D&E

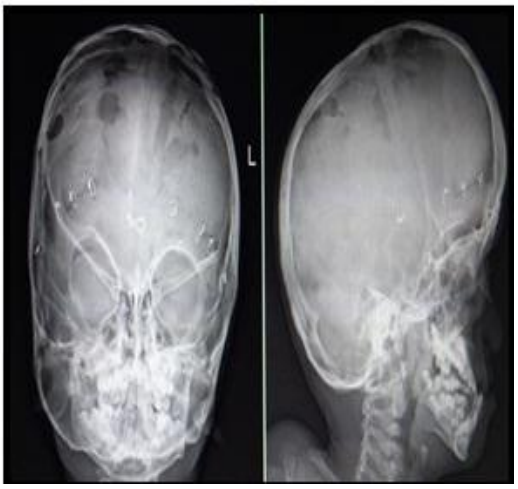
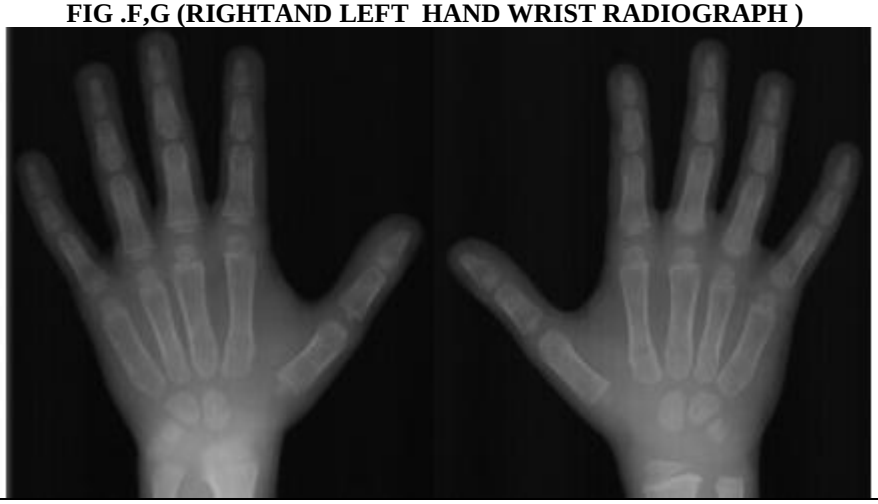


FIG .F,G (RIGHTAND LEFT HAND WRIST RADIOGRAPH)



DISCUSSION

The Crouzon's Syndrome is the most frequent of the craniofacial diseases and is characterized for being a rare genetic disorder that can be diagnosed upon the birth or during the childhood [13]. The dominant transmission range is of 100% and the large scale penetrance with

phenotypic expression is highly variable [9,13-18] CS is inherited as an autosomal dominant fashion but there is an equal incidence of sporadic cases which probably represent new mutations [5]. The sporadic cases are postulated to be associated with advanced paternal age and some investigators have found that this mutation is more common in the sperm of older men [5,19]. The phenotypic features of CS may be absent at birth and evolve gradually during the first few years of life [5,26]. The variability in both cranial and facial malformations (ravikumar) 50% of the Crouzon's syndrome incidents are not inherited but result from new spontaneous mutations [13-17]. The fibroblast growth factors are intrinsically related to the extracellular matrix. When the extracellular matrix presents FGFR2's mutation, it begins to secrete cytokines both in autocrinous and paracrinous manner and these may modify the very matrix. It is allegeable that such changes are in the osteogenic process change genesis, which explains the pathologic variations found. [13,24,25]. This syndrome was originally described in 1912 by a French neurosurgeon. He described four essential characteristics including exorbitism, retromaxillism, inframaxillism and paradoxic retrogonia [4,7].

The variability in both cranial and facial malformations depends on the order and rate of progression of sutural synostosis. Premature synostosis commonly involves the sagittal and coronal suture. Lambdoidal sutures are occasionally involved. The craniosynostosis of the sagittal is predominant in boys, while the coronal is more common in girls [5,13]. The type of obliterated sutures determines the shape of the cranial vault. The skull shape can vary from brachycephaly (most commonly observed) to scaphocephaly (boat-shaped head), oxycephaly, plagio, cephaly, trigonocephaly (triangle-shaped head) or in severe disease cloverleaf skull (kleeblattschädel) like deformity [5,13,3]. The obstruction of the upper respiratory passages develops, following the septal diversion, abnormalities to the center of the nose and epipharynx narrowing [13,17]. The optical atrophy may be a complication resulting from the narrow optical channel. Blindness following the optical atrophy by the intracranial hypertension may also occur. Other characteristics generally seen in these patients are visual disturbances relating to a muscular unbalance. The patients have hyperemia, bilateral ocular irritation and sensation of long-term nuisance for being constantly rubbed [13,17].

Acanthosis nigricans, a disorder that causes brown to black velvet stains, generally on the neck, under the arm or in the groin region is the main Crouzon's syndrome dermatologic manifestation, and it is detectable after the childhood [13,17]. Generally, the psychomotor development is normal and the mental ability of these patients is usually within the normality [17]. Other less frequent characteristics are associated. The diminished mental function is present in about 12% of the patients; headaches and apprehensions are ascribed to the high intracranial pressure; a progressive hydrocephaly occurs in 30% of these patients and accompanying the cephalea there also may be vomits and/or convulsions. The Crouzon's syndrome early diagnosis is critical to avoid cranial hypertension, as well as visual disturbances and blindness, etc. Therefore, it is important to pay close attention to the patients that have some Crouzon's syndrome carrier relative precedent or that have a certain level of exophthalmia. We must be attentive to the cerebriform impressions development in the cranium-occipital region, cranial hypertension and the appearing of other characteristics of the syndrome [13,17].

Cervical region radiologic abnormalities include butterfly-shaped vertebra and fusion of the posterior bodies and elements, present in about 18% of the patients. C2-C3 and C5-C6 are equally affected (5,6). The magnetic resonance is used to view corpus callosum occasional agenesis and optical atrophy [13-17].

Radiographs, MRI, genetic testing, X rays and CT scans can be used to confirm the diagnosis. Ultrasonic prenatal diagnosis of crouzon syndrome has been reported, however molecular testing is more accurate and reliable than ultrasonography. CT scan brain shows signs of raised intracranial pressure, fusion of coronal and sagittal sutures and 3d images will reveal copper beaten appearance. Preimplantation genetic diagnosis for crouzon syndrome by blastomere biopsy samples from cleavage staged embryos may be detected by mutational analysis [20].

Five autosomal dominant craniosynostosis syndromes (Apert, Crouzon, Pfeiffer, Jackso-Weiss and Crouzon syndrome with acanthosis nigricans) result from mutations in FGFR genes. The TWIST gene, which is also known to cause Saether-Chotzen syndrome, serves as transcription factor and work with FGFR gene family, affect head and limb region [4].

Management of Crouzon's disease is multidisciplinary and early diagnosis is important. In the first year of life, it is preferred to release the synostotic sutures of the skull to allow adequate cranial volume thus allowing for brain growth and expansion. Skull reshaping may need to be repeated as the child grows to give the best possible results.] If necessary, mid-facial advancement and jaw surgery can be done to provide adequate orbital volume and reduce the exophthalmoses

to correct the occlusion to an appropriate functional position and to provide for a more normal appearance. Prognosis depends on malformation severity [21-23].

CONCLUSION

Crouzon syndrome is a generic disorder caused by mutant gene. Crouzon syndrome is an autosomal dominant disorder diagnosed in infancy and referred to a major hospital that has a craniofacial unit. Medical care focuses on managing the symptoms and surgically correcting problems. A team of specialists are involved in the care. An understanding of these abnormalities is necessary so the pediatric nurses can make the appropriative referral to insure the children receive the best available care.

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