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EDİTÖRE MEKTUP / LETTER TO THE EDITOR

Crouzon syndrome in two siblings

İki kardeşte Crouzon sendromu

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Dear Editor,

Crouzon syndrome is an autosomal dominant disorder with complete penetrance and variable expressivity[1]. In the year 1912, French neurosurgeon Octave Crouzon described this autosomal dominant rare genetic disorder[2]. Crouzon syndrome is a disorder characterized by pre-mature closure of cranial sutures, mid-facial hypoplasia and orbital deformities[3]. The reported occurrence of Crouzon syndrome is 1:25000 live births, which makes it the most common of over 70 conditions which has pre-mature fusion of the cranial sutures as one of its features. A positive family history is stated to occur in approximately 44-67% of the reported cases[4].

The diagnosis is established based on the findings of the clinical and radiological examination. There is no significant gender predilection. Both genders are equally affected. The mutation in the Fibroblast Growth Factor Receptor-2 (FGFR-2) gene is believed to be the cause in both the sporadic as well as inherited cases. The risk factor increases with increased paternal age, children of those parents with the manifestations of the disorder or may be carrier of the mutated gene[5].

In the familial type, the syndrome is inherited as an autosomal dominant condition. It will manifest in each generation in the family so that one out of two children will have Crouzon syndrome. The severity of the condition varies from patient to patient. In this article we report Crouzon syndrome in siblings. A 5 year old female patient reported to the Department of Oral Medicine and Radiology with chief complaint of decay in the upper front teeth since 3 months. The history was recorded as told by the parents. Patient noticed the decay in the maxillary incisors 3 months back. No pain or other associated symptoms. There was no history of systemic illness or any hospitalization since birth. Parents gave a history of defects in the face and skull since the time of birth. Family history revealed that the patient was first of the two siblings. Grandmother and younger brother are known to have the same syndromic features. There was no history of consanguineous marriage between the parents.

The mothers age at the time she conceived her first and second child were 25 and 27 respectively, while the fathers age during the first child birth was 30 and the second child birth was 32. Patient was conscious, co-operative, well oriented to time, place and person, moderately built and nourished. On extraoral examination patient was found to have straight facial profile, brachycephaly, parietal bossing, flattened forehead, shallow orbits, ocular proptosis, hypertelorism, flattened nasal bridge, malar hypoplasia, midface hypoplasia, malformation of the toe and incomplete polydactyly [Figure 1].

Intraoral examination revealed high arched palate, decayed primary maxillary central and lateral incisors, missing primary mandibular left lateral incisor and mandibular right central incisor [Figure 3].

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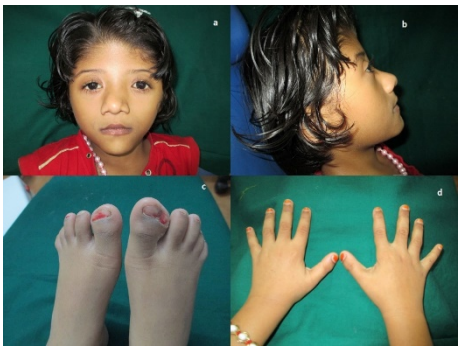


Figure 1. Extraoral features of case 1

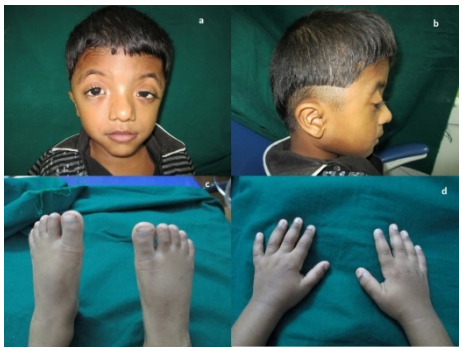


Figure 2. Extraoral features of case 2

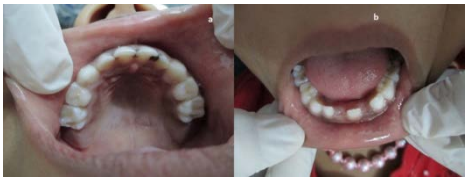


Figure 3. Intraoral photograph of Case 1.

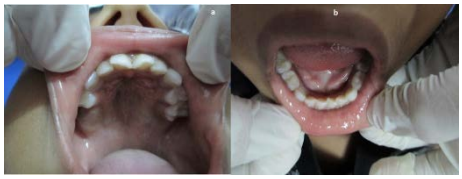
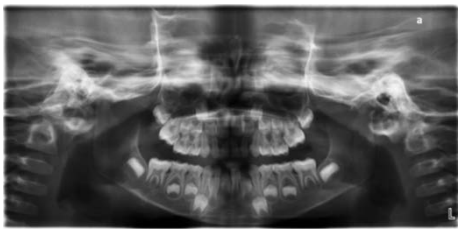


Figure 4. Intraoral photograph of Case 2.



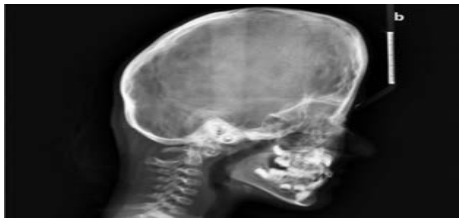


Figure 5. Panoramic radiograph and lateral Cephalogram showing radiographic features of case 1.

Panoramic radiograph revealed the presence of full complement of maxillary and mandibular teeth, decayed primary maxillary central and lateral incisors, missing primary mandibular left lateral incisor and mandibular right central incisor. Erupting tooth buds of permanent teeth are also visible. Lateral cephalogram revealed presence of multiple overlapping layers of bone characteristic of beaten metal appearance of the skull and flattening of frontal bone [Figure 5].A 3 year old male patient accompanied Case 1 with a chief complaint of defects in the face since birth. On eliciting the medical and family history it was revealed that the 3 year old boy was the brother of Case 1 and younger to her for 2 years. They are the only two children of the parents.

Patient was conscious, well oriented to time, place and person, moderately built and nourished. He was co-operative for clinical examinations but non-compliant for radiographic investigations. Hence radiographic investigations could not be performed.

On extraoral examination patient was found to have straight facial profile, brachycephaly, parietal bossing, flattened forehead, shallow orbits, ocular proptosis, strabismus, hypertelorism, flattened nasal bridge, malar hypoplasia, midface hypoplasia and brachydactyly [Figure 2].Intraoral examination revealed high arched palate and unerupted maxillary right primary second molar [Figure 4]. A provisional diagnosis of Crouzon syndrome was arrived at. Apert syndrome, Pfeiffer syndrome, Carpenter syndrome and Saethre-Chotzen syndrome were considered as differential diagnosis.

Crouzon syndrome is an autosomal dominant disorder with complete penetrance and variable expressivity, but, about one third of all the cases are sporadic and spontaneous[1]. The mutation in the genes that codify receptor 2 of the (FGFR2) fibroblast growth factor, is responsible for the deformities observed in Crouzon syndrome. 25 mutations have already been recognized in the FGFR2 and is associated with the pathogenesis of

Crouzon's Syndrome[6].

The fibroblast growth factors are inherently linked to the extracellular matrix. When the FGFR2's mutation is presented to the extracellular matrix, it starts secreting cytokines in autocrinous and paracrinous manner. This might transform the extracellular matrix. It is suspected that such changes in the osteogenic process elucidates the pathologic variations found in the syndrome[7]. There is yet another hypothesis postulated which states that the malformations in the cranium is responsible for the premature fusion of the cranial sutures. The midfacial hypoplasia and the shape of the cranium changes in agreement with the sutures that are involved in premature fusion[8]. The anomalies found show too many variations from one case to another. Some variations are seen even in between members affected from the same family. The order and range in which the suture fuses decide the degree of malformation and incapacity[9].

The trio composed of cranial deformities, facial anomalies and exophthalmia that were described by Crouzon in the year 1912, forms the Crouzon's syndrome that we know today. The brachycephaly in Crouzon syndrome is due to the premature closure of cranial sutures, midfacial sutures and premature synostosis of the cranium.[9]

The affected individuals always have high and large forehead, with convexity in the region of the anterior fontanelle, flattening of the occipital region and occipital protuberance. This gives the appearance of tower shaped cranium. Maxillary hypoplasia, midfacial hypoplasia are responsible for a number of alterations in the facial aspect. Apart from this, V shaped dental arch, altered occlusion, spacing in between teeth are seen. Occasionally there is presence of narrowing or congenital cleft in the roof of the mouth, cleft uvula, short upper lip and inferior lip, prominent tongue, maxillary hypoplasia and relative maxillary prognathism and micrognatia. Conductive hearing deficit, atresia of acoustic meatus, hypacusis and malformations of the middle ear are other manifestations[9].

Ocular abnormalities like shallow orbits, bilateral ocular proptosis, hypertelorism, divergent strabismus, optical atrophy, conjunctivitis or exposure keratoconjunctivitis and a non-explained loss of visual accurateness may also be seen in few cases. Rarely, nystagmus, coloboma of the iris, anisocoria, microcornea or megalocornea, cataract, blue sclera, glaucoma and globe luxation may be seen[9]. Brown to black velvet stains on the neck, underarm or in the groin region called Acanthosis nigricans may be noticeable after the childhood[9].

Crouzon syndrome must be differentiated from Apert syndrome. The Apert syndrome has features very similar to those found in the Crouzons syndrome. Apert syndrome is accompanied with deformity of the hands and feet, with symmetric syndactyly of the second, third and fourth digits. Hyperacrobrachycephaly is commonly observed and the occiput is flattened. Apart from these differences significant number of patients with Apert syndrome are mentally retarded[10]. Differential diagnosis is also made with the syndromes like Pfeiffer, Carpenter and Saethre-Chotzen. In Pfeiffer syndrome apart from craniosynostosis there is presence of broad thumb, broad great toes, partial soft tissue syndactyly involving the digits 2 and 3 and sometimes digits 3 and 4 of both hands and feet. The skull is usually turribrachycephalic in nature. Carpenter syndrome is autosomal recessive rare disorder, showing tower-shaped skull, additional or fused digits, obesity, intellectual disability and reduced height. Saethre-Chotzen syndrome shows clinodactyly of the fifth finger, syndactyly high forehead, bilateral single plamar transverse creases, brachydactyly and brachycephaly[11].

The treatment for Crouzon syndrome is multidisciplinary and gives acceptable results. Symptomatic treatment with hearing aid, phonotherapy, psychopedagogy, family orientation, genetic advice, speech therapy can contribute for improving the quality of life. Several surgical techniques are employed to prevent the early fusion of craniofacial sutures and thus reduce the head pressures thereby reducing the cranial and facial bone deformities. The appropriate age to carry out a surgery is before 1 year of the child's life. This is beacuse the bones are more flexible at this age. In the first year of life, it is desirable to release the craniosynostosis so as to allow brain growth and expansion[7].

The plastic surgery can be valuable in Crouzons syndrome. The methylmethacrylate is a polymer that has been used in the cosmetic surgery to smooth and harmonize the facial contour[12].

Crouzon syndrome is one of the few syndromes in which the cosmetic and esthetic results may be very

effective, satisfying and strikingly effective. These patients may ultimately come to lead a relatively normal life. Early recognition and prompt treatment of such cases will help the patients lead and very normal life. Patients with a positive family history should be counselled for a possible manifestation of the syndrome in their offspring.

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