

# Peripheral Ossifying Fibroma in a Child with Existing Crouzon Syndrome- A Case Report

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## ABSTRACT

**Introduction:** Crouzon syndrome represents an autosomal dominant syndrome, characterized by craniosynostosis. Other features like exophthalmous, proptosis, midface hypoplasia and dental features such as misaligned teeth or dysphasia can be evident. Whilst Peripheral ossifying fibroma is a relatively common reactive gingival growth of uncertain pathogenesis.

**Case presentation:** A 11 years old male child, reported with the chief complaint of discomfort, associated with a growth in the upper right front teeth region. Markedly visible facial and skull asymmetries were also evident along with a short stature. Based on clinical, radiological and histopathological features, and a thorough history, a diagnosis of Peripheral ossifying fibroma in a child with existing Crouzon syndrome was made.

**Management:** Complete surgical excision of the peripheral ossifying fibroma mass was done, and no recurrences were noted. Regarding the Crouzon syndrome, the patient was advised Orthodontic treatment for correcting malocclusion and Dentofacial orthopedics, for managing the skeletofacial symmetries. However the Mother of the child refused any orthodontic intervention.

**Conclusion:** FGFR2 genetic mutation is held responsible for Crouzon syndrome, which needs to be differentiated from other craniosynostoses like Apert syndrome. Peripheral Ossifying fibroma is a nodular, usually ulcerated growth which originates from interdental papilla. Our particular case is unique, because, very few instances of Peripheral ossifying fibromas with existing Crouzon syndrome have been reported in the literature.

**Keywords:** Craniosynostosis, Crouzon syndrome, FGFR2 gene, peripheral ossifying fibroma.

Oral and Maxillofacial Pathology Journal (2021): <https://www.ompj.org/archives>.

## INTRODUCTION

The Craniosynostoses syndromes comprise a group of conditions, denoted by premature fusion of the cranial sutures, within utero, accompanied by varied other anomalies. Crouzon syndrome is the commonest among the bunch.<sup>1</sup> It was first described by a French Neuro Surgeon, Louis Crouzon, in 1912.<sup>2</sup> The syndrome, is observed in 1 among per 25000 births as an autosomal dominant condition.<sup>3</sup>

The craniofacial syndromes are usually attributable to a number of genetic mutations. Crouzon syndrome, likewise, is caused by mutation of FGFR2 gene.<sup>4</sup> This FGFR2 gene encodes a protein called Fibroblast growth factor receptor, which is responsible for normal bone growth and development.<sup>5</sup>

Craniosynostosis is the hallmark of this syndrome. It is a condition emphasized by premature fusion of the fibrous joints of the cranial bones, in utero. Coronal and sagittal sutures are normally affected. These sutures allow for the growth and expansion of the infant head along proper anatomical orientation.<sup>6</sup> The premature closure of the sutures results in abysmal, distorted growth and development of the craniofacial bones. Malformations like brachycephaly (short and broad head) or dolichocephaly (narrow and long head) can be noted. Severely affected persons can demonstrate a "cloverleaf" skull. The orbits are shallow, resulting in

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**How to cite this article:** Sarangi S, Dutta S, Mitra S. Peripheral ossifying fibroma in a child with existing Crouzon syndrome- A Case report. Oral Maxillofac Pathol J 2021; 12(2):73-77

**Source of Support:** Nil

**Conflict of Interest:** None

proptosis. Exophthalmous can be evident too. Visual and hearing impairments might occur along with headaches owing to compression of the nerves within their foramina by the premature closure of sutural plates and increased intracranial pressure.<sup>7</sup> The retruded maxilla along with the midface hypoplasia are noteworthy features.<sup>8</sup>

Mandibular prognathism, reverse overjet, narrow high arched or cleft palate accompanied by crowded teeth might also be noted.<sup>9</sup>

Peripheral ossifying fibroma is a benign, reactive, well encapsulated neoplasm usually affecting young persons in first and second decades of life. Females are usually involved and most of the cases tend to occur in the maxillary incisor-canine region, as a firm pedunculated mass.

Histopathologically, it is characterized by fibrous connective tissue stroma, containing variable amounts of mineralized or calcified material, which represent osteoid or cementoid, or a combination of both.<sup>10</sup>

## CASE REPORT

A male child, aged about eleven years, hailing from a rural area of Bankura district, reported to the Dept. Of Oral Pathology and Microbiology, Burdwan Dental College and Hospital with the chief complaint of discomfort, associated with a growth located in the upper right front teeth region. The child visited our institution for alleviation of the discomfort associated the growth. Family history of the patient showed nothing significant. The hematological assays revealed results that were within normal limits. The patient's mother told that the extra oral features started developing gradually after birth. The intelligence level of the patient was satisfactory. Previous medical and surgical histories were non contributory.

A thorough examination of the child was done and it yielded significant findings.

1.1 **General examination** of the patient pointed towards a short stature.(Fig 1A)

1.2 **Skull findings** revealed that the child had a short and broad face (brachycephaly). In the head region, a prominent dome like bulge was observed involving the midline of the skull, (Fig 1B) in relation to anterior fontanelle. On palpation, a slight fluctuation could be elicited involving the midline of the face, tracing from the

nasal bridge and root of the nose and coursing towards the bulge in the head.

1.3 **Extra oral analysis** was performed. A depressed midface along with flattened nasal bridge, retruded upper jaw and concurrent mandibular prognathism were observed. Somewhat flattened upper lip and philtrum, along with a beak like nose was there. (Figs. 1B and 1C)

1.4 **Ophthalmologic findings** revealed the presence of wide set bulging eyes. Exophthalmous and proptosis along with strabismus were also evident. The patient also had increased intercanthal distance (hypertelorism). (Fig 1B)

1.5 **Intraorally**, a narrow high arched palate was evident along with malocclusion and crowding of the teeth. Class III malocclusion and anterior cross bite were evident. Mandibular prognathism and retrognathia of maxilla were marked. The patient also had a garbled and slurry speech. A soft to firm, pedunculated, mass measuring about 2cmx3cm in diameter was seen in relation to labial attached gingiva of upper right lateral incisor- canine region. The colour the overlying mucosa pertaining to the mass was similar to adjacent gingival tissue. (Figs 1D and 1E)

A skull skiagram, antero posterior view was performed, which revealed the characteristic "beaten copper" appearance of the skull. Multiple convolutions on the inner bony aspect of the skull were evident, indicating the remodeling and anatomical restructuring of the brain, necessary for the growth and expansion, so pathognomonic of Crouzon syndrome. The dome shaped bulge which was observed externally on the head, could be corroborated perfectly with the radiological findings, which demonstrated a marked mound like elevation in the anterior fontanelle region. Malocclusion of the dentition was also noted. (Fig 2) Based on these clinical and radiological features, a provisional diagnosis of



**Fig 1A:** Short stature of the patient



**Fig 1B:** Extraoral findings - A dome shaped bulge in the anterior fontanelle region along with brachycephaly, hypertelorism, flattened nasal bridge along with a depressed midface and a flattened upper lip and philtrum



**Fig 1C:** Exophthalmous and proptosis along with maxillary retrognathia and beak-like nose observed

Crouzon syndrome was made. Complete analyses of the diagnostic aspects of the child were done and, then he was referred to the Dept. of Oral and Maxillofacial Surgery, for surgical removal of the intraoral pedunculated mass, and Dept. of Orthodontics regarding orthodontic correction for the dental anomalies viz malocclusion and high arched palate and correction of facial contours ie retruded maxilla and depressed midface. However the mother of the patient refused to undertake any orthodontic intervention and was willing to go for only surgical removal of the soft tissue mass in the upper jaw.

Accordingly, surgical excision of the pedunculated soft tissue mass, involving the upper jaw, in upper right lateral incisor-canine region, was performed.

Histopathological analysis revealed the presence of a stratified

squamous epithelium, backed by fibro vascular connective tissue stroma, being characterized by numerous variably shaped and sized basophilic calcifications. Collagen fibres were arranged haphazardly and some of the bony trabeculae exhibited osteoblastic rimming and contained osteocytes within a moderately cellular fibrous stroma. An isolated multinucleated giant cell was also noted within the connective tissue.

The overall histopathological features were corroborative to that of Peripheral ossifying fibroma. (Fig 3A, 3B)

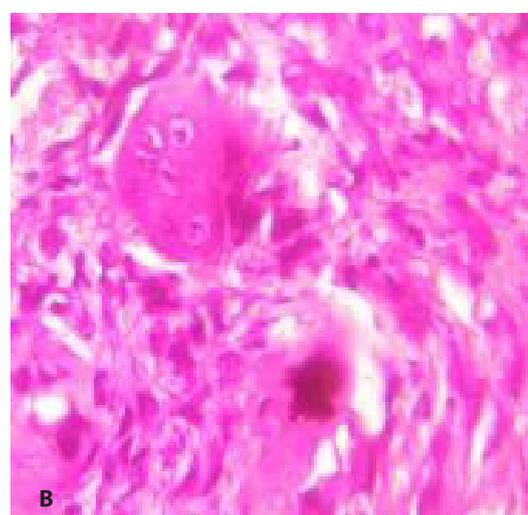
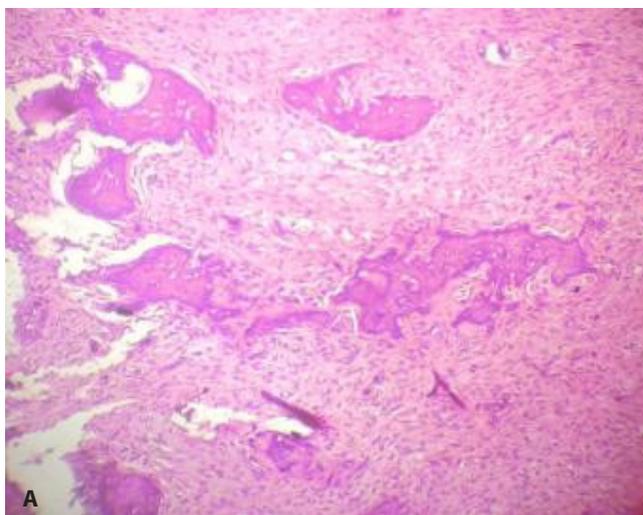
## DISCUSSION

Crouzon syndrome, an autosomal dominant condition, is signified by craniosynostosis-the term used to denote intrauterine, premature amalgamation of single or many cranial sutures.<sup>11</sup> This was quite apparent in the skull radiograph done in our case.



**Figs 1D and 1E:** Intraoral findings (D) A soft to firm pedunculated mass in relation to upper right anterior attached gingiva- lateral incisor-canine region was noted; (E) Narrow V shaped high arched palate and malocclusion of teeth were evident.

**Fig 2:** Cephalogram: "beaten copper" appearance along with convolutions involving the inner bony aspect of the skull. Malocclusion and crowding of teeth were observed. Dome shaped bulge in the midline of skull in the anterior fontanelle region



**Figs 3A and 3B:** (A) Numerous variably shaped and sized basophilic calcifications dispersed in a highly cellular and fibrous connective tissue stroma; bony trabeculae exhibit osteoblastic rimming and embedded osteocytes within the fibro cellular stroma. (H and E stain, 10X). (B) An isolated multinucleated giant cell in the connective tissue (H and E stain, 40X).

This craniosynostosis can also be observed in a host of other syndromes like Carpenter syndrome, Apert syndrome, Pfeiffer syndrome, etc. Crouzon syndrome needs to be differentiated from likewise conditions. Treacher Collins syndrome is characterized by hypoplastic mandible, downward slanting palpebral fissure and ear deformities which are not seen in Crouzon syndrome. For Apert syndrome to occur, syndactyly must be there, which was not evident in our case. Achondroplasia patients exhibit short stature, disproportionately long trunk and limited joint movement- notable characteristics which were not observable in our case, except for the short stature.<sup>12</sup>

Although the coronal and sagittal sutures are commonly affected, other ones like the lambdoid sutures at the posterior segment of the skull are also susceptible. Thus the normal, usual growth and expansion of the skull is hindered owing to the early fusion of cranial sutures. As a result, the architecture and size of the face are altered. It is observed in approximately 16 million newborn children across the globe.<sup>13</sup>

FGFR2 genetic mutations are held accountable for the syndrome. This gene encodes a specific protein, which is the fibroblast growth factor receptor 2 protein. A critical role, of this protein, is to orchestrate immature mesenchymal cells to differentiate into osteoprogenitor cells during initial embryonic developmental phase. FGFR2 mutations, presumably lead to an upregulation of fibroblast growth factor protein, thereby causing excessive and anomalous osteoblastic activity, causing premature fusion of the concerned cranial sutures.<sup>14</sup>

The craniosynostosis can lead to expression of a host of external facial features. Premature amalgamation of the cranial sutures can cause the head to look like brachycephaly (short and broad face) or dolichocephaly (long and narrow face). Brachycephaly was seen in the child. A rare condition, known as "clover leaf skull" deformity, might arise, when early integration of multiple cranial sutures are involved. However, this feature was notably absent in our case. The characteristic features of this syndrome generally are apparent, by the 1st year of life, with the features becoming more pronounced by two to three years of age.<sup>15</sup>

Anomalous bone growth and development leads to formation of wide set, bulging eyes and shallow depth of the orbital sockets, causing visual impairments. Exophthalmous and proptosis are observed. The orbits generally tend to focus on different directions, which are known as strabismus. These findings were also seen in our subject, but visual impairment was not there. Inflammatory changes in the anterior compartment of the eye, such as keratitis and conjunctivitis might develop too, although absent in our instance.<sup>16</sup> Frontal bossing, hypertelorism, midface hypoplasia and retruded maxilla along with relative mandibular prognathism can be observed, as evident in our case. A curved beak like nose and a short upper lip might be seen, as noted in our case.<sup>17</sup> Headaches due to enhanced intracranial pressure; as a result of abysmal cranial bone expansion and development, along with diminishing visual and hearing capabilities, owing to compression of the nerves in their respective foramina, due to excessive bony deposition, as a result of upregulated osteoblastic activity, is a significant feature. Respiratory deficits owing to airway obstruction can take place.<sup>18</sup> However, these features could not be found in our subject. Persons with Crouzon syndrome usually have normal intelligence.

Intraorally, cleft lip and cleft palate might be observed in some patients. Alongside that, narrow high arched palate, malocclusion and crowding of teeth and dysphasia might be evident.<sup>19</sup> Barring cleft lip and palate, rest of the features were present in our case.

Crouzon syndrome might be accompanied by Acanthosis nigricans, which is the presence of velvety, papular, keratotic plaques in various areas of the body such as trunks, neck, abdomen etc, owing to mutation of FGFR3 gene.<sup>20</sup> Acanthosis nigricans was not there, clinically in our case.

Combating Crouzon syndrome calls for a multidisciplinary approach and early diagnosis is the need of the hour. During the 1st year of life, if the synostotic sutures are released, it will lead to optimum brain growth and expansion, by allowing necessary cranial volume. Orthodontic appliances like rapid maxillary expansion facemask can be employed in prepubertal patients. Orthognathic surgeries might play a pivotal role for betterment of aesthetics.<sup>21</sup> However, as the mother accompanying the child refused any sort of orthodontic intervention, the patient did not undergo any sort of orthodontic/paedic treatment. Surgical excision of the gingival soft tissue mass was performed followed by a histopathological analysis, as desired by the patient party.

The peripheral ossifying fibroma is a relatively common, gingival growth, which exhibits reactive growth pattern. Researchers believe that these masses develop as fibrous maturation of pyogenic granulomas that undergo subsequent calcification. It appears as a nodular pedunculated or sessile mass that emanates from interdental papilla. This was evident in our case. The lesions are most often found in the gingiva, located anterior to the molars and in the maxilla, and young persons in the first decade of life are affected. The color is identical to that of the gingiva. Again this finding could be corroborated in our case.<sup>22</sup>

Histopathological analysis exhibits, an overlying epithelium, backed by fibrous connective tissue stroma, showing variable mineralized component such as osteoid, cementoid or both. In some cases, multinucleated giant cells might be found. Findings alike this, were clearly observed in our case.<sup>23</sup> Surgical excision is the treatment of choice, which was performed in our case. After obtaining the histopathology report, the child and his mother were properly counseled regarding the outcome of the diagnoses as well as the syndrome status; which would not otherwise lead to any hindrance in the daily life of the child, or might not cause any life threatening complication. The patient was duly followed up after a period of 02 and 04 weeks respectively, and the healing of the surgically excised gingival region was satisfactory and uneventful, with the patient being fully cooperative.

## CONCLUSION

Crouzon syndrome and craniosynostoses syndromes require early and timely diagnosis, during the early years of life, for delivery of optimum treatment, for improvement regarding the quality of life for the patient, which is very significant. It might mean that the condition, can be handled conservatively by orthodontic/paedic approaches rather than going for mutilating procedures at later phases of life, which could be psychologically challenging for the patient. Whilst, Peripheral ossifying fibromas, post a proper diagnosis, require surgical excision, which is the modus operandi. Crouzon syndrome usually necessitates a multimodal approach,

involving Orthodontists, Orthopaedic surgeons, Oral Pathologists, Pedodontists, Otolaryngologists, Psychologists, Neurosurgeons and Speech therapists. Improvements regarding molecular genetics and imaging assays in the days to come will only broaden the horizon in this regard.

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