Case Report

Crouzon Syndrome in a Ten-week-old Infant: A Case Report

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Abstract

Crouzon syndrome is a rare genetic disorder. We report a rare case of Crouzon syndrome in a very young infant with distinct features of craniofacial malformations. A 10-week-old male child presented with features of craniofacial dysostosis with abnormal shape of the skull, proptosis, hypertelorism, curved nose and frontal bossing. Radiological findings revealed a predominant premature fusion of sagittal sutures. The infant had airway obstruction. Features of hydrocephalus, papilledema and optic atrophy were not evident. We chose to manage the symptoms and prevent complications, and the surgery was deferred for later, depending on the degree of malformation and psychological needs. Diagnosis of this rare condition at an early stage can help in preventing the development of complications. A careful follow-up and appropriate surgical intervention can improve the prognosis of this condition, which carries the risk of respiratory complications, poor vision and, in some cases, mental retardation as the age advances.

Keywords: Cranial sutures, craniofacial, Crouzon syndrome, dysostosis, infant

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INTRODUCTION

Crouzon syndrome (CS) is a rare genetic disorder affecting about 1.6/100,000 people in the general population.[1] It is characterized by craniofacial dysostosis, which is described as the malformation of the skull and facial bones due to premature fusion of the cranial suture that leads to the abnormal skull and facial bone growth patterns. CS is an autosomal dominant disorder with a mutation in one of the fibroblast growth factor receptor (FGFR) genes (FGFR2 and FGFR3). The degree of cranial malformation varies, depending on the specific cranial sutures involved as well as the order and rate of progression. Most commonly, premature closure of coronal or sagittal sutures is found. Brachycephaly (caused by the fusion of the coronal suture), scaphocephaly (fusion of the sagittal suture), plagiocephaly (unilateral premature closure of the lambdoid and coronal sutures), oxycephaly (fusion of the coronal and lambdoid sutures) and complex craniosynostosis (premature closure of some or all sutures) are various abnormal skull shapes in CS. The condition is often associated with additional craniofacial abnormalities that are mostly secondary to abnormal skull growth. Proptosis (protrusion of the eyeball), hypertelorism (wider space between the eyes), strabismus, prominent forehead (frontal bossing), a curved nose, underdeveloped mid-facial regions and a short upper lip are some described abnormalities. A small, underdeveloped upper jaw (hypoplastic maxilla) with protrusion of the lower jaw (relative mandibular prognathism) may also occur. About 25% of individuals develop hydrocephalus,[2] and restricted airways and

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breathing difficulties have also been reported in some cases. However, few cases have been reported at very young, infantile stages in the literature.[3,4] We report such a case of CS, diagnosed at an early stage (at about 2.5 months of age) with a classic presentation of craniofacial abnormalities.

CASE REPORT

A 10-week-old male infant presented to our pediatric outpatient department with complaints of gradually progressive noisy breathing since birth. The parents also noticed a bulge over the anterior fontanelle in the past 1 month, which was reportedly increasing in size. Noisy breathing was not associated with the posture but was attenuated during sleep. No history of fever was reported. Birth history revealed normal full-term vaginal delivery with immediate cry. No history of seizure episodes was found. The infant has two older siblings (6 and 2.5 years in age) with no significant ailments. Developmental milestones were normal. Social smile and neck holding were developed. Clinical examination revealed proptosis, abnormal shape of the head with an occipitofrontal diameter of 40 cm. Bulging of the anterior fontanelles and overriding of the cranial sutures were noticeable. Facial development appeared abnormal, which revealed hypertelorism, curved nose and frontal bossing [Figure 1a-c]. Respiratory, cardiovascular, abdominal and central nervous system examinations were normal. Ear, nose and throat examination was performed because of the noisy breathing. Flexible laryngoscopy was performed but was not successful, as the scope could not be negotiated until the nasopharynx. Computed tomography (CT) of the paranasal sinuses suggested the presence of bilateral ethmoid sinusitis, otomastoiditis and deviated nasal septum. Nasopharynx appeared normal. Bilateral lateral ventricles, third and fourth ventricles were prominently evident. Features of hydrocephalus were not evident. There was benign prominence of the subarachnoid space.

Three-dimensional volume-rendering technique CT images revealed the fusion of the sagittal sutures. A focal fusion of the right coronal suture along with decreased space of the coronal and lambdoid sutures could also be noticed [Figure 2a-c]. Mild dilatation of the bilateral lateral ventricles was found [Figure 3]. Hypoplastic maxilla was noticeable [Figure 2c]. Both the orbits appeared normal and no intra-orbital mass/collection was noted. Ultrasonography (USG) of the cranium revealed prominent ventricles, while USG of the abdomen was normal. Retinoscopy findings were +0.25−1 × 90° (right eye) and +0.25−1.5 × 90° (left eye), which were not suggestive of significant refractive errors.[5] The fundus examination was normal with no disc edema.

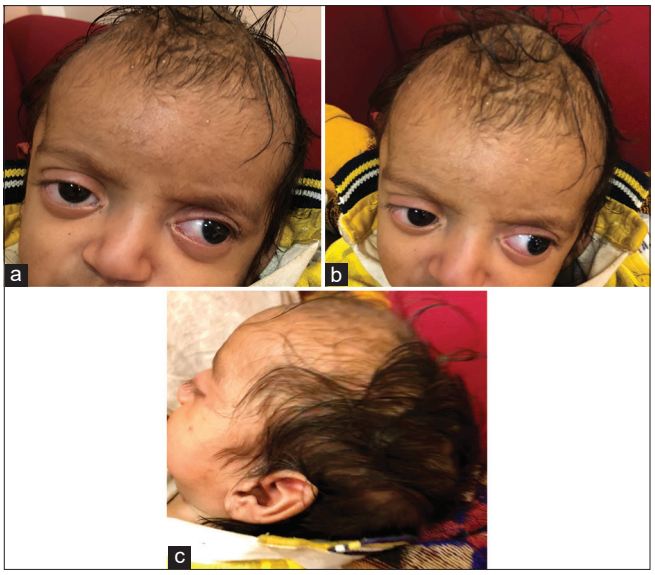

Figure 1: (a and b) Proptosis, hypertelorism and dolichocephaly are noticeable. (c) Abnormal long (dolichocephalic) shape of the skull

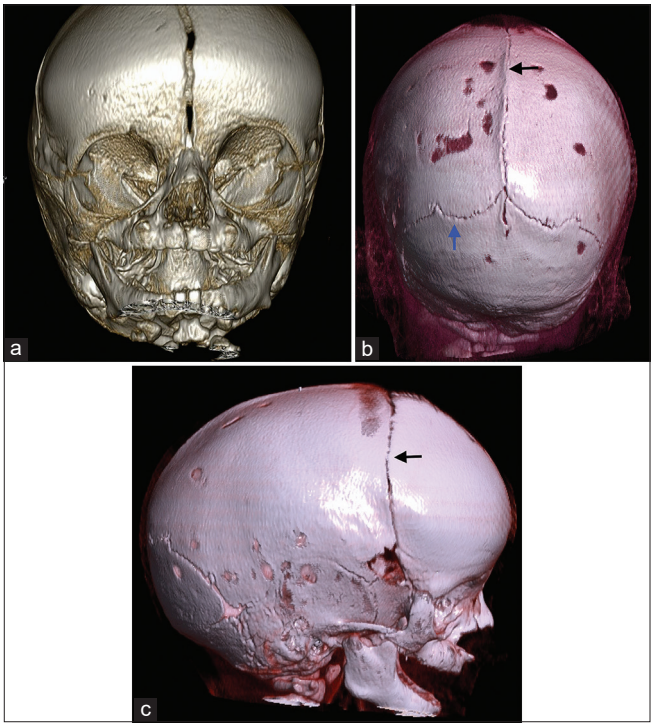

Figure 2: Three-dimensional volume-rendering technique computed tomography image showing (a) fused sagittal sutures; (b) fusion of sagittal suture (black arrow) and decreased space of the lambdoid suture (blue arrow); (c) dolichocephalic head with focal fusion of the right coronal suture (black arrow) and reduced space of rest of the coronal suture

Visual evoked potential (VEP) test was also performed for the electrophysiological evidence of the secondary signs of raised intracranial pressure (ICP). Flash VEP was performed by light-emitting diode goggle stimulation. VEP waveforms were recordable and reproducible in both the eyes. P100 latencies were 127 milliseconds and

119 milliseconds in the right and left eyes, respectively [Figure 4]. Interocular latency difference was increased (right eye with slightly greater P100 delay). If VEPs are recordable (indicating maturation of P100) and replicable (the sign of the validity of responses) in the patient of infantile age group (<6 months), it reveals little possibility of optic nerve dysfunction at this stage.

Based on the clinical features and characteristic radiological findings, the diagnosis was confirmed as CS. The patient was started on oral acetazolamide (45 mg/kg/day in three divided doses) (total 187.5 mg daily) and nutritional supplements. As the infant did not show signs of hydrocephalus at the time of presentation, an expectant approach with careful clinical, ophthalmological, respiratory and radiological monitoring for raised ICP was adopted. The parents of the child were instructed to consult with no delay if the child developed symptoms such as vomiting, loss of consciousness, episodes of seizure or head size enlargement. The result of genetic studies revealed heterozygous mutation of FGFR 2 gene, located on chromosome 10. At the patient's follow-up visit after 3 months of initial presentation, multistage surgical correction procedures for the craniofacial deformity were advised; however, despite adequate counseling, the parents refused this treatment.

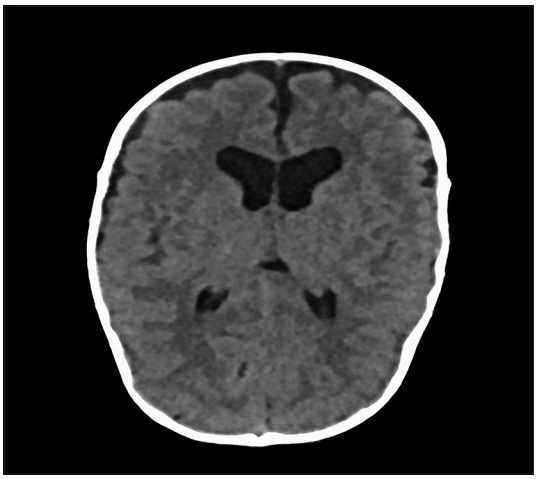

Figure 3: Computed tomography image showing mild dilatation of bilateral lateral ventricles

DISCUSSION

CS is epitomized by craniofacial dysostosis involving premature fusion of skull bones resulting in abnormal head shapes and abnormal development of facial bones. Most often, coronal, and sometimes, lambdoid or sagittal sutures are reported to be prematurely fused. Hypoplastic maxilla with receded zygoma, proptosis, curved nose and frontal bossing are some characteristic facial features. Our patient with this rare condition was diagnosed at a very early stage. This young infant had a premature fusion of the sagittal sutures as the most prominent cause of abnormal skull shape, a scaphocephalic abnormality. Clinical and radiological examination could confirm associated abnormal facial features including hypertelorism, beaked/curved nose, hypoplastic maxilla with relative prognathism and frontal bossing in the patient [Figures 1 and 2].

In general, CS has been suggested to be defined on the basis of the patient's phenotypic appearance, as no single mutation described provides a molecular genetic definition of CS craniosynostosis due to other causes (Crouzon-like phenotypes). The Pfeiffer syndrome was excluded because

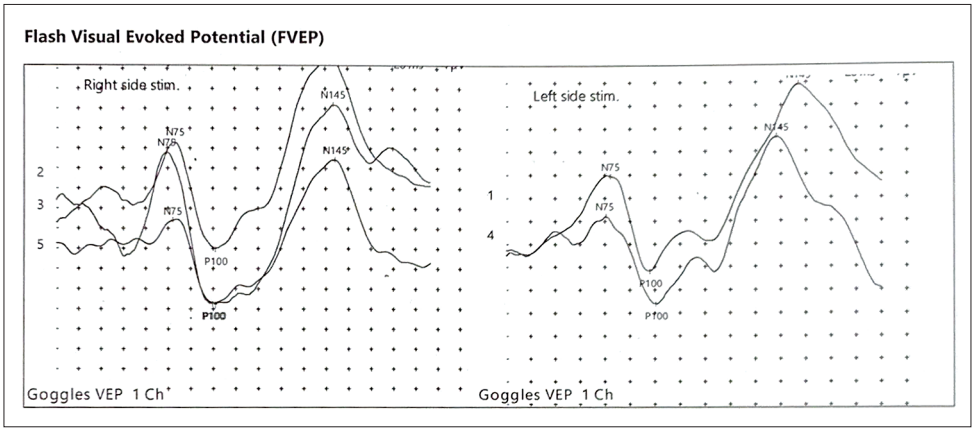

Figure 4: Flash visual evoked potential (to light emitting diode goggle stimulation) with recordable and replicable waveforms in both the eyes

in such cases, the coronal suture prematurely fuses and the resultant abnormal shape of the head forms a brachycephalic (turribrachycephalic) skull with a high prominent head, whereas our patient had dolichocephalic features [Figure 1c and 2c].[6] The Pfeiffer syndrome also includes abnormalities of the hands and feet, which were not present in our patient. Acrocephalic (cone shaped) head with a diminished anteroposterior diameter, flat occiput (due to involvement of coronal suture) and syndactyly excluded Apert syndrome in our patient.[7] Further, Jackson–Weiss syndrome was excluded because it presents with foot abnormalities as a consistent feature apart from craniosynostosis, while Muenke syndrome was excluded because broad toes and brachydactyly are some important distinguishing features in it.[8,9] Cloverleaf skull and a specific skin abnormality, called cutis gyrata, characterized by a furrowed and wrinkled appearance in the face and palms and soles of the feet along with acanthosis nigricans excluded Beare–Stevenson cutis gyrata syndrome, which is another form of craniosynostosis and abnormal skull shape.[10] Nonsyndromic craniosynostosis had readily been excluded owing to the absence of dysmorphism of the face, trunk or extremities and typical involvement of a single suture in the same.[11]

Some features in the CS have been described as secondary to the abnormal skull structure such as hydrocephalus, papilledema, optic nerve atrophy, sensorineural hearing loss and restricted airways.[12] Narrow/high-arched palate, posterior bilateral crossbite, hypodontia and crowding of the teeth are other common features described. However, our patient was very young to manifest dental and secondary features of abnormal skull growth. Nonetheless, the signs of noisy and difficult breathing suggest that he might be at risk of developing airway restriction secondarily later during development. He had deviated nasal septum; upper airway obstruction has been reported to develop secondary to septal deviation, mid-nasal abnormalities and nasopharyngeal narrowing.[13] However, noisy breathing was found to be ameliorated on clinical examination after 15 days of initial presentation, and SpO_2 levels were 96.5% (both in awake state and during sleep).

The mental capacity of patients with CS has been described to be usually in the normal range; however, increased ICP has resulted in a mental delay in some cases.[14] As our patient has proptosis, corneal damage from exposure needs to be prevented to impede visual disturbances. Primary optic atrophy leading to reduced vision has been another common finding in such patients. We attempted to rule out the presence of optic atrophy by recording VEP by flash stimulation. The findings demonstrated the presence of the prominent P100 wave at a slightly delayed latency. However, recordability and replicability of the waveforms at this younger age excludes the development of optic atrophy at this stage.

Treatment options for the children with CS are open surgical approaches as well as a minimally invasive approach. The exact timing and sequence for surgical procedures depends to a large extent on the functional and psychological needs.[15] The selection of the appropriate surgical technique remains a subject of substantial debate among surgeons. In addition, the timing and course of the surgical treatment is highly individualized. Minimally invasive (endoscopic) surgeries are suggested for infants usually younger than 6 months of age and with a single sutural involvement. Our patient is a syndromic case of craniosynostosis who demonstrated involvement of other cranial sutures in addition to the sagittal sutures. Open surgeries in infancy (cranioplasties) include skull expansion and remodeling for the cosmetic benefit and to release the stenosis. Remodeling techniques have been suggested to be performed in children <1 year of age. These can be deferred up to 11 months of age if features of hydrocephalus are not evident.[15] CS was detected in our patient at the age of 2.5 months, without the evidences of hydrocephalus, and the patient was planned to be regularly followed up to manage the symptoms. Open surgical treatment in a staged fashion was decided to be performed during the patient's follow-up visit, but the parents dissented. Therefore, the child remains under regular follow-up with careful monitoring and conservative management.

CONCLUSION

CS, a craniofacial dysostosis, exhibits distinct features of abnormal skull growth and facial development. Radiological examination contributes to a conclusive diagnosis. Early diagnosis of the condition can help in appropriate management of the adverse symptoms and also surgical intervention can be planned accordingly to improve the prognosis of the disorder.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's parents have given their consent for his images and other clinical information to be reported in the Journal. The patient's parents understand that his name and initial would not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Peer review

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Conflicts of interest
There are no conflicts of interest.

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