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CASE REPORT-A RARE CASE OF CROUZON SYNDROME

General Medicine

Dr. Abishek N* Postgraduate student Department of General Medicine Raja Rajeswari Medical College and Hospital, Bangalore, Karnataka, India *Corresponding Author

DR. Prajwal.K.C Assistant Professor Department of General Medicine Raja Rajeswari Medical College and Hospital, Bangalore, Karnataka, India

ABSTRACT

Crouzon syndrome is a rare autosomal dominant disorder caused by fibroblast growth factor receptor 2 gene mutation . This gene is required for the normal growth and development of the skull. Any abnormalities in this gene can result in early fusion of the skull suture lines, affecting the adequate growth and development of the skull resulting in altered shape of the skull. It is characterized by craniosynostosis,hypertelorism,bilateral ocular proptosis,maxillary hypoplasia, diminished mental function, and progressive hydrocephalus. The worldwide prevalence rate approximately is 1 per 25,000 live births .We found one such rare case of Crouzon's syndrome presenting with complaints of protruding eyes, dimness of vision to close objects and right focal seizures with generalization.

KEYWORDS

Craniosynostosis,hypertelorism,maxillary hypoplasia,crouzon syndrome,seizures

INTRODUCTION

Crouzon syndrome, named after Octave Cruzon is a syndromic craniosynostosis, first described in 1912(1). It is a rare autosomal dominant genetic disorder known as branchial arch syndrome affecting the 1st branchial arch precursor of maxilla and the mandible caused by fibroblast growth factor receptor 2(2)gene mutation, resulting in craniofacial dysostosis caused by premature obliteration and ossification of two or more sutures, most often coronal and sagittal and sometimes involving the lambdoidal sutures(3,4)

Craniosynostosis examples include:
trigonocephaly (fusion of the metopic suture),
brachycephaly (fusion of the coronal suture),
dolichocephaly (fusion of the sagittal suture),
plagiocephaly (unilateral premature closure of lambdoid and coronal sutures), oxycephaly (fusion of coronal and lambdoidal sutures),
Kleeblattschaedel (premature closure of all sutures) (cloverleaf skull deformity)(5)

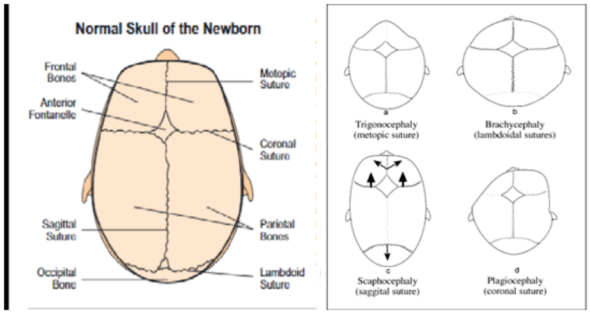


Figure 1a. Normal skull of newborn
Figure 1b. Types of craniosynostosis anomaly

Crouzon syndrome with oxycephaly and Apert syndrome with oxycephaly and syndactylia (acrocephalosyndactyly) are the most common types of dysostosis. Some authors connect those syndromes as one, calling it Crouzon-Apert syndrome.(6)

CONDITION	LOCATION OF ABNORMALITY CONDITION (CHROMOSOME/GENE)	PRIMARY CHARACTERISTICS
Alpert's syndrome(6)	10q25.3-q26/FGFR2 Exon 7(U)	Acrocephaly, brachycephaly, flat face, large fontanelle, shallow orbits,hypertelorism, down-slanting palpebral fissures, maxillary hypoplasia, narrow palate, syndactyly, short fingers, broad thumbs and great toes, fusion of cervical vertebrae, mental retardation (in 50%), acne.
Cruzon syndrome(6, 7)	10q25.3-q26/FGFR2 Exon 9(B)	Shallow orbits, hypertelorism, frontal bossing, maxillary hypoplasia, curved beak-shaped nose, A-shaped palate, conductive hearing loss
Jackson-Weiss syndrome(6)	10q25.3-q26/FGFR2 Exon 9(B)	Shallow orbits, hypertelorism, mid-facial hypoplasia, syndactyly, broad great toe
Pfeiffer syndrome(6)	10q25.3-q26/FGFR2 Exon 9(B) and 8p11.2-p12/FGFR1 Exon 5	Brachycephaly, full high forehead, hypertelorism, up-slanting palpebral fissures, small nose, broad thumbs and great toes, syndactyly

Crouzon syndrome is characterized by craniosynostosis, hypertelorism, bilateral ocular proptosis,shallow orbits , Maxillary hypoplasia . The order and rate of suture fusion determines the degree of deformity and disability .(7,8)

One of the most serious effects of craniosynostosis is an increased intracranial pressure, which generally is not a problem if one suture is involved, but becomes more likely as the number of involved sutures increases. This increased pressure may be acute, leading to signs and symptoms such as headache and vomiting, or papilledema and optic atrophy with loss of vision.(9)

Craniosynostosis can affect the visual system severely. If the bony orbits are shallow, proptosis may occur, which in addition to its cosmetic effect, may lead to exposure keratopathy. Asymmetry of the orbits may lead to ptosis or strabismus, both of which can result in amblyopia. Papilledema and optic atrophy, which initially may be asymptomatic, may occur due to increased intracranial pressure. Hypertelorism, the result of coronal synostosis, may affect conjugate vision.(8,10)

Patients with midfacial hypoplasia due to craniosynostosis of the sutures of the base of the skull may have problems with the upper airway, leading to stridor and apnea. Midfacial hypoplasia may lead to dental problems such as malocclusion. rarely, involvement of the lower airway, can lead to lower airway obstruction. (7)

Crouzon syndrome, are associated with abnormalities of hearing. Patients who have associated cleft palate may have an increased incidence of ear infections as well. Rarely, children will have difficulty with swallowing if the mandible is involved. Craniosynostosis severe enough to cause noticeable deformity of the skull and/or face can raise psychosocial concerns.

Central nervous system findings include hydrocephalus (25%), chronic tonsillar herniation (72%), jugular foramen stenosis with venous obstruction (30%), seizures (10.5%), frequent headaches (29%), and mental deficiency (3%). The worldwide prevalence rate is approximately 1 per 25,000 live births indicating the rarity of the syndrome.

CASE REPORT

A 24yr old male presented with complaints of protruding eyes since 3 months of age,gradually progressive and noticed reduced vision to close objects from age of 12,developed seizures 3-4episodes per month since 8 months, not controlled with medications,right focal seizures with secondary generalization. He gives history of underachieving in school. Further detailed family and medical history revealed that he was born out of a non-consanguineous marriage, by normal vaginal delivery, cried on birth and had no NICU stay.There were no anomalies in any siblings or near relatives.

Examination- Shallow orbit,ocular proptosis,hypertelorism,maxillary hypoplasia,v-shaped maxillary dental arch,overcrowding of upper teeth were observed.

Preliminary investigations showed Thyroid profile-within normal limits,MRI brain with orbit screening showed gliotic changes in left parietal lobe with calvarial defects,empty sella,bilateral proptosis. Based on the examination and MRI brain findings a diagnosis of Crouzon syndrome was made.

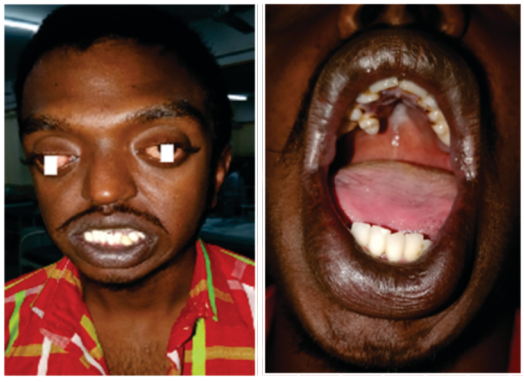
The Treatment Plan–

a multidisciplinary approach was taken
The patient was started on antiepileptics tab.carbamazepine 300mg 1-0-1 and tab.Phenytoin 100mg 1-0-1 for the focal seizure.
Genetic and occupational counseling was done.

As there was no hydrocephalous on MRI , no CSF shunting procedure was done.

Ophthalmology consultation was taken for the proptosis and for preventing exposure keratitis.

Dental opinion was taken for tooth crowding and gingivitis.
Patient was then discharged and regularly followed up.



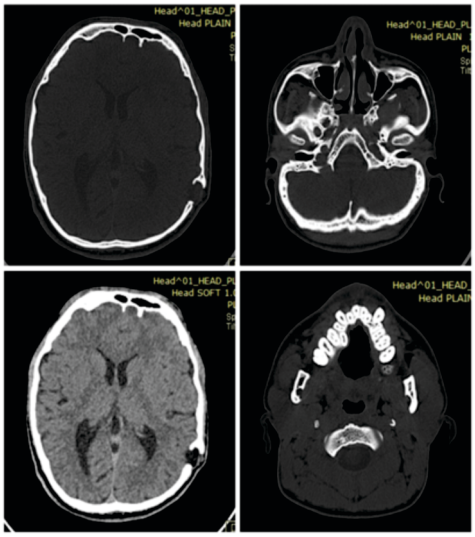


Figure 2a. Bony deformities such as hypertelorism
Figure 2b.Crowding of teeth, v-shaped maxillary arch
Figure 2c.CT showing- Calvarial defect noted in the parietal bone.

DISCUSSION

The French neurologist, Octave Crouzon (1912) first described this syndrome in a mother and son with the characteristic Triad of calvarial deformities, facial anomalies, and exophthalmos.

Crouzon's syndrome has no racial or sex predilections.(2)

Crouzon syndrome is a part of various syndromes of craniosynostosis. These skull deformities are due to dysplasias of the skeleton (including craniofacial dysostosis) , caused by the malformations of the mesenchyme and ectoderm. Dysplasias are inherited in an autosomal dominant pattern. Inheritance may come from an affected parent(s), although cases exist in which mutations arise de novo. Mutation of the gene (locus 10q26) for fibroblast growth factor receptor 2 (*FGFR2*) has been identified as a causative factor for Crouzon syndrome.(3) Typically, the mutations occur on exons 8 or 10. Moreover, the mutation in the transmembrane region of *FGFR3* (locus 4p16.3) was detected in this syndrome. Mutation of the FGFRgene is also responsible for other craniosynostosis such as Apert's, Pfeiffer's, Jackson-Weiss's, and Saether-Chotzen's syndromes . (11)

Premature fusion of the cranial sutures results in craniosynostosis, and this initiates changes in the brain and adjoining structures, such as increase in intracranial pressure, reduced orbital volume, exophthalmos (proptosis)(7,8), severe maxillary hypoplasia and occlusal derangement . Complications of Crouzons syndrome may include conjunctivitis or keratitis, exotropia, poor vision due to optic atrophy and corneal injury, (12)Frequent headaches, seizures, mental deficiency, increasing hydrocephaly, conductive hearing deficit, upper airway obstruction develop secondary to septal deviation, midnasal abnormalities, choncal abnormalities and nasopharyngeal narrowing,(13) Other findings include nystagmus, iris coloboma, aniridia, anisocoria,corectopia, microcornea, megalocornea, keratoconus, cataract, ectopia lentis, blue sclera and glaucoma.

Imaging studies-are a necessary part for diagnosis of Crouzon syndrome, treatment planning, management, and monitoring .Preliminary diagnosis of craniosynostosis done by- brain computed tomography (CT)(7,8,12) scanning or magnetic resonance imaging (MRI) are used to evaluate the patient for hydrocephalus and structural anomalies.(5)

Treatment-

Patients with Crouzon syndrome require interdisciplinary and multidisciplinary care and management.Educating the patient regarding the condition is of high priority in order to allay the patients' and caregivers' concerns about the condition, the etiology and management of the patient. The patients are treated for hydrocephalous with V-P shunting; tooth, eye and facial deformities are treated by the concerned departments either conservatively or by surgery as deemed appropriate . Surgeries for craniosynostosis include- skull reshaping surgeries, fronto-orbital advancement, mid facial advancement, rhinoplasty, genioplasty etc. Antiepileptics are given in case of seizure disorder. Occupational and vocational physiotherapy along with genetic counselling is done.

Prognosis depends on severity of malformation. Innovations in craniofacial surgery have enabled patients to achieve their full potential by maximizing their opportunities for intellectual growth, physical competence and social acceptance.

It is imperative to recognize this syndrome early so that prompt intervention can be done to prevent complications of raised ICT and if needed cosmectic surgeries can be done so that the patient may lead a normal physical and social life.

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