Crouzon Syndrome: A case report with review of literature

Priyanshi Awasthi [1,*], Rajendra P. Maurya[2], Virendra P. Singh[3], Tanmay Srivastav[4]

[1]Junior Resident, [2]Assistant Professor, [3]Professor, [4]Senior Resident, Dept. of Ophthalmology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India

***Corresponding Author:**
Email: mauryarp_bhu@yahoo.com

Abstract
Crouzon syndrome is a rare congenital malformation of cranium and face. It is an autosomal dominant disorder characterized by premature fusion (craniosynostosis) of coronal and sagittal sutures leading to craniodentofacial deformities. We report here a case of 5 year old female with ocular, skeletal and dental features of Crouzon syndrome.

Keywords: Craniosynostosis, Crouzon syndrome, Exophthalmos, FGFR 2 gene mutation, Prognathism.

Introduction
Crouzon syndrome was first described by French neurosurgeon, Octave Crouzon (1874-1938) as one of the variant of craniofacial dysostosis.(1) It is a rare genetic disorder having autosomal dominant inheritance with complete penetrance.(2) Crouzon syndrome is caused by mutation in the fibroblast growth factor receptor-2 (FGFR-2) gene. Syndrome is characterized by abnormal fusion of one or more cranial sutures in utero, resulting in craniofacial deformities since birth or begins in the first year of life.(3,4) Most common ocular findings are shallow orbits, proptosis, hypertelorism, strabismus, papilloedema and optic atrophy.(5-7) Other abnormalities are intraoral manifestations including mandibular prognathism, V-shaped maxillary dental arch, high arched or cleft palate and bifid uvula.(7,8)

Case Report
A 5 year old female child presented to our departmental OPD with complaint of outward protrusion of both eyeballs since birth. Her mother also complained of deviation and occasional dislocation of left eye which she was able to retroplace by her own. Detailed family and medical history was taken which revealed mother had normal hospital based vaginal delivery. In family, siblings and near relatives were normal. Examination was done and clinical photographs were taken after taking prior consent from parents. On general examination, it was noted that her head was elliptical in shape with beak-like nose, broad nasal bridge, high arched palate and low set ears. The patient had a concave profile with lip incompetence.

On local ocular examination, patient had bilateral proptosis, hypertelorism and divergent squint in both eyes. Anterior segment including pupil was normal. Fundus showed clear media with normal cup disc ratio, engorged and tortuous vessels with normal foveal reflex.

There was no distal anomaly. In the systemic examination it was found that she had cardiopulmonary abnormality. So, she was referred to department of paediatrics where she was planned for surgery.

She was diagnosed as a case of Crouzon syndrome with these ocular abnormalities on clinical basis. Patient was started on lubricant eye drops and ointment to prevent exposure keratopathy. Amblyopia management was done and the patient was advised close follow-up.

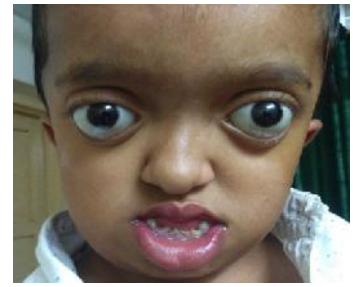

Fig. 1: Showing acrocephaly, bilateral proptosis, strabismus, hypertelorism and maxillary hypoplasia

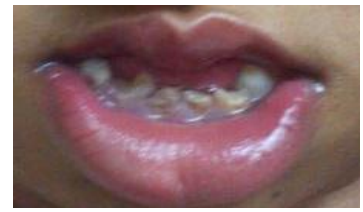

Fig. 2: Showing dental deformities

Discussion
Craniosynostosis is defined by premature fusion of one or more cranial sutures in utero. Cohen has listed upto 57 craniosynostosis syndromes in 1979.(9) It has an incidence of approximately 16.5 cases per one million live births with prevalence of 333–476 per million births.(10) Crouzon syndrome is an autosomal-dominant condition caused by specific point mutations in the FGFR-2 genes which play an important role in suture development. FGFRs are transmembrane tyrosine kinase proteins receptor.(11) There are four types of tyrosine kinase receptors. Among this 3 are reported to be mutated in majority of craniosynostosis conditions namely FGFR1, FGFR2, and FGFR3. It does not show any gender predilection.(12)

Crouzon syndrome is characterized by maxillary hypoplasia, shallow orbits, craniosynostosis, proptosis, and dental malocclusions due to arrested growth of the maxilla and zygoma.[13] Chronic papilloedema may also be associated leading to optic atrophy. Other ocular associations include ectopia lentis, aniridia, coloboma, blue sclera, cataract and optic nerve hypoplasia.[14-16] The patients often present with decreased vision at least in one eye in 35% of patients and 9% in both the eyes.[17] The shape of the head depends on the time and order of fusion of suture and brachycephaly is the most frequently seen abnormality. Children with Crouzon syndrome may also have hearing difficulties which may be associated with narrow auditory canals. The patients may have upper airway obstruction leading to respiratory distress.[18] Management of Crouzon syndrome requires a multidisciplinary approach and early diagnosis of this syndrome is important.[19] During period of infancy it is preferable to release synostotic sutures of the skull to allow for the growth of adequate cranial volume thus allowing normal brain development and expansion.[20-22] Ophthalmic evaluation should be done at young age in these patients. Nonsurgical management of Crouzon syndrome include orthopedic appliances and orthodontics therapy.[23] Newer techniques do promise for cosmetic reconstruction of facial bones. Prognosis depends on degree of severity of malformation. Patients usually have live a normal lifespan.

Conclusion

To diagnose Crouzon syndrome, of relevant importance are ophthalmic examination, radiological examination– CT, cranial MR imaging, and genetic analyses. Early detection of eye problems to reduce amblyopia by correction of refractory errors and timely treatment of strabismus and patching is recommended. Management of craniofacial deformities often requires multidisciplinary team involvement. Clinicians must be able to recognize the characteristic features of the various craniofacial syndromes so that an early diagnosis and referral for specialized care can be done. Craniofacial syndromes, if diagnosed at any early stage, can be managed by orthopedic growth modification, thus avoiding the need for major facial surgeries and additionally benefiting the psychological development of the patient.

References

1. Marsh JL, Vannier MW. Cranial deformities comprehensive care for craniofacial deformities. St. Louis: Mosby;1985.p.154.
2. Fogh-Andersen P. Craniofacial dysostosis (Crouzon's disease) as a dominant hereditary affection. Nord Med 1943;18:993-6.
3. Fries PD, Katowitz JA. Congenital craniofacial anomalies of ophthalmic importance. Surv Ophthalmol 1990;35:87-119.
5. Padmanabhan V, Hegde AM, Rai K. Crouzon's syndrome: A review of literature and case report. Contemp Clin Dent 2011;2:211-4.
6. Singer SL, Walpole I, Brogan WF, Goldblatt J. Dentofacial features of a family with Crouzon syndrome. Case reports. Aust Dent J 1997;42:11-7.
7. Gray TL, Casey T, Selva D, Anderson PJ, David DJ. Ophthalmic sequelae of Crouzon syndrome. Ophthalmology 2005;112:1129-34.
8. Hlongwa P. Early orthodontic management of Crouzon syndrome: A case report. J Maxillofac Oral Surg 2009;8:74-6.
9. Cohen MM Jr. Craniosynostosis and syndromes with craniosynostosis: Incidence, genetics, penetrance, variability, and new syndrome updating. Birth Defects Orig Artic Ser 1979;15:13-63.
10. Ingersoll RG, Paznekas WA, Tran AK, Scott AF, Jiang G, Jabs EW. Fibroblast growth factor receptor 2 (FGFR2): Genomic sequence and variations. Cytogenet Cell Genet 2001;94:121-6.
11. Wilkie AO, Slaney SF, Oldridge M, Poole MD, Ashworth GJ, Hockley AD, et al. Apert syndrome results from localized mutations of FGFR2 and allelic with Crouzon syndrome. Nat Genet 1995;9:165-72.
12. Jabs EW, Li X, Scott AF, Meyers G, Chen W, Eccles M, et al. Jackson- Weiss and Crouzon syndromes are allelic with mutations in fibroblast growth factor receptor 2. Nat Genet 1994;8:275-9.
13. Reardon W, Winter RM, Rutland P, Pulleyn LJ, Jones BM, Malcolm S. Mutations in the fibroblast growth factor 2 gene cause Crouzon syndrome. Nat Genet 1994;8:98-103.
14. Järund M, Lauritzen C. Craniofacial dysostosis: Airway obstruction and craniofacial surgery. Scand J Plast Reconstr Surg Hand Surg 1996;30:275-9.
15. Hlongwa P. Early orthodontic management of Crouzon syndrome: A case report. J Maxillofac Oral Surg 2009;8:74-6. References [1] Gray TL, Casey T, Selva D, et al. Ophthalmic sequelae of Crouzon syndrome. Ophthalmology. 2005;112:1129–34.
16. Maloth S, Padamashree S, Rema J, et al. Diagnosis of Crouzon's syndrome. Hong Kong Dental Journal. 2010;3:95–100.
16. Reardon W, Winter RM. Mutations in the fibroblast growth [3] factor receptor 2 gene cause Crouzon syndrome. Nature Genetics.1994;8:98–103.
17. Bowling EL and Burstein FD. Crouzon syndrome. [4] Amer Optometry Assoc. 2006;77:217-22.
18. Wen MH, Hsiao HP. Growth hormone deficiency in a case [5] of Crouzon Syndrome with hydrocephalus. International Journal of Pediatric Endocrinology. 2010;4:101-07.
19. Cohen MM Jr. An etiologic and nosologic overview of [6] craniosynostosis syndromes. Birth Defects Orig Artic Ser. 1975;11(2):137-84.
20. Gorlin RJ, Cohen MM, Levin LS. Syndromes of the head [7] and neck. Oxford: Oxford University Press.2001;4:658-59.
21. Phupong V, Srichomthong C, Shotelersuk V. Prenatal [8] exclusion of Crouzon syndrome by mutation analysis of FGFR2. Southeast Asian J Trop Med Public Health. 2004;35:977-79.
22. Kaur H, Singh WH, Sharma CM. Crouzon syndrome: A [9] case report and review of literature. Indian J Otolaryngol Head Neck Surg. 2006;58:381-82.
23. Gray TL, C asey T, Selva D, et al. O phthalmic sequelae of Crouzon syndrome. Ophthalmology 2005;112:1129–34.