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Ocular Manifestations of Crouzon Syndrome

KEYWORDS: Crouzon syndrome, Craniosynostoses, Strabismus, Proptosis, Optic atrophy

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ABSTRACT *Seven patients with a clinical diagnosis of Crouzon syndrome were assessed before any surgery in the Department of Ophthalmology, Maharani Laxmi Bai Medical College, Jhansi. The ocular features were assessed in these patients. The mean age (in years) in the study group was 13.2 ± 6.7 (range 8 to 27 years). Visual impairment in at least 1 eye occurred in 2 patients (28.6%) and was bilateral in 5 patients (71.4%). The most common cause of visual impairment was amblyopia, which was present in 4 (57%) of patients, followed by optic atrophy in 2 (28.6%). Ametropia occurred in 85.7% of patients; 57% had hypermetropia of ≥ +3 diopters (D) and 28.5% had myopia of ≥ -1.5 D. Strabismus occurred in 57% of patients. Although exposure keratopathy was observed in 2 patients, this complication was well managed and caused no reduction in visual acuity. Ocular protosis, dystopia and hypertelorism were other features seen. Early detection to reduce amblyopia by correction of refractive errors, timely treatment of strabismus, and patching should be a priority. Optic atrophy remains an important cause of visual impairment in such patients.*

INTRODUCTION

Cleidocranial dysplasia (CCD) / Craniosynostoses is an uncommon genetic skeletal condition. The craniosynostoses comprise a clinically and genetically heterogeneous group of disorders characterised by premature fusion of the skull bone sutures. Several recognisable entities are identifiable within this broad group, among them Crouzon, Apert, Pfeiffer, and Jackson- Weiss syndromes[1].Originally it was described by Crouzon in a mother and son in 1912[2].

Inheritance is autosomal dominant with virtually complete penetrance. It is caused by multiple mutations of the fibroblast growth factor receptor 2 gene, FGFR2[3]. Crouzon syndrome with a reported incidence of 1:25000 live births is the most common of over 70 conditions in which premature fusion of the cranial sutures may be a feature[4]. A positive family history is reported to occur between 44-67% of cases. Those most at risk for Crouzon syndrome are children of parents with either the menifestus disorder parents or carrier of the gene and fathers at an older age at the time of conception. Both genders are equally affected.

The syndrome is principally characterised by craniosynostosis, shallow orbits, ocular proptosis, strabismus, hypertelorism, maxillary hypoplasia and relative mandibular prognathism[5]. Features of the skull are variable. The skull may have associated brachycephaly, trigonocephaly, or oxycephaly. These occur with premature fusion of sagittal, metopic, or coronal sutures, with the coronal sutures being the most common. In addition, combinations of these deformities may be seen.

The diagnosis is based on clinical findings and radiological examination. Examination of the eyes by an ophthalmologist is essential to assess for papilledema, which indicates elevated intracranial pressure. Another finding may be optic atrophy with deterioration of vision. This consists of standard radiology to produce anteroposterior, lateral, and cephalometric views. The information gained is the position of the maxilla relative to the mandible. This is class III, with the upper teeth lying behind the lower teeth when they are in occlusion. Patients show evidence of elevated intracranial pressure and have "paw marking" of the skull due to the gyri of the brain indenting and thinning the calvaria, with, in severe cases, erosion. The fusion of the involved sutures can be seen. A CT / MRI scan helps to confirm the findings of standard radiographs and provides information on orbit and other cranial structures.

MATERIALS AND METHODS

Overview of clinical records was made with documentation of patient age, gender, visual acuity, refractive error, diagnosis of amblyopia, squint, eye movement dysfunction, nystagmus, fundus examination, examination of the anterior segment, interpupillary distance, and intercanthal distance. Standard radiology including X-ray, CT or MRI scans were also evaluated. Quantitative data were expressed in terms of mean with standard deviation (SD) while qualitative data were inacted as 'present' or 'not present'. No surgical interventions were given during the study to any of the patients.

RESULTS

The mean age (in years) in the study group was 13.2 ± 6.7 (range 8 to 27 years). 4 patients were male and 3 patients were female (Table1).

We describe here a case from our study group for relevance.

Case : A 13 years old female patient was brought to our department by her parents with complaints of large eyes since birth, difficulty in speaking and chewing. She had history of sleep apnoea with upper airway problems. Family history revealed consanguineous marriage iof her parents. There was positive family history and the father also had frontal bossing without maxillary hyperplasia. One of her cousin was also suffering from skull deformity. On clinical examination, patient had brachycephalic head, maxillary

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retrusion, malar deficiency, hypertelorism, divergent strabismus, bilateral ocular proptosis, psittichorhina (beak like nose) (Figure 1a) and moderate mental retardation. Her best corrected visual acuity (BCVA) was 6/60 in right eye with +4.5 DS/ +2.5 DC AT 105° while 6/36 in left eye with + 5.00 DS/ +2.75DC AT 95°. Fundus examination revealed vitreous degeneration and optic atrophy both eyes. Intraoral examination revealed class III incisor relationship. The dental arches were U-shaped with unilateral cleft in the upper arch. On radiological examination, patient had bilateral ocular proptosis, shallow orbits, hypertelorism, presence of metopic suture (Figure 1c), corpus callosum agenesis (Fifure 1b) and right sided defect in cribriform plate with encephalocoele (Figure 1b,2a). The approximate interpupillary distance (IPD) was 68.7 mm and distance between anterior margin of frontal processes of zygomatic bones at level of plane of optic nerves was 97.4 mm. The anteroposterior diameter of eyeball was 33.4 mm in right eye and 31.3 in left eye and transverse diameter of eyeball was 27.4 mm in right eye and 26mm in left eye. In the absence of hand and feet lesions a provisional diagnosis of Crouzon syndrome was made.

In this study group, visual impairment in at least 1 eye occurred in 2 patients (28.6%) and was bilateral in 5 patients (71.4%). The most common cause of visual impairment was amblyopia, which was present in 4 (57%) of patients, followed by optic atrophy in 2 (28.6%). Ametropia occurred in 85.7% of patients; 57% had hypermetropia of ≥ +3 diopters (D) and 28.5% had myopia of ≥ -1.5 D. Strabismus (exotropia) occurred in 4 (57%) patients which was bilateral in 2 cases. One patient had clinical signs of bilateral papilloedema. Inability to close eyes properly/ lid lag was seen in 5 patients (71.4%). Although exposure keratopathy was observed in 2 (28.6%) patients, this complication was well managed and caused no reduction in visual acuity. Proptosis was seen in 5 cases (71.4%) which was bilateral in 3 such patients. Hypertelorism was present in 6 patients (85.7%) (Table 1).

On CT scan and MRI, the mean IPD was 67.8 mm (Figure 2b), mean distance between anterior margin of frontal processes of zygomatic bones was 99.3 mm (Figure 2c), mean anteroposterior diameter of eyeball was 29.2 mm and mean transverse diameter of eyeball was 27.0 mm (Table 1).

The craniofacial features seen were : frontal bossing 6 patients (85.7%), open fontanells in 5 patients (71.4%), maxillary hypoplasia in 4 cases (57%), frontal bossing 4 patients (57%), prognathism in 3 cases (42.9%), corpus callosum agenesis in 2 patients (28.6%) and presence of metopic suture and encephalocoele in one patient (Table 1).

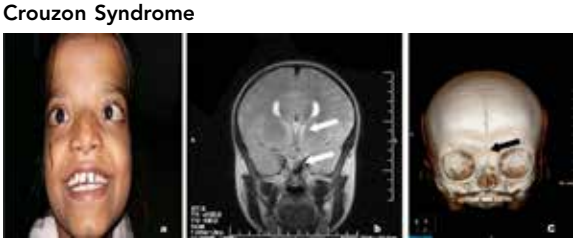
FIGURES AND TABLES

TABLE 1

Demography and Oculo-craniofacial Manifestations in patients of Crouzon Syndrome

Parameters	Value / no.of patients (%) n=7
Mean Age	13.2 ± 6.7 (range 8 to 27 years).
Gender	
Male	4 (57%)
Female	3 (43%)
Ocular Manifestations	
Visual imapairment	Unilateral 2 (28.6%) Bilateral 5 (71.4%)
Ametropia	Hypermetropia 4 (57%) Myopia 2 (28.6%)
Amblyopia	4 (57%)
Optic atrophy	2 (28.6%)
Strabismus	4 (57%)
Hypertelorism	6 (85.7%)
Proptosis	5 (71.4%)
Papilloedema	1 (14.2%)
Exposure keratopathy	2 (28.6%)
Lid lag	5 (71.4%)
Mean IPD (interpupilary distance)	67.8 mm
Mean distance between anterior margin of frontal processes of zygomatic bones	99.3 mm
Mean anteroposterior diameter of eyeball	29.2 mm
Mean transverse diameter of eyeball	27 mm
Other manifestations	
Open fontanels	5 (71.4%)
Maxillary hypoplasia	4 (57%)
Frontal bossing	4 (57%)
Corpus callosum agenesis	1 (14.2%)
Metopic suture	1 (14.2%)
Encephalocoele	1 (14.2%)

Figure 1 : A 13 years old female patient suffering with Crouzon Syndrome

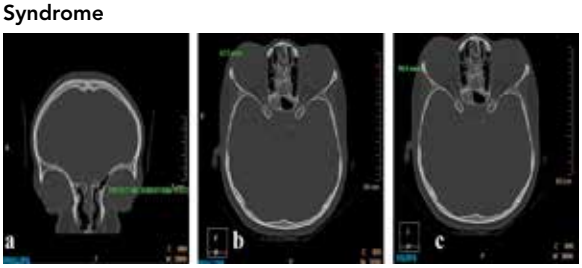


frontal bossing, proptosed eyeballs, hypertelorism, strabismus, beaked nose, prognathism and crowded teeth

Coronal view MRI showing corpus callosum agenesis and encephalocoele (arrows)

Volume rendered CT showing presence of metopic suture (arrow) and round small orbits

Figure 2 : Radiological features in patients of Crouzon Syndrome



Coronal bone window CT showing right sided defect in cribriform plate with encephalocoele

Interpupillary distance (IPD)

Distance between anterior margin of frontal processes of zygomatic bones

DISCUSSION

This syndrome was originally described in 1912 by a French neurosurgeon as an autosomal hereditary

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disease. He described four essential characteristics including exorbitism, retromaxillism, inframaxillism and paradoxic retrogonia. The affected individuals in this study presented with varying degree of craniosynostosis, ocular proptosis, hypertelorism and class III malocclusion strongly suggestive of Crouzon syndrome. The associated features of Crouzon syndrome are given in Table I. Abnormalities of the calvarial shape in Crouzon syndrome are dependent on the sutures involved[6].The most common clinical appearance as seen in both the patients, is brachycephaly. Hydrocephaly and mental retardation may develop due to premature closure of cranial sutures. Exophthalmos, which was evident in our cases, is regarded as a universal feature of Crouzon syndrome[1]. In Crouzon syndrome, ocular proptosis is primarily caused by retrusion of the lateral and inferior orbital margins with a very short orbital floor. Hypertelorism was also a universal finding and is thought to arise due to a decrease in the growth of sphenozygomatic and sphenotemporal sutures. In the diagnosis of craniofacial anomalies, thorough radiographic inspection of the cranial vault, orbits, facial bones, and temporal bones and their interrelationships yields useful diagnostic information[7]. CT is particularly useful in identifying bony and soft-tissue features in these regions. The bony interorbital distance is an essential measurement in diagnosing orbital hypotelorism or hypertelorism[8]. Before CT the principal methods used for such measurements have been based on conventional posteroanterior projection and cephalometric radiography.

CONCLUSION

Early detection to reduce amblyopia by correction of refractive errors, timely treatment of strabismus, and patching should be a priority for ophthalmologists and a goal of the craniofacial teams managing patients with Crouzon syndrome. Optic atrophy remains an important cause of visual impairment in these patients before decompressive craniectomy. Patients with Crouzon syndrome are often best cared for by a team of craniofacial experts in which professionals in plastic surgery, ear/nose/throat surgery, dentistry, orthodontics, genetics and audiology can address the patient's multiple needs.

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