Rare Presentation of Crouzon Syndrome in Siblings with Bilateral Ectopia Lentis

Atul Thadani[1], Abhishek Katiyar[2], Yusuf Rizvi[3], Abhilasha Dhankhar[4]

[1]Third Year Junior Resident, Department of Ophthalmology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India. [2]First Year Junior Resident, Department of Ophthalmology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India. [3]Professor, Department of Ophthalmology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India. [4]Third Year Junior Resident, Department of Ophthalmology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India.

PRESENTATION OF CASE

Two sibling patients aged 16 & 18 years reported at this tertiary hospital with symptoms of bilateral painless diminution of vision noticed for previous 4 & 2 years respectively. Refractive corrections did not result in tangible visual improvements. Unaided visual status of counting fingers at 1 metre (OD) & ½ metre (OS) in the 16 years old female and ½ metre (OD) and 4 metres (OS) in the 18 years old male patient foretold a similar clinical handicap. Anterior segment evaluations revealed overt superonasal subluxation of lens in the female patient while an inferior temporal zonular dehiscence, phacodonesis & a propensity for ectopia lentis were observed in the male sibling.

Intra ocular pressures of 15 mmHg (OD) & 17 mmHg (OS) in the male and 14 & 16 mmHg respectively in the female patient as on Applanation tonometry ruled out glaucomatous aetiology for poor vision. Similarly, all biometric evaluations of the globe in both patients were within normal range. Posterior segment evaluation employing fundus photography noted oval hyperaemic disc with blurred margins and absent cup with tessellated background. Optical coherence tomographic picture was unremarkable except for a pigment epithelial defect in one of the eyes.

Facial contour expressed striking features of Crouzon syndrome with Brachycephaly, prominent parrot beak nose, maxillary hypoplasia, telecanthus & low set of ears. In addition, a high arched palate, irregular dentition and a vacant expression noticed in multiple cranio facial dysostosis highlighted the quintessential features of the syndrome.

General examination revealed stunted growth and poor nutritional status in both patients. Height of 140 cm in female sibling was equal to the arm span with an Upper lower segment ratio of 0.59. There were no deformities in the extremities and no characteristic skin changes. General physical changes in male sibling were less prominent. Psychological assessment of the cases revealed a subnormal Intelligence quotient (IQ of 82) in the female but an average normal in the male. Pure tone audiometry revealed normal hearing status for both patients. X-ray chests and Echocardiographic assessments ruled out cardio-vascular malformations.

A multi-disciplinary approach, involving an Internist, Paediatrician, Clinical Psychologist, Neurosurgeon and Otorhinolaryngologist conferred the diagnosis of Crouzon syndrome.

CLINICAL DIAGNOSIS

Crouzon Syndrome with Ectopia Lentis

Corresponding Author:
Dr. Yusuf Rizvi,
Department of Ophthalmology,
Rohilkhand Medical College and Hospital,
Bareilly, Uttar Pradesh, India.
E-mail: yrizavi06@yahoo.co.in

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DIFFERENTIAL DIAGNOSIS

- Apert syndrome
- Pfeiffer's syndrome
- Carpenters syndrome
- Marfan's syndrome
- Weil Marchesani syndrome
- Homocystinuria
- Saethre-Chotzen syndrome

Figure 1. Facial Contour of Female Sibling Along with Anterior Segment and Fundus Photograph

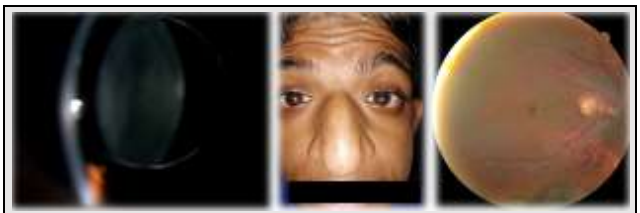

Figure 2. Facial Contour of Male Sibling Along with Anterior Segment and Fundus Photograph

PATHOLOGICAL DISCUSSION

Cranio-synostosis or premature closure of skull bones is a genetic disorder usually presenting at birth or early infancy. Depending on the number and order of affected cranial sutures it accords various shapes to the skull which characterize the clinical facies of a particular syndrome.[1] A number of these syndromes have a similar genetic aetiopathogenesis associated with mutation of 'Fibroblast growth factor receptor - 1 (FGFR-1) gene and FGFR-2 genes that bear an autosomal dominant transmission.[2,3]

Even though the syndromic presentation of Crouzon was first described by Octave Crouzon in 1912 based on its characteristic clinical features, genetic studies have proscribed it to be a variant of a group of conditions like Pfeiffer syndrome, Apert syndrome, Beare-Stevenson syndrome, Jackson-Weiss syndrome and Muenke syndrome with the common denominator of mutations in the FGFR genes.[4] With a prevalence of 16.5 per million newborns, Crouzon syndrome comprises nearly 5% of all craniosynostosis conditions.[5]

Ectopia lentis described as the displacement or malposition of the crystalline lens of eye was first noted by Beryat in 1749. The term 'Ectopia lentis' was however coined first by Stellwag in 1856, who also observed its congenital background.[6] Even though the commonest cause of Ectopia lentis is trauma, a large proportion of them present with concomitant hereditary systemic disease and associated ocular disorders.[7] This subset of patients present early in life and may present with life threatening conditions apart from the visual symptoms. The syndromic ectopia lentis conditions are hypothesized to have defective protein synthesis of microfibrils that apart from supporting many body tissues, form the architecture of lenticular zonules.[8] The Ectopia lens syndrome is hence considered an inheritable connective tissue disorder that may share some of the features of Marfan's syndrome, viz; disproportionate growth of extremities, joint laxity, pectus or spinal deformities and cardiac abnormalities like dilation of the ascending aorta with aortic insufficiency.[9] An interesting feature of these lens dislocations is their propensity to get displaced in a particular direction; superotemporal in Marfan's, Inferonasal in Homocystinuria and inferiorly or anteriorly in Weil Marchesani syndrome. The genetic zonular dysgenesis of a particular sector is hence not ruled out in explaining directional luxation of these lenses.

A disturbing feature of Crouzon syndrome as of other Cranio-synostosis conditions are the symptoms of neuropathy due to brain compression on account of early closure of cranial sutures. These may manifest as an 'Internal hydrocephalus', conductive deafness, post papilloedemic compressive optic neuropathy or mental retardation. The defects contributed by these dysgenetic changes are hence permanent and apart from the morbidity they lead to decreased life expectancy.

DISCUSSION OF MANAGEMENT

The management of these cases were strategized on two fronts. The first was the management of the subluxated lens which was causing visual symptoms. This was planned in the female sibling on account of its overt manifestation and gross visual disturbance. A capsular tension ring segment was placed to institute an extracapsular lens extraction along with a posterior segment intraocular lens implant. The male patient was only provided with conservative management that included prescription of protective glasses to save the eye from an inadvertent trauma, circumventing a more visually handicapping luxation of lens. Close monitoring of Intra ocular pressures were instituted to rule out glaucomatous effects.

The post papilloedemic optic atrophy was managed with the involvement of Neurosurgeon. Since release of prematurely fused sutures was not an option at this advanced age, the possibility of other intracranial de-compressive measures was explored like shunts. The conservative management of oral Acetazolamide, (sustained release 250 mg tablets twice a day) and oral Glycerol (0.75 gm/Kg body weight) were instituted. A prolonged multi-disciplinary follow-up along with genetic counselling were advised.

The variant nature of the reported cases were their relatively late presentation and sibling affection. Crouzon syndrome generally is noticed during infancy and despite the auto dominant genetic trait, is frequently detected sporadically with near normal siblings. The prominent clinical

feature of this syndrome is bilateral proptosis on account of the shallow orbits. The visual affection due to exposure keratopathy is the imposing challenge apart from the enhanced intra cranial pressure. The latter condition entails early neurosurgical intervention to release the pre-maturely fused cranial sutures and subvert the ill effects of compression of a developing brain.

The present two patients differ, with their late presentation with visual complaints that can easily be attributed to simple refractive errors. In addition, their near normal mental faculty, absence of other systemic affections or absence of a history of compressive neurological symptoms like frequent headaches, vomiting or seizures makes them conspicuous.

Associated ocular abnormalities in Crouzon syndrome like Iris coloboma, nystagmus, microcornea, megalocornea, anisocoria, congenital glaucoma, blue sclera or ectopia lentis have very few reports in literature. Bilateral ectopia lentis among siblings in Crouzon syndrome has not been reported to the best of our knowledge. Again, the superonasal shift of the crystalline lens or even the dysgenesis of the inferotemporal zonules is an observation not mentioned in existing literature.

The essence of this clinical report lies in the existence of craniofacial anomalies that may present late with ocular symptoms. Conversely all cases of ectopia lentis, optic disc oedemas, or ocular malformations must be explored for craniofacial dysostosis. Clinical data is perhaps as forthcoming as molecular biological reports which may not be accessible even at tertiary centres. The multidisciplinary approach in such cases again needs to be emphasized. This is essential not just for the sake of ophthalmic management but also due to the probability of other systemic abnormalities like cardiovascular defects (patent ductus arteriosus, coarctation of aorta, etc.,) or skin conditions such as acanthosis nigricans.[10] Equally important is the screening of close relatives of such patients who may be detected with different stages of the disease.

CONCLUSION

Ectopia lentis constitutes an integral feature of cranio facial synostosis syndromes. Although rarely reported in Crouzon syndrome, its possibility should be considered in ocular management especially among siblings.

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