Crouzon Syndrome: A Rare Case of Severe Intrauterine Craniosynostosis

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Introduction

Crouzon syndrome is characterized by severe premature craniosynostosis of coronal and sagittal sutures, a rare genetic disorder with brachycephaly reported in a male baby with distinctive facial features and low set ears known as branchial arch syndrome, caused by mutation in the fibroblast growth factor receptor 2 (FGFR2) gene located on chromosome 10 being an autosomal dominant disorder with complete penetrance and variable expressivity [1], was first described by a French neurosurgeon Octave Crouzon in 1912 [2]. Normally the bones of the skull fuse after the growth of brain which begins in the first year of life. Early fusion of skull bones both endochondral (nasal, occipital) and membranous (frontal, parietal, interparietal) interfere with development of brain with raised intracranial pressure and multiple sutural synostoses of skull base causing mid-facial hypoplasia, shallow orbit resulting in abnormal head shape and abnormal facial features and occasional upper airway obstruction [3-5].

Keywords

Crouzon’s Syndrome; Severe Craniosynostosis at Birth

Case Report

A single live term boy baby was born by normal vaginal delivery to a second gravida mother with one normal living child. The baby was severely asphyxiated at birth required resuscitation with nasopharyngeal airway and intermittent positive pressure ventilation, and despite establishing respiration continued to have respiratory distress with subcostal recession requiring supplemental oxygen with Apgar score 3 at 1 min and 7 at 5 min. Obvious external congenital malformations included brachycephaly, frontal bossing, shallow orbits with marked proptosis of eyes, external strabimus, hypertelorism with downward slanting of palpebral fissure, mid facial or hypoplastic maxilla with prognathism or chin appears to protrude inspite of normal growth of mandible giving the effect of a concave face, beak like nose or psittichorhina and low set abnormally shaped ears with bulging mastoids. Additionally there were noticeably short humerus and femur bones relative to the rest of the body.

Radiographic analysis by a computed axial tomographic scan is the gold standard for diagnosing craniosynostosis confirms the diagnosis of Crouzon syndrome with calcifications or craniosynostosis of coronal and sagittal sutures while ultrasonogram and chest and abdomen revealed no internal congenital malformations. The baby was subsequently started on oral feeds and was...
discharged on seventh day as parents refused any further treatment and management for craniostenosis, however the patient returned for follow up at six weeks of age and on bottle feeds. Father had mild features of Crouzon’s Syndrome, hence the importance of prenatal genetic counselling. Newborn baby with severe craniosynostosis - Crouzon’s syndrome is seen in Figure 1.

Discussion

Crouzon syndrome is a rare genetic disorder and an autosomal dominant genetic disorder also known as branchial arch syndrome as the first or pharyngeal arch the precursor of the maxilla and mandible is affected with premature synostosis, first called as “craniofacial dystosis” by French neurosurgeon Octave Crouzon in 1912 [2], caused by mutation of fibroblast growth factor receptor 2 (FGFR2) located on chromosome 10 which regulated the production of a protein known as fibroblast growth factor receptor (FGFR) [1]. Genetic mutation disrupts functioning of such proteins causing abnormalities of bone development and growth with malformation of craniofacial area [3-5].

The incidence of Curozon’s Syndrome is estimated to occur in 1.6 out of every 100,000 people [6]. There is greater frequency in families with a history of the disorder; approximately 50% of children in syndromic cases will be affected as it is autosomal dominant, only one parent needs to be a carrier for a child to inherit the condition. About 97 percent of these children have normal intelligence. Most genetic diseases require two copies of a gene, one received from the father and one from the mother; however in dominant genetic disorders only a single copy of an abnormal gene can be inherited from either parent. The risk is same for both males and females. Spontaneous (de novo) genetic mutations may occur in ova or sperm cell, when the disorder is not inherited from parents. Crouzon syndrome comprises approximately 4.8% of all cases of craniosynostosis, no known race or sex predilection exists [6, 7].

The resulting shape of skull depends on pattern of growth with premature fusion of different sutures, fusion of metopic suture causes trigonocephaly, fusion of coronal suture brachypehaly, fusion of sagittal suture dolichocephaly, unilateral fusion of lamboid and coronal sutures plagiocephaly, fusion of coronal and lamboidal sutures oxycephaly and complex or severe fusion or some or all sutures results in cloverleaf shaped head or skull to be abnormally divided into three lobes also known as kleeblattschadel type Craniosynostosis [5].

Craniostenosis is classified as ‘simple’ or isolated if only one of four sutures close prematurely. When two or more are involved it is ‘complex’. A second classification depends on clinical description of resulting shape of skull, while a third classification is called ‘nonsyndromic’ or isolated craniosynostosis with no extracranial deformations and ‘syndromic’ when extracranial malformations involving limbs, heart, central nervous system or respiratory tract is present [4].

Prominent characteristics in Crouzon’s syndrome is brachycephaly with short broad head and prominent forehead, more severe cases may have cloverleaf shaped head. Shallow orbits after early fusion of surrounding bones, causes exophthalmos with hypertelorism, external strabismus and downward slanting palpebral fissure of eyes, may cause exposure keratitis as exposure conjunctivitis. Hypoplastic maxilla with insufficient growth of midface results in relative prognathism where chin appears to protrude despite normal growth of mandible giving the face a concave effect. Low set ears are a pronounced feature of the branchial arch syndromes in the developing embryo. In the fetus the ears are much lower than in the adult and during normal development the ears “travel” upwards on the head which is disrupted in Crouzon’s syndrome compounded by ear canal malformations leading to some hearing loss and in some cases Meniere’s disease. Increased intracranial pressure leads to optic atrophy with visual impairment, sleeping disorders, eating difficulties or impairment of mental development with significant reduction in IQ and approximately one-third may develop hydrocephalous. Some infants with upper airway obstruction lead to acute respiratory distress, clefting of lip and/or palate occur rarely. Typical dental problems include high arched narrow palate with crowded teeth and malocclusion. Crouzon’s syndrome may also be associated with patent ductus arteriosus (PDA) and aortic coarctation. Partial syndactyly appears in “Type II’ Crouzon syndrome. In addition for reasons not entirely clear Crouzon patients also have a noticeably shorter humerus and femur bones relative to the rest of the body [2-4].

Differential diagnosis of syndromes associated with fibroblast growth factor receptors include Apert syndrome where there is also syndactyly or fused fingers or toes and flat midface, Pfeiffer syndrome have acrocephalosyndactyilia with unusually broad short fingers and toes brachydactyly, webbed or fused fingers and toes. Jackson Weiss Syndrome has in addition enlarged bent
toes preaxial foot polydactyl, tarsal synostosis and flat midface [8].

Diagnostic investigations include CT scanning and MRIs to detect craniosynostosis [9], molecular genetic testing can detect mutations in the FGFR2 gene to confirm Crouzon syndrome [10].

Management of Crouzon’s syndrome is multidisciplinary and early diagnosis is important even as the abnormal head shape resulting from craniostenosis in infants and children continues to be a diagnostic and therapeutic challenge. Surgery to release synostotic sutures is the main treatment to expand and reshape skull in the first year of life to allow adequate cranial volume for brain growth and expansion. Skull reshaping may need to be repeated as the child grows to give best possible results and best started in late infancy between six to twelve months. Also midfacial advancement and jaw surgery to provide adequate orbital volume and reduce the exophthalmos and to correct occlusion to a more appropriate functional position and to provide for a more normal appearance. Multidisciplinary approach include a team of specialists paediatricians, neurosurgeons, plastic surgeons, otolaryngologists, audiologists, ophthalmologists, dental specialists, social workers and other health care workers. Genetic counselling and psychosocial support for the family is also essential. Prognosis depends on malformation severity [11-13].

References