Surgical treatment of craniofacial dysostosis in monozygotic twins

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A family with craniofacial dysostosis affecting a father and his monozygotic twin sons is described. The father had no surgery until linear craniectomy when 3 years old; he is of normal intelligence but legally blind. Prophylactic coronal craniectomy and orbital decompression were done on the twins. One had an uncomplicated course and is developing normally. The other developed neonatal meningitis and ventriculitis with secondary hydrocephalus, plus poor vision and retarded development.

KEY WORDS monozygotic twins · Crouzon's syndrome · craniofacial dysostosis · craniosynostosis · blindness

CRANIOFACIAL dysostosis, characterized by craniosynostosis and facial malformation, was described as a hereditary syndrome by Crouzon in 1912. A report in 1933 by Günther in the German literature mentioned a family with affected twin sisters. In a Swedish publication Fogh-Anderson noted an affected mother who had dizygotic twins, one of whom was also affected.

Flippen was the first to describe a hereditary case in the English literature in 1950, but to our knowledge there are no reports in English of affected twins. We have had the opportunity of caring for twins with hereditary Crouzon's syndrome from birth, and planning early preventive surgical procedures to avert possible blindness and mental retardation.

Case Reports

Monochorionic twin boys were born of a 19-year-old healthy mother with borderline intelligence and a 25-year-old father with craniofacial dysostosis, average intelligence, and amaurosis. Pregnancy was uneventful and delivery uncomplicated at 36½ weeks' gestation. There were no other affected relatives.

Case 1

In Twin B, features of Crouzon's syndrome were noted at birth: brachycephaly, mild frontal bossing, ridging of coronal sutures, proptosis, hypertelorism, and maxillary hypoplasia (Fig. 1). Optic discs were normal. Head circumference was 31.5 cm (below 3rd percentile), weight 2550 gm, length 50 cm. Skull films demonstrated bilateral coronal synostosis and a shallow posterior fossa.

Bilateral coronal craniectomy was done at 3 weeks for the synostosis and a repeat right coronal craniectomy at 5 months because of refusion. Persistence of proptosis necessitated left orbital decompression at the age of 3½ months and right orbital decompression at the age of 5 months. Head circumference
had increased to 43.0 cm (25th percentile) at 6 months, and to 44.5 cm (40th percentile) at 7\(\frac{1}{2}\) months. When the infant was 14 months old, psychometric studies suggested a mental age of 12.6 months (Cattell Scale) with an I.Q. of 90. The Vineland Social Maturity Scale recorded his social age as equal to his chronological age. Repeated fundoscopic examinations continue to show normal fundi.

**Case 2**

The twin of Case 1, Twin A, had identical features of Crouzon's syndrome at birth. Head circumference was 31.5 cm, birth weight 2200 gm, length 50 cm. At 1 week of age neurological examination was considered normal. Skull films showed bilateral fusion of coronal sutures, shallow orbits, and shallow posterior fossa.

When the infant was 11 days old, he developed *E. coli* sepsis, which 2 days later advanced to meningitis and ventriculitis in spite of Kanamycin treatment. A 1-week course of intraventricular Polymyxin B was instituted, and, although he developed focal seizures, ventricular fluid was sterile 2 weeks after the onset of ventriculitis. Obstructive hydrocephalus was evident by air study the following week. Numerous CSF shunting procedures were necessary but by the time he was 9 months old a left ventriculoperitoneal shunt was functioning well.

Bilateral coronal craniectomy was done at 2 months, repeat right coronal craniectomy and right orbital decompression at 5 months, and a left orbital decompression at 11 months. Orbital decompression was performed because of failure of resolution of proptosis even though papilledema was not present. Head circumference was 44.5 cm (50th percentile) at 6 months. At 9 months, vision and cranial nerves appeared intact, but he did not sit alone or actively reach for objects and his deep tendon reflexes were hyperactive. On the Cattell Infant Intelligence Scale administered at age 18 months, he achieved a mental age of 14 months with a corresponding I.Q. of 77. Generalized seizures developed at 1 year and were easily controlled by Dilantin. Repeated ophthalmological evaluations revealed normal fundi.

Blood typing on the twins was identical as follows: types A, D/c/E, N, K--, Fy.

Chromosomal analysis was normal male karotype on both patients.

**Case 3**

The twins' father was the second of five children, the siblings being normal (Fig. 2). Progressive loss of vision was noted at 3 years, at which time he underwent a series of three linear craniectomies. Intelligence remained normal. He attended sight-saving classes in grammar school and graduated from a regular high school. At present he directs a small business. He has light perception only in one eye but can read newsprint at close range with the other. The optic discs are atrophied. He is acrocephalic with mild proptosis, exotropia, hypoplastic mid-facies.

**Discussion**

Crouzon's syndrome of craniofacial dysostosis results from defective bone formation involving the skull and face. The combination of defects in Crouzon's syndrome consist of: 1) premature synostosis of sutures, most commonly the coronals, with resulting brachycephaly or acrocephaly; 2) facial malformation consisting of maxillary hy-
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poplasia, short nasal bones and beaking of the nose, shallow orbits, and prominent bregma; 3) eye changes including proptosis, exotropia, optic atrophy, and blindness.

Etiology of the syndrome is unknown. The cranial synostosis is a result of disturbed membranous bone formation, with loss of continuous growth of interstitial mesenchymal tissue between the bone margins of the sutures. Intramembranous ossification occurs in the following bones of the head: 1) skull vault—frontal, parietal; 2) skull base—interparietal segment of the occipital, orbitotemporal segment of the greater wing of the sphenoid, squamosal segment, and zygomatic process of the temporal; 3) face—mandible, maxilla, malar, lacrimal, and nasal bones.

Defective growth of intramembranous facial bones results in hypoplastic mid-facies. Imbalance of growth between intramembranous and endochondral bones of the skull base apparently explains the shallow orbits and hypertelorism (the latter from the relatively greater growth of the lesser wings of the sphenoid compared to the lateral portion of the greater wings.).

The majority of cases of Crouzon's syndrome are hereditary and transmitted in the pattern of a Mendelian dominant trait; one quarter of the cases are sporadic. Hereditary origin was apparent in 60 of 86 cases cited by Atkinson. Flippen described a family in which 10 of 21 progeny in four generations were affected. Dodge, et al., accumulated two hereditary and three sporadic cases at the Mayo Clinic. Vulliamy and Normandale reported a family in which 14 members were known to have Crouzon's syndrome. Pinkerton and Pinkerton found four cases in a family of seven: the mother and three of her five children.

In the family we have reported, the condition appeared in the third generation as a mutation of the dominant gene, and the twins showed concordance for the syndrome (Fig. 2). Monozygosity of these twins is established by their monochorial placentaion, as there is no established case of dizygous twins with such a placenta. Schiller reported a sibship of 15 with seven affected, including two sets of dizygotic twins; in each set one member was affected and one was not. Shillito and Matson state that coronal or multiple synostoses have a higher familial incidence than other types. Of their 519 patients, nine families had two involved siblings including one pair of identical twins, but the authors make no mention of Crouzon's syndrome among these.

There is no published documentation known to us of the incidence of mental retardation expected in untreated Crouzon's syndrome or other craniostenoses. Generally ac-
cepted concepts hold that craniosynostosis can impair normal brain growth, lead to increased intracranial pressure, and cause mental retardation and optic atrophy. Probably there is no intrinsic malformation of the brain in uncomplicated craniostenosis. Autopsy on a 2-year-old boy who had had fusion of the coronal and lambdoid sutures which was surgically treated (Dodge, et al.) showed a normal brain on gross and microscopic examination. The four cases of Crouzon's syndrome among 38 patients with cranial synostosis treated by Andersson and Gomes all showed normal mental development.

Since it is known that even single suture synostosis may cause increased intracranial pressure, and that there is a suggestion that surgical correction of craniosynostosis under 1 year of age may relate to a lower incidence of mental retardation compared to untreated cases, early craniectomy is advocated to prevent constriction of the brain. Andersson and Gomes summarized the evidence in favor of early craniectomy and point out the necessity of early surgery in all cases because of the impossibility of predicting which ones may result in brain damage.

Optic atrophy and loss of vision cause a second problem and one that may result from either increased intracranial pressure associated with craniosynostosis, or encroachment on the optic nerve by a shallow orbit and narrow optic foramen. Therefore, the treatment of our twins was prophylactic from a dual approach; craniectomy to prevent increased intracranial pressure, and orbital decompression to alleviate distortion of orbital contents.

It was our initial hope that synostectomy alone would help resolve the orbital proptosis, an approach supported by Matson. However, the continued protrusion of the orbital contents along with the attendant possible risks of optic nerve compression and corneal ulceration prompted us to proceed with the decompressions which have subsequently proven effective. The nature of the mid-facial multiple bone deformities in this particular syndrome argues against resolution of orbital proptosis following simple synostectomy, and one should probably seriously consider orbital decompression in the routine management of these patients.

In Twin B with uncomplicated disease, the resulting psychomotor development and vision seem to be normal. Twin A's course has been complicated by meningitis, ventriculitis, and secondary hydrocephalus; he now has functioning vision, but retarded development. As the twins grow, periodic refraction or visual acuity testing and psychological testing will be performed, to assess function and aid in school planning.

References


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