Acta Genet Med Gemellol 33:501-504 (1984)

TWIN RESEARCH 4 - Part C: Clinical Studies
Proceedings of the Fourth International Congress on Twin Studies (London 1983)

Discordance for Skeletal and Cardiac Defect in Monozygotic Twins

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Abstract. A case of monozygotic male twins discordant for skeletal and cardiac defect is reported. One twin had the hemifacial microsomia type of the oculo-auriculo-vertebral dysplasia. The cotwin had no asymmetry of the face and normal ears, but preaxial polydactyly and ventricular and auricular septal defects. The cotwins were concordant for craniostenosis with a ridge metopic suture. Karyotypes were normal.

Key words: Craniostenosis, Oculo-auriculo-vertebral dysplasia, Twins

The frequency of structural defects in morphogenesis is increased in twins as compared to singletons. This excess is entirely due to the increased incidence of aberrations in monozygotic twins [5,9]. We wish to report a case of MZ male twins discordant for skeletal and cardiac defect, as a contribution to the understanding of birth defects.

CASE HISTORY

The twins are born at 36 weeks gestation to a healthy mother. They were monoamnionic and concordant for blood groups and HLA. The parents come from healthy families, have never been ill, and denied consanguinity. Mother had no radiation, no teratogenic contact and no illness during pregnancy. At the birth of the twins the father was 33 and the mother 32 years of age. They had a daughter of 5 years with dislocation of the hip. The mother never had a miscarriage nor practiced contraception.

Twin A was the first born with a length of 45 cm and a weight of 2500 g. He showed a clear underdevelopment of the left half of the face and a deviation of the chin to the left. The left external ear was hypoplastic. The auditory meatus was missing. Anterior to the left ear there were several cutaneous tags. There was no detectable fistula. He had a ridged ectopic suture. He had no heart murmur and no mental retardation. At X-ray examination the skull shows metopic cranio-stenosis, asymmetry of mandibula; maxilla, base of the skull and petrosa visible detrimental to the left. The external auditory meatus is lacking. No abnormality is visible on photographs of the spine.

Twin B was born with a length of 41 cm and a weight of 1800 g. He was cyanotic at birth and required intubation. He had a narrow and prowshaped forehead with a ridged metopic suture, shallow supraorbital ridges and lateral displacement of the inner canthi. He showed no asymmetry of the face.

His ears were normal. He had preaxial polydactyly of the left thumb with partial syndactyly of the 2d and 3d toes. A heart murmur was heard. He had no mental retardation. He sat at 6 months. He had bilateral cryptorchidism. At X-ray examination the skull shows metopic cranio-stenosis. The second phalanx of the thumb was duplicated. At cardiac catheterization a ventricular septal defect type II_B and an auricular septal defect were demonstrated.

Karyotypes (R and G-banding) were normal in both twins and their parents.

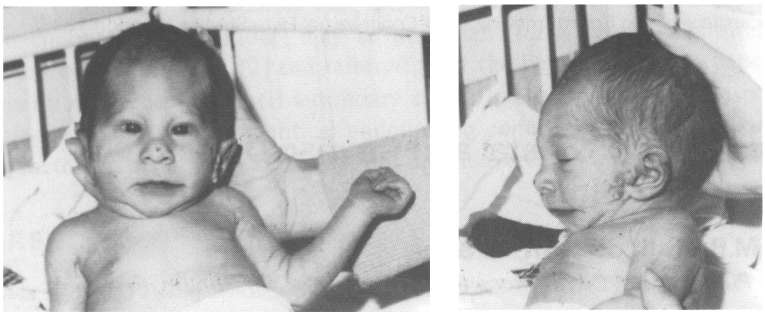

Fig. 1 - Twin A.

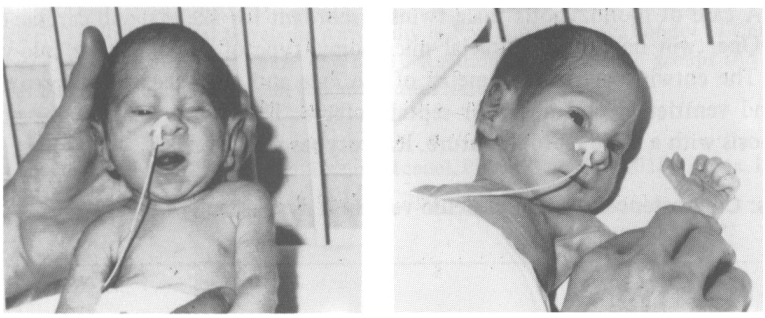

Fig. 2 - Twin B.

DISCUSSION

Gorlin et al [3] gave an excellent review of the great variation in the Goldenhar syndrome. Because of the frequent deviations of the spinal column, they introduced the name oculo-auriculo-vertebral dysplasia and indicated the relation with hemifacial microsomia. Their view that both syndromes are manifestations of the same dysmorphogenesis was confirmed by Pashayan et al's [10] patient, who had the characteristics of both hemifacial microsomia and oculo-auriculo-vertebral dysplasia. Etiology of this syndrome is controversial. There are few indications for teratogenesis or heredity. Twin pairs have been described, all but two discordant [13].

Acrocephalopolysyndactyly (Carpenter Syndrome) was described by Carpenter [2] in two sisters and a brother exhibiting a syndrome consisting of acrocephaly, peculiar facies, preaxial polydactyly and syndactyly. Additional features were obesity, mental retardation and hypogonadism. Autosomal recessive inheritance was considered likely [16]. Greig, in his discussion of oxycephaly [4], described association of digital malformation with cranial deformity in a mother and her daughter. The thumbs were short and flat with an attempt at bifidity of the distal phalanges. A sporadic case with similar cranial and digital malformations was reported by Korting and Ruther [8]. This entity is characterized by the association of peculiar skull shape, which is not oxycephaly, with polysyndactyly. The inheritance is autosomal dominant [16].

In 1973 Quan and Smith [12] introduced the acronym Vater to characterize an association of vertebral anomalies, tracheoesophageal fistula, anal atresia with renal and/or radial dysplasia. Limb abnormality includes reduction, hypoplasia, polydactyly and syndactyly of radial, preaxial axis, ie, thumb, first metacarpus and radius of upper limbs. Temtamy and Miller [15] later added cardio-vascular defects, eg, ventricular septal defects, Fallot, atrial septal defect, duodenal atresia and anomalies of the external genitalia. The spectrum of manifestation ranges from the full picture to individual isolated feature. This syndrome has generally been a sporadic occurrence.

In 1960 Holt and Oram [6] described a syndrome of skeletal and cardiovascular abnormality. Hypoplasia and proximal placement of the thumb is the most common defect but triphalangeal thumb and extracarpal bones may occur [11].

Twin A has the oculo-auriculo-vertebral syndrome. He has no epibulbar dermoids nor vertebral malformation. He shows a clear underdevelopment of the left half of the face with hypoplastic left ear and preauricular tags. He has the hemifacial microsomia type of the syndrome. He has metopic craniostenosis.

Twin B is a patient with features of the Carpenter and Greig cephalopolysyndactyly syndromes and of the Vater and Holt-Oram syndromes. Carpenter syndrome and Greig syndrome both have cranial and digital malformations. However, in Greig syndrome the peculiar skull shape, which is not oxycephaly, is due to expansion of the cranial voult leading to a voluminous forehead and a high bregma with no evidence of premature synostosis of cranial sutures. Digital malformations are bilateral in hands and feet: short and flat thumbs, webbing between the toes, bifid terminal phalanx. Our patient has unilateral duplication of one thumb. His head deformation is not oxycephalic-like. Obesity is not noted but it is too early. As in Carpenter syndrome, stenosis of cranial sutures and hypogonadism were noted, but no mental retardation. Preaxial polydactyly usually involves the big toe in Carpenter syndrome, but cases with duplication of the thumb were reported. Turner's [17] patient had pedunculated post-minimi on both hands, a frequent finding in patients with preaxial polydactyly. Both syndrome are inherited, Carpenter syndrome as autosomal recessive and Greig syndrome as autosomal dominant. The parents of our patient were healthy and not related.

Vater association is more frequent in twins than in singletons [13]. Twin B had two abnormalities of the Vater association and of the Holt-Oram syndrome, radial and cardiac, but he had not the other defects of these syndromes. Holt-Oram is inherited as autosomal dominant. Vater association is generally sporadic but Auchterlonie and White [1] had seen the syndrome in two brothers. King et al [7] reported a tracheoesophageal fistula in a pair of MZ twins, in one being an isolated finding and in the other part of the Vater association.

Oculo-auriculo-vertebral dysplasia is already found in 13 MZ twin pairs (for review see Schinzel [13]), 2 of them being concordant. However, there are few data to conclude for an exogenous or endogenous origin of this dysplasia. The absence of consanguinity and the few familial accumulations (the majority of cases being sporadic) fail to support a hereditary etiology, while the absence of clear disturbances of pregnancy fail to support a teratogenic etiology. The concordance in MZ twins is so striking that it seems possible to assume a genetic form of the syndrome. It may be only a genetic predisposition which is realised under unfavourable circumstances. No exogenous influence could be demonstrated, but this does not exclude one acting on a genetical predisposition. Up to now only few agents were demonstrated to be teratogenic in man, but many are in animals.

It is unlikely that the two syndromes could have occurred together by chance. The

frequency of the oculo-auriculo-vertebral dysplasia is unknown. We have registred only one oculo-auriculo-vertebral dysplasia and one Vater association in a survey of near 20,000 consecutive births [14]. Therefore, the probability that both syndromes occurred by chance is at maximum 1/20,000 x 1/20,000 = 1/400,000,000.

Variable expression is a common problem encountered by those who study syndromes. The features displayed by our cases could be variable expression of the same disease. Such variations between MZ twins affected by congenital malformations exemplify the potential range of expression of an anomaly rather than suggesting separate genetic factors for individual features [13]. Little is known about the mechanism for MZ twinning, including those examples with additional early malformations. Our case supports the hypothesis that an early developmental defect of an unknown origin (vascular ?) produces craniosynostosis in both twins and hemifacial microsomia in one and cardiac with skeletal defect in the other.

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