

MONOZYGOTIC TWINS WITH CONCORDANCE FOR DOWN'S SYNDROME AND CONGENITAL HEART DISEASE

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Cytogenetic, clinical, and other findings are presented on a pair of same-sex, monochorial MZ twins concordant for both trisomy 21 and congenital heart disease. The literature on Down's syndrome in twins and on congenital heart disease in twins is reviewed and the exceptional occurrence of concordant congenital heart disease in MZ twins is stressed.

Among those suffering from mental retardation, we can frequently find patients originating from multiple pregnancy. Berg and Kirman (1960) found twice as many twins, among the mentally retarded, as in average births. It is noteworthy that, in spite of the high incidence of Down's syndrome relatively few 21-trisomic twins are known in the literature (Richards 1971). It is considered possible that the unbalanced chromosome substitution leads to prenatal death more easily in twins.

Studies of twins with Down's syndrome might be expected to give useful evidence in determining the etiology. Down's syndrome has been reported in 107 pairs by Oster (1953), 31 pairs by Allen and Baroff (1955), 162 pairs by Keay (1958), 146 pairs by de Wolff et al. (1962), and 185 pairs by Zellweger (1968).

The incidence of congenital heart disease is high among twins of identical sex, but the concordance rate is rarer (Hay and Wehrung 1970, Telfer et al. 1972). The case of a pair of MZ twins, concordant for both Down's syndrome and congenital heart disease, may therefore prove of some interest.

CASE HISTORY

The mother of the children is 22 years old and has been married 2 years, with a normal delivery in her obstetrical anamnesis. Her first child is living and healthy. She was admitted in the 39th week of her second pregnancy. Hydramnion was established on the basis of external examination as well as on account of the large abdomen, and, considering that her sister also had a twin pregnancy, we thought of a twin pregnancy. Because of Rh incompatibility, she was under immunological control, which once indicated a mild sensitization. She gained 2 Kg, took no drugs, and underwent chest X-ray in the third month.

Her husband is her second cousin; from the two marriages of his mother, 4 children were born who died in infancy, in addition to the healthy offspring.

On the day following admission, spontaneous delivery took place. Two girls were born, with skull presentation, respectively weighing 2300 and 2350 g (weight percentiles lower than 25), and 44 and 45 cm of length. The placenta was monochorial diamniotic.

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TABLE
BLOOD GROUPS OF TWINS AND THEIR PARENTS

Blood Group	Father	Mother	Twin A	Twin B
ABO	B	A	AB	AB
Rh	DCE	dce	dce	dce
K	k	k	k	k
MN	MS NS	MS NS	MS NS	MS NS
Duffy	a + b +	a — b +	a — b +	a — b +
Xg ^a	—	+	+	+

The newborns showing characteristics of Down's syndrome, cord-blood lymphocytes were cultured (Papp and Gardó 1970). The assumed hydramnion was also verified, approximately 3000 ml of amniotic fluid being discharged during delivery.

Changes observed in the newborns: oblique palpebral fissures, epicanthal folds, large tongue, flexed helix (especially in twin A), flat profile and nose-bridge, muscle hypotension, weak patella reflex, deficient Moro reflex. The palms were square, the fingers short. The palm prints of both twins provided clear evidence of Down's syndrome. On every finger-tip of both newborns there was an ulnar loop — excepting the fourth finger of the right hand showing an arch.

Immediately after delivery, auscultation indicated a possible heart defect in twin A.

In the lymphocyte cultures of the newborns, 35-38 metaphases were evaluated. They proved unequivocally to be regular G-trisomies, with no other structural or numerical deviation (karyotype: 47,XX,21+). There was no evidence of mosaicism.

The further fate of twin A: frequent dilute stools lasting for days in the fifth week, vomiting, lack of appetite, so that it became necessary to treat her for debility. There was a blowing systole murmur above the heart, a diffuse, rasping breathing above the lungs, sanguine pharyngeal formations, gaseous intestines, and fungus in her mouth. Bacterial stool culture: negative. She weighed 3280 g after recovering from influenza. In her fifth month, she was again treated for acute enterocolitis and influenza. Her cardiac status: a punctum maximum above the stoma, a blowing, rasping-like systole murmur of the V degree in the left parasternal IV intercostal space.

EKG: sinus rhythm. Normal stimulation development and conduction. Principal axis deviating to the left. P congenitale in chest recording. Signs indicating biventricular hypertrophy.

Dg.: Vitium cordis cong. Vero similiter defectus septi ventriculi et stenosis aortae.

The cardiac status did not change after Isolanid treatment. She was repeatedly treated for bronchitis and gripe at 8 and 12 months. Her dyspnea and cyanosis became moderate after hospital treatment. Her general condition is satisfactory at the age of 1½ years, her mental level corresponds to Down's syndrome.

Twin B was under pediatric control for months from the age of 4 weeks. When she had been cured of enterocolitis and gripe, her congenital heart disease, dystrophy, and — from the age of 6 month — her bronchopneumonia, came to the fore. The chest X-ray showed cardiac enlargement, primarily right ventricular, with increased pulmonary vascularity, and a systole blowing-like murmur was to be heard in the IV intercostal space. EKG: almost identical to that of twin A. In spite of being treated with antibiotics, she died at the age of 7 months, probably in consequence of pneumonia. The autopsy was not carried out in our university, so we could only find an imprecise description later, in which there was a ventricular-septal defect.

The karyotype of the parents is normal, we were not able to demonstrate any trisomic cells in the form of mosaicism. The family was counseled that their risk of recurrence for Down's syndrome was not high nor significantly increased because of having had twins concordant for Down's syndrome. In the next pregnancy, a healthy boy, weighing 3850 g, was born in the 40th week of gestation.

DISCUSSION

In 1954, Young gave an account of MZ twins, both with Down's syndrome. He gave a survey of the literature and collected altogether 102 cases in which one or both twins suffered from Down's syndrome.

MZ twins usually show concordance for trisomy 21, though less than expected (Lipovetskaia 1964, Rasore-Quartino 1967, Shiono et al. 1971). From a study on 26 MZ pairs with Down's syndrome (Zellweger 1968), concordance was reported in 22 pairs and discordance in 4. Twenty-six pairs assumed to be MZ, over a total of 185 pairs, would represent an incidence of 14.1%. This is lower than the calculated expectation, estimated as 26.3% by Smith (1955) and 30% by Allen and Baroff (1955). Keay (1958) endeavours to explain this contradiction by stating that very often one of the twins with Down's syndrome probably dies before birth. Many more MZ twins were described than expected, of which only one suffered from Down's syndrome (Lejeune et al. 1962, de Wolff 1962, Citterio 1964, Turpin 1964 and 1970, Dekaban 1965, Nielsen 1967).

Male MZ twins concordant for Down's syndrome and female MZ twins discordant for trisomy 21, were found in a study by Shapiro and Farnsworth (1972).

Examples of possible DZ twins concordant for Down's syndrome have been reported in the past, but with no cytogenetic findings (MacKaye 1936, Gordon and Roberts 1938, Jervis 1943, Keay 1958, Nicholson and Keay 1959, McDonald 1964).

Theoretically, it could be assumed that DZ twins do not show greater concordance for Down's syndrome than simple siblings (Kiossoglou et al. 1963, Wright et al. 1963, Massimo et al. 1966). McDonald (1964) made a study of 67 pairs of twins and only in the case of 2 sets of twins of opposite sex did he find concordance for Down's syndrome. On the basis of theoretical calculations, there should be a much smaller ratio of concordance among DZ twins. McDonald (1964) sets the rate of concordance at 14% among same sex, and 6% among opposite sex DZ twins. Friedman (1955) found concordance for Down's syndrome to be 30% among 71 same sex pairs, and 0% among 42 opposite sex pairs of twins.

It is an old observation that congenital heart defect can be found in only one of MZ twins (Weitz 1936, Forsyth and Uchida 1951, Morison 1959). In the 26 pairs of Uchida and Rowe (1957), and in the 38 pairs of Campbell (1961) there was not a single instance of concordance.

The observation of concordant congenital heart disease is extremely rare in MZ twins (Nora et al. 1967). Lamy et al. (1957) described a pair of twins both afflicted with pulmonary stenosis, but this observation was made on DZ twins.

Not long ago, Telfer et al. (1972) gave an account of a 21-trisomic MZ pair of twins discordant for congenital heart disease. The associated occurrence of Down's syndrome and heart defect in twins is not frequent.

According to Hay and Wehrung (1970), the high incidence and low concordance of congenital heart disease among twins of the same sex indicates that the placental anastomosis may play a significant role in the development of this disorder.

In contrast, the data referring to Down's syndrome show a high concordance and a low incidence among twins of the same sex. Friedman (1955) points out that, in spite of the high incidence of Down's syndrome (1:500-1000), there are relatively few occurrences of twins, probably on account of the early death of the MZ embryos.

In the cases reported before the introduction of cytogenetic examinations, no light was thrown upon the type of the trisomy, an incidental mosaicism, or a double aneuploid, or,

consequently, on their percentile ratio, either. Richards (1969) found mosaicism in MZ twins; Hustinx et al. (1961) were able to demonstrate 21 trisomy and XXY gonosomal constitution in male twins. Turpin et al. (1964) also emphasize the necessity of careful cytogenetic examinations in the case of all MZ twins suspected of having Down's syndrome.

In our case, a regular trisomy was found, and no mosaicism. Our case can be considered an exception, in that congenital heart disease could also be demonstrated in both MZ twins. The only question is whether this was caused by genetic or environmental factors. Rowe and Uchida (1961) studied 184 children with Down's syndrome and found that 40% had cardiac and cardiovascular malformations.

In the majority of MZ twins, fetal circulation is common, and can theoretically become unbalanced, thereby causing disorder in one of the fetuses (Price 1950). According to Uchida and Rowe (1957), heart disease is not more frequent in twin than in single pregnancies. This argues against a genetic origin. The generally reported discordance in MZ twins also argues against genetic factors.

It could even be imagined that congenital heart disease may be associated with Down's syndrome in 40% of the cases, so that the congenital heart defect in our twins would not result from environmental factors.

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RIASSUNTO

Gemelle Monozigotiche Concordanti per Sindrome di Down e Cardiopatia Congenita

Vengono presentati i risultati di esami citogenetici e clinici ottenuti su di una coppia di gemelle MZ, concordanti sia per trisomia 21 che per cardiopatia congenita.

Viene passata in rassegna la bibliografia sulla sindrome di Down e sulle cardiopatie congenite in gemelli e viene sottolineato il carattere eccezionale della concordanza in gemelli MZ per una cardiopatia congenita.

RÉSUMÉ

Jumelles MZ Concordantes pour Syndrome de Down et Cardiopathie Congénitale

Les auteurs présentent une analyse cytogénétique clinique d'un couple de jumelles concordantes pour trisomie 21 et cardiopathie congénitale.

La bibliographie sur le syndrome de Down et les cardiopathies congénitales chez les jumeaux est analysée et le caractère exceptionnel d'une concordance chez des jumeaux MZ pour une cardiopathie congénitale est souligné.

ZUSAMMENFASSUNG

Konkordanz von Down Syndrom und angeborener Kardiopathie bei EZ

Es werden die Ergebnisse der klinischen und zytogenetischen Untersuchungen bei einem weibl. EZ-Paar mit Konkordanz sowohl für eine 21-Trisomie als für ein angeborenes Herzleiden berichtet.

Es folgt eine Uebersicht über die Fälle von Zwillingen mit Down Syndrom und mit angeborener Kardiopathie im Schrifttum, und es wird betont, dass die Konkordanz von angeborenem Herzleiden bei EZ eine Ausnahme darstellt.

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