

Twins with nonconcordant sexual aneuploidy

SUMMARY We present a pair of dizygotic twins with different abnormal karyotypes. The chromosome anomaly is a sexual aneuploidy in both cases: 48,XXXXY in one, 47,XXY in the second. The origin of the chromosomal anomaly and the hypothetical relation between sexual aneuploidy and twinning is discussed. It is concluded that further studies in twins are necessary to prove the not yet solved problems of non-disjunction and double ovulation.

Several authors (Ferguson-Smith, 1958; Hoefnagel and Benirschke, 1962; Nielsen, 1966, 1970) have found a major incidence of twins among sibs of patients with Klinefelter's syndrome.

Case report

The propositus came to our department with a previous diagnosis of unilateral cryptorchidism, growth retardation, and talipes equinovarus.

The child was born after an uneventful pregnancy. The mother was 26 years old and the father 24 years old at the time of delivery. Both parents are living and healthy. Neither of them had a familial history of twins or of congenital malformations. The twins were the product of their mother's first and only pregnancy.

The twins were both male. There was a single placenta and 2 chorionic sacs. The birthweight of the propositus was 2400 g and the twin brother weighed 3100 g.

When seen by us, the propositus was 8 months old. His weight and stature were below the third centile. There was a flat facial profile and flat occiput, low nasal bridge, and macroglossia. Examination of the genitalia showed a small penis, undescended right testis, and hypoplastic scrotum. The limbs were short; and he had talipes equinovarus, clinodactyly in the fourth and fifth fingers, and limited pronation of elbows.

The radiology showed normal skeletal growth, hypoplasia of the mid-phalanx of the fifth fingers, and large metaphyses in both femur and ulna.

The child had a congenital heart disease compatible with pulmonary stenosis and a ventricular septal defect.

The levels of FSH and LH were increased. The 17 ketosteroids and 17-hydroxycorticosteroids were normal.

The twin brother was physically normal. His weight and stature were on the 75th centile.

CYTOGENETICS

The propositus had 49 chromosomes. With the trypsin G-banding method the karyotype was found to be 49,XXXXY (Fig. 1).

The twin brother had 47 chromosomes and his karyotype with the G-banding method was 47,XXY (Fig. 2).

Both parents had a normal karyotype.

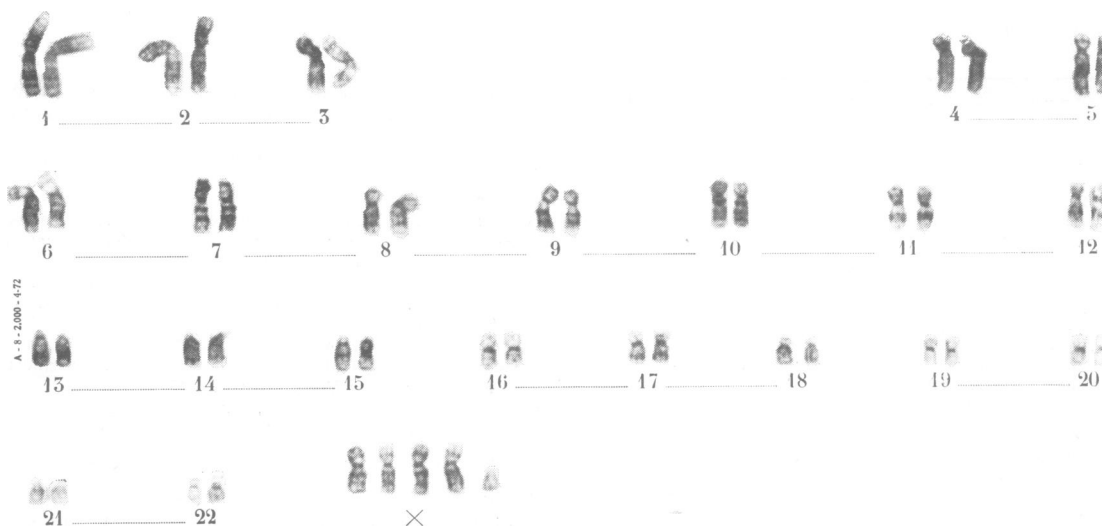


Fig. 1 G banded karyotype of the proband with 49,XXXXY.

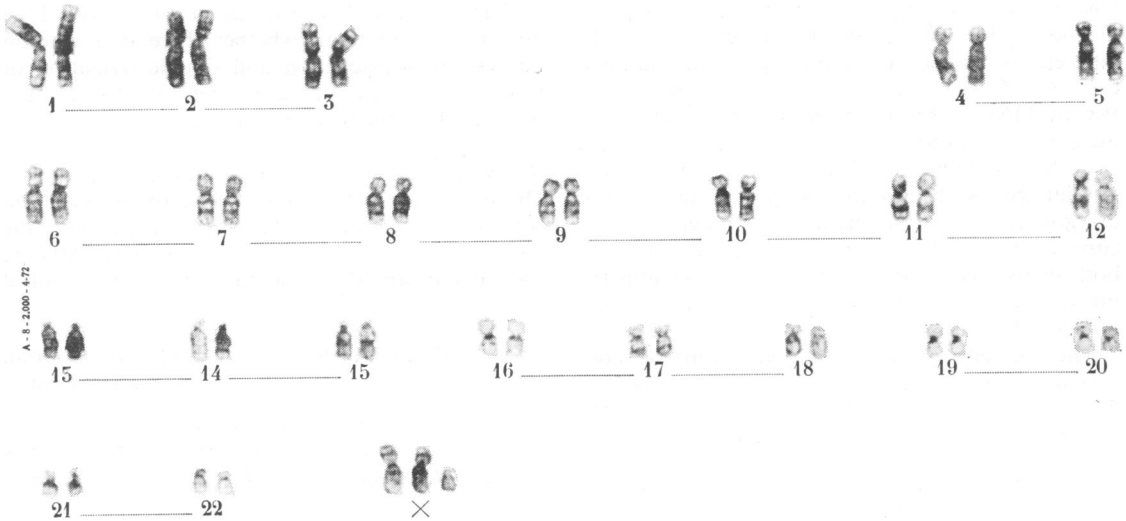


Fig. 2 G banded karyotype of the twin brother with 47,XXY.

DERMATOGLYPHS (Table 1)

Propositus. There was a whorl in each thumb. The remaining finger patterns were arches. The total finger ridge count (TFRC) was 18. The axial palmar triradius was in t' position in both hands.

The twin brother had a TFRC of 130. The finger patterns were whorls in fingers 1, 4, and 5, and ulnar loops in the rest. The palmar axial triradius was in t° position and he had a radial loop in the hypothenar area of right hand.

BLOOD GROUPS

All the blood groups studied (Table 2) were identical in both twins (ABO, Le, MNS, P, Kell, Lu, Fy, and Xg) with the exception of the Rh; the propositus' phenotype was CCDee as was that of the mother. The twin brother had cCDee like the father.

Discussion

The clinical and analytical data in our case support the assumption that the twins are dizygotic. The

Table 1 *Dermatoglyphs of twins*

	<i>Propositus (49,XXXXY)</i>					<i>Twin brother (47,XXY)</i>														
	<i>Right hand</i>					<i>Left hand</i>														
Finger Pattern	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Pattern	W	A	A	A	A	W	A	A	A	A	W	U	U	W	W	W	U	U	W	W
FRC	11	0	0	0	0	7	0	0	0	0	17	15	8	14	11	12	17	14	9	13
TFRC						18						130								
t	t'					t'	t°					t°	t°							
atd angle	53					65	47					55	—							
Hypothenar pattern	—					—	Radial loop					—	—							

FRC, Finger ridge count; TFRC, Total finger ridge count.

Table 2 *Blood groups*

	<i>Father</i>	<i>Mother</i>	<i>Twin brother (47,XXY)</i>	<i>Propositus (49,XXXXY)</i>
ABO	A ₁	A ₁	A ₁	A ₁
Rh	cCDee	CCDee	cCDee	CCDee
Lewis	Le (a-b+)	Le (a-b+)	Le (a-b+)	Le (a-b+)
MNS	M+ N- S+ s+	M+ N+ S- s+	M+ N- S+ s+	M+ N- S+ s+
P	P ₁ + T _J ^a +	P ₁ + T _J ^a +	P ₁ + T _J ^a +	P ₁ + T _J ^a +
Kell	K- k+	K+ k+	K+ k+	K+ k+
Lutheran	Lu (a-b+)	Lu (a+b+)	Lu (a+b+)	Lu (a+b+)
Duffy	Fy (a-b+)	Fy (a+b+)	Fy (a+b+)	Fy (a+b+)
Xg	Xg (a+)	Xg (a+)	Xg (a+)	Xg (a+)

placenta and chorionic sacs were of no help for diagnosis. The dermatoglyphs are expected to be different, even if they were monozygotic, in relation to the total finger ridge count; since according to Penrose (1967), when the number of X chromosomes increases, the TFRC decreases in about 30 per each extra X. The difference of 112 found in our case is so striking that we believe that we are facing a case of dizygosity. On the other hand, the blood groups were conclusive. All the systems studied were alike in both twins except for the Rh. In the propositus the phenotype was CCDee while in the brother it was cCDee, which rules out monozygosity.

The incidence of dizygotic twins with nonconcordant chromosomal aneuploidy appears to be low. To the best of our knowledge we think that ours is the first reported case of dizygotic twins with this specific anomaly.

As the Xg blood group was positive in the parents and the twins, it was not possible for us to know the origin of the X chromosomes.

In the wide study carried out by Race and Sanger (1969), the origin of the X chromosomes could be established only in 3 of the 29 patients with 49,XXXXY by assessing the Xg blood group. In those 3 cases, the 4 X chromosomes were of maternal origin. We are inclined to believe that the same occurs in our case, i.e. a double non-disjunction during maternal oogenesis. If this were true, the most probable origin of the 47,XXY twin was also a non-disjunction in the mother.

Ferguson-Smith (1958), Hoefnagel and Benirschke (1962), and Nielsen (1966) have described an increased incidence of twins in the sibships of patients with the Klinefelter's syndrome. Later on Soltan (1968) estimated the incidence of twins among sibs in Klinefelter's syndrome, and he found it to be higher than expected. Both Hoefnagel and Nielsen explain this major proportion of twins through an maternal age effect.

It seems evident that in the case of dizygosity, the tendency to non-disjunction and to twinning increases with the age of the mother. In our case the age of the mother was 26 years and thus it does not agree with this hypothesis. However, the ages in 2 of the 5 families described by Nielsen (1966) were between 20 and 23 years.

Tumba (1974) has shown that the incidence of 49,XXXXY patients is related to the age of the mother. In his series the mean age was 28, with two peaks corresponding to ages 29 and 35.

On the other hand, we should not underestimate the hypothetical environmental influence that may be the cause of both, the meiotic non-disjunction and the twin pregnancy, either as separate events joined by chance or as a single event.

Further cytogenetic studies in twins would be necessary to find out whether there is a relation between non-disjunction and double ovulation or whether these 2 events are independent but could occur at the same time by chance.

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Ring chromosome 4

SUMMARY A mentally and physically retarded boy with a 46,XY,ring(4) (p16q35) chromosome complement is described. Chromosome banding showed that the amount of chromosome material deleted from the ring chromosome 4 was minimal, apparently no more than the telomeres. Chromo-