45,X Turner's syndrome in monozygotic twin sisters

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Summary. A 7-year-old girl was admitted to the hospital for anaemia, secondary to intestinal blood loss (melaena). She was found to have 45,X Turner's syndrome. Her identical twin sister also had Turner's syndrome with a 45,X chromosome complement. According to various criteria the probability of monozygosity was 0.9905. Although the incidence of twinning is greater than usual in families of patients with Turner's syndrome, affected cases have only been observed in twin sisters on six occasions. It seems therefore that the 45,X chromosome complement itself is not a factor predisposing to twinning, but that in some families, a factor is at play, which causes either twinning or the 45,X aneuploidy, or both.

Turner (1938) in his original publication reported that one of his patients with the triad 'infantilism, pterygium colli and cubitus valgus' had a normal twin sister. Since Turner's original paper, the association of Turner's syndrome and twinning in the same family has been recorded on 28 occasions. The purpose of the present paper is to report the case of two monozygotic sisters with non-mosaic 45,X Turner's syndrome.

Case reports

The proposita, the second born twin, a 7-year-old girl, was admitted to our paediatric service for investigation of hypochromic anaemia due to recurrent melaena. Family history was negative for consanguinity, small stature, sterility, or anaemia. Twinning has occurred on two occasions on the maternal side (see pedigree, Fig. 1).

Pregnancy was complicated by protracted vomiting during the first 4 months, and by a threatened abortion at 3 months. Delivery occurred on 15 June 1966, in the estimated 30th week of gestation. V.1 weighed 1950 g at birth, and V.2 (propositus) 1720 g. Placenta was unique. The mother was 22 years old and the father 23.

The neonatal period was uneventful. Psychomotor development of both twins was slow, they walked at 18 months, and began to speak only at 4 years. Longitudinal growth was regular but slower than that of other children.

V.2 experienced her first episode of melaena, followed by palor and fatigue, at the age of 4 years. A second episode occurred at the age of 6 years, and a third, at the age of 7 years, prompted the hospital admission. V.1 never experienced any gastrointestinal bleeding.

On physical examination (Fig. 2), the proposita (V.2) was a shy, slightly retarded (2 years retardation) 7 year-old girl. Height was 117 cm (10th to 25th centile) and weight 2400 g (50th centile). Skin was pale, with several pigmented naevi on the trunk and a few areas of hyperpigmentation on the extremities. Palpebral fissures were slanted downwards, and a divergent squint was

FIG. 1. Family pedigree.

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FIG. 2. The twins, aged 7.

noted. The mouth was small, with an inverted V shape and an open bite, a narrow arched palate (Fig. 3), and irregular teeth implantation. The neck was short, without pterygium. The thyroid gland was not enlarged. On the neck, the hair was not low but it grew upwards, particularly at the sides. A discrete cubitus valgus was present on both sides and a mild hyperlaxity was noted. There was no lymphoedema. The thorax was shield-like with widely spaced nipples. Heart and lung examination were within normal limits. There was no abdominal mass. External genitalia were those of a normal prepubertal female.

Laboratory tests confirmed the diagnosis of hypochromic anaemia secondary to intestinal blood loss. Radiology of the gastrointestinal tract failed to reveal the origin of the blood. The origin of the melaena remained therefore obscure. An intravenous pyelogram showed normal kidneys and excretory pathways.

The association of the minor physical abnormalities mentioned above with digestive bleeding (telangiectases?) suggested the possibility of Turner's syndrome. Cytogenetic determinations were therefore undertaken in the patient and in her twin sister.

Physical examination of V.1 was similar to that of V.2 (see Fig. 2 and Table III).

Cytogenetics

Methods. Sex chromatin was examined according to the method of Moore and Barr (1955) in buccal mucosa smears, and according to that of Davidson and Robertson-Smith (1954) in peripheral leucocytes.

The chromosome complement was determined from peripheral blood lymphocyte cultures. Seabright's technique (1971) was used for examining the G-banding of chromosomes.

FIG. 3. The strikingly similar appearance of the mouth and palate of the twin sisters.

Results

Sex chromatin was negative in both sisters. In both of them the chromosome complement was 45,X (Table I). The unpaired chromosome belonged to group C, by size and morphological appearance. In this chromosome, G-bands corresponded to those of an X chromosome (Fig. 4). No evidence of mosaicism was found.

Dermatoglyphics

The data from the study of dermatoglyphics are summarized in Table II and Figure 5.

TABLE I
SUMMARY OF THE CYTOGENETIC DATA

Case	Sex Chromatin		Chromosome Complement
	Barr Bodies	Drumsticks	
V.1	0/200	0/500	45,X
V.2	0/200	0/500	45,X

FIG. 4. 45,X karyotype of one of the twins showing G-banding.

FIG. 5. Dermatoglyphic patterns of the hands of the twins.

Two of the measurable characteristics, the *a-b* ridge count and the maximal *ard* triradius angle corresponded to the values recorded in Turner's syndrome (Holt and Lindsten, 1964/65). The total ridge count (TRC), by contrast, was particularly low in both sisters.

Other dermatoglyphic characteristics usually associated with Turner's syndrome were observed in the two patients: loops in both fourth interdigital areas, well developed hypothenar patterns, T-lines terminating in the second interdigital interval, and similar orientations of the A-line (Fig. 5).

Finger and palm prints of the two sisters were strikingly similar. Moreover, a higher total finger ridge count in the right hand as compared to the left hand was noted in both twins; this feature was recorded by Lamy *et al* (1956/1957) in monozygotic twins. The dermatoglyphics, therefore, as the other anatomical features, strongly suggest monozygosity.

Morpho-anthropometrics

The striking clinical similarity of the twins was recorded in a more objective fashion by comparison of specific morpho-anthropometrical data (Table III). The only discordance noted was laterality; such a difference is not exceptional in monozygotic twins. Annett (1964) constructed a model on the heredity of laterality and concluded that in the

TABLE II
DERMATOGLYPHIC ANALYSIS

Finger patterns	V.1		V.2	
	Left Hand	Right Hand	Left Hand	Right Hand
	UL, RL, UL, UL, UL	UL, UL, UL, UL, UL	UL, UL, A, UL, UL	UL, UL, UL, UL, UL
Position of axial triradius	t''	t, t''	t''	t, t''
Total ridge count	23	39	18	40
a-b ridge count	89		88	
Maximal <i>atd</i> angle	137°		121.5°	

TABLE III
ANTHROPOMETRIC DATA FROM THE TWINS
According to Martin and Saller (1957)

	V.1	V.2
Weight	26.0 kg	24.0 kg
Height	118.0 cm	117.0 cm
<i>Head</i>		
Maximal AP diameter	163 mm	160 mm
Maximal transverse diameter	135 mm	132 mm
Head circumference	53.5 cm	51.3 cm
Inner canthal distance	31 mm	31 mm
Outer canthal distance	86 mm	89 mm
Interpupillary distance	54 mm	51 mm
Zygomatic diameter	99 mm	99 mm
Nose length	42 mm	44 mm
Nose width	25 mm	25 mm
Gonion diameter (mandible)	79 mm	86 mm
Right ear width	30 mm	35 mm
Right ear height	57 mm	56 mm
Facial height	97 mm	99 mm
<i>Hands</i>		
Right hand length	145 mm	146 mm
Right hand width	58 mm	57 mm
<i>Other characteristics</i>		
Iris pigmentation	10 (blue-green)	10 (blue-green)
Hair pigmentation	N (blond)	N (blond)
Skin	Fine, white-pink	Fine, white-pink
Hair	Not curly	Not curly
Hair whorl	Whorl, clockwise	Whorl, clockwise
Occiput	Slightly flattened	Slightly flattened
Nose shape	Slightly concave	Slightly concave
Forehead	High, slightly prominent	High, slightly prominent
Ears	Attached earlobes	Attached earlobes
Lower lip	Moderately thick	Moderately thick
Palate	Highly arched	Highly arched
Tongue curling	Absent	Absent
Laterality	Right handed	Left handed
PTC tasting	Non-taster	Non-taster
<i>Indices</i>		
Robusticity index of KAUP: $\frac{\text{weight (kg)} \times 1000}{\text{height (cm)}}$	1.84	1.76
Cephalic index: $\frac{\text{maximum transverse diameter} \times 100}{\text{Max. AP diameter}}$	82.8	82.5
Type of skull	Brachycephalic	Brachycephalic
Facial index: $\frac{\text{face length} \times 1000}{\text{zygomatic diameter}}$	104.3	100.0

TABLE IV

CALCULATED RELATIVE CHANCE (PROBABILITY OF A DIZYGOTIC PAIR p^D) IN FAVOUR OF A DIZYGOTIC TWIN PAIR

Character	Relative Chance
Initial odds	2.3333
Likeness in sex	0.5000
Likeness in ABO	0.6891
Likeness in MNS	0.4556
Likeness in Rhesus	0.5021
Likeness in P	0.8489
Likeness in Kell	0.9485
Likeness in Duffy	0.8036
Difference of total ridge counts	0.2300
Difference of <i>aid</i> angles	1.3600
Difference of height	0.4700
Difference of cephalic index	0.5500
Total relative chance, p^D	0.0096217
Total chance, $p^D (1 + p^D)$	0.0095

The absolute probability of monozygotism for our twin pair is:
 $1/(1 + p^D) = 0.9904699$

TABLE V

BLOOD GROUPS OF THE TWINS

V.1	O	MNS _s	CCDee	PP	kk	Fy ^a Fy ^b
V.2	O	MNS _s	CCDee	PP	kk	Fy ^a Fy ^b

heterozygotic situation lateralization was a variable characteristic. Furthermore, Rife (1940) observed a discordant lateralization more often in twins born in families with left handed members. In the present family, two near-relatives of the parents are left handed.

The probability of monozygosity (Table IV) was established in accordance with Smith and Penrose's statistical method (1954/1955) which takes into account sex, blood groups (Table V), and some morphological and anthropological features. The probability of monozygosity, in the present case, was 0.9905.

Discussion

The present observation raises several interesting questions. There was very strong evidence that the 45,X sisters were monozygotic twins. Twinning occurs, on the average, once in 85 pregnancies and only 25% of all twins are monozygotic. On the other hand, the incidence of 45,X Turner's syndrome in Europe and north America is estimated to be of 1/3000 female births (Mikamo and de Watterville, 1969). Therefore the occurrence of 45,X Turner's syndrome in monozygotic twins is theoretically not higher than 1/1 000 000 pregnancies. Such an event has been recorded on six occasions. In other reported instances (Table VI) the twins

TABLE VI

TURNER'S SYNDROME AND TWINNING: LITERATURE REVIEW

Phenotype	Report	Zygosity		Chromosome Complement or Sex Chromatin
		MZ	DZ	
Female twins; both affected	Turner and Zanartu (1962)	+		45,X and 45,X
	Lemli and Smith (1963)	+		45,X and 45,X
	Decourt <i>et al</i> (1964)	+		45,X and 45,X
	Edwards <i>et al</i> (1966)	+		46,XX/45,X and 46,XX/45,X
	Yarema and Borgaonkar (1970)	+		45,X and 45,X
	Ferrier <i>et al</i> (1970)	+		46,XX,qi/46,XX/45,X and 47,XXX/46,XX/45,X
	Riekhof <i>et al</i> (1972)	+		45,X and 45,X
	Present report	+		45,X and 45,X
Female twins; one affected, one unaffected	Turner (1938)	?		? and ?
	Boyer <i>et al</i> (1961/1962)	?		? and chromatin-X negative (two sets of twins)
	Almqvist <i>et al</i> (1963)		+	46,XX and 46,XX,qi
	Lindsten <i>et al</i> (1962/1963)		+	46,XX and 46,XX,qi
	Mikkelsen <i>et al</i> (1963)	+		46,XX/45,X and 46,XX/45,X
	K. Benirschke and M. M. Sullivan (personal communication, 1965)	+		46,XX and 45,X
	Shine and Corney (1966)	+		46,XX and chromatin-X negative
	Ross <i>et al</i> (1969)	+	+	47,XXX/45,X and 47,XXX/45,X
Female twin: affected, male twin: unaffected	Yarema and Borgaonkar (1970)	+		46,XX and 45,X
	Potter and Taitz (1972)	+		46,XX/45,X and 46,XX/45,X
	Turpin <i>et al</i> (1961); Turpin (1970)	+		46,XY and 45,X
	De la Chapelle (1962)	?		? and 45,X
	Almqvist <i>et al</i> (1963)	+	+	46,XY and 45,X
Females twins with no characteristics of Turner's syndrome	Dent and Edwards (1965)	+		45,X and 45,X
	Edwards <i>et al</i> (1966)	+		45,X and 46,XY/45,X
	Muller <i>et al</i> (1970)	+		47,XXX/46,XX/45,X and 47,XXX/46,XX/45,X
	Van der Horst <i>et al</i> (1971)	+		46,XX/45,X and 46,XX/45,X

were monozygotic but heterocaryotic, or monozygotic but mosaic, or dizygotic. The total number of cases of Turner's syndrome occurring in one or two of twins is relatively high (28 pregnancies, see Table VI). Nance and Uchida (1964) suggested that monozygotic twinning (which had occurred in seven out of their 34 sibships identified by the presence of a case of Turner's syndrome) was significantly more frequent than expected by chance alone in families of patients with Turner's syndrome. The present report would be in keeping with their observation.

Monozygotic twins are thought to originate from the activity of a factor operating at an early cleavage division (causing the formation of two individuals from one fertilized egg). It seems reasonable to postulate that the 45,X aneuploidy, when it is associated with twinning, arises from the activity of the same factor, at the same period of cleavage. The high incidence of mosaicism in these pairs of twins may be taken as evidence in favour of such a post-fertilization event. One may therefore conclude that in some families, a factor is at play, which causes sometimes twinning, sometimes the 45,X aneuploidy, and sometimes both. It seems likely that this factor is not the one which causes meiotic non-disjunction in the male (most frequent cause of the 45,X aneuploidy according to colour-blindness and Xga studies, Polani, 1971). Indeed in the present family twinning was observed on the maternal side only.

The propoita, V.2, came to medical attention because of melaena. Occult blood loss or melaena have been reported in patients with Turner's syndrome. This is either due to telangiectasias (Haddad and Wilkins, 1959) or to ulcerative colitis (Williams *et al.*, 1966). In V.2 appropriate investigations failed to reveal the origin of the haemorrhage, which may be the case in some instances of small telangiectasias.

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