Turner's Syndrome in Monozygotic Twins

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The clinical picture of short stature, neck webbing, and cubitus valgus was first described by Ullrich (1930) in males and females with normal pubertal development. In his classical description, Turner (1938) described a similar clinical picture in females who had primary amenorrhoea.

Since the original description, numerous contributions have been made to the study of this syndrome: sex chromatin was found to be absent (Polani, Hunter, and Lennox, 1954; Wilkins, Grumbach, and Van Wyk, 1954), and subsequently it was discovered that there was a missing X chromosome (Ford, Jones, Polani, de Almeida, and Briggs, 1959). It is now known that there can be various chromosome mosaic patterns in association with both chromatin negative and positive patients (Polani, 1961), and this author mentions that the clinical features of the syndrome may be found in men and women who have normal chromosomes.

It is interesting to note that in his original description in 1938 Turner described twin girls aged 16 years, one of whom showed the typical features of the syndrome, while her twin was apparently normal, the menarche having been established at the age of 12 years. 24 years later he described twins of proven monozygosity concordant for the syndrome, each having an XO chromosomal pattern (Turner and Zanartu, 1962), and there have been several reports of the syndrome in one or both of monozygotic and dizygotic twins (Table I).

We wish to report a further pair of discordant monozygotic twins: they are of particular interest because of associated abnormalities, necropsy findings, and Xg blood grouping.

**Case Report**

This was the second pregnancy of a 20-year-old mother who was delivered of twin girls at the 37th week of gestation at the Horton Maternity Hospital, Banbury, after a normal pregnancy. The first baby weighed 4 lb. 5 oz. (1956 g.) and was delivered as a vertex; the cord was wound three times round the neck and regular respirations were not established for 12 minutes. The second baby weighed 6 lb. 2 oz. (2777 g.) and was an assisted breech delivery; she cried well at birth and no abnormality was apparent on clinical examination. Reviewed at 6 months, she appeared to be developing normally.

The placenta was reported as single but was not available for detailed examination.

The first baby showed numerous abnormalities (Fig. 1); the face was rather small, the skin dry with little subcutaneous fat. A large omphalocele was present.
with an ectopia vesicae, and an intestinal fistula (ex-

of the cloaca). The external genitalia were
difficult to identify, the labia were rudimentary, 
and there was no evidence of a phallus or testes. 
The anus was imperforate. No abnormalities were noted in
the respiratory, cardiovascular, or central nervous systems,
and there was no webbing of the neck and no cubitus 
valgus or oedema of the feet.

Multiple defects of the cervical and lumbo-sacral
spine, and widening of the symphysis pubis were seen
on radiography, and subsequent excretion urography
showed excretion from the right kidney, but no evidence
of the left kidney.

After consultation it was decided that surgical treat-
ment was not possible; a conservative régime was
adopted, no drugs were given, and the child died at 2
months.

The father was 27 years old and unrelated to his wife.

**Necropsy Findings.** The intestines proved to be
malfixed, and were mainly present within the ompha-
locoele, where there were foci of intussusception; the
terminal part of the intestine was small in calibre and
opened into the ectopic area. The liver, biliary system,
and pancreas were normal. The right kidney and ureter
appeared normal, but there was a gross hydrenephrosis
on the left side, with a dilated tortuous ureter that was
stenosed at its lower end; both ureters opened to the
exterio in the ectopic bladder. Fallopian tubes and
ovaries were present, but there was no uterus or vagina,
and histological examination of the ovaries showed
normal tissue.

**Determination of Sex.** At birth both twins were
thought to be female. Smears taken from the buccal
mucosa from the abnormal baby at the end of the first
week and again at the age of 1 month were examined,
using the mounting, fixing, and staining procedures
described by Ross (1962). No sex chromatin was found
in 500 cells, but 1% of them had small deeply staining
areas that were possibly atypical sex chromatin. Chromo-
some analysis was not performed because sufficient
peripheral blood could not be obtained. However
suggestive evidence was available from the analysis of
the Xg blood group system. This blood group is sex-
linked (Mann, Cahan, Gelb, Fisher, Hamper, Tippett,
Sanger, and Race, 1962) and follows the rules of sex-
linked dominant inheritance, so that fathers carrying the
gene on their X chromosome and so phenotypically
Xg(a+), always have Xg(a+) daughters. In this case
the father was Xg(a+) and the abnormal twin was
Xg(a−) proving that she had not received her father’s
X chromosome.

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**TABLE I**

**REPORTS OF TURNER’S SYNDROME IN TWINS**

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of Pairs</th>
<th>Zygosity</th>
<th>Method of Determining Zygosity</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner (1938)</td>
<td>1</td>
<td></td>
<td></td>
<td>Twin 1 normal female; co-twin typical stigmata</td>
</tr>
<tr>
<td>Boyer, Ferguson-Smith, and Grumbach (1961)</td>
<td>2</td>
<td></td>
<td></td>
<td>Twin 1 apparently normal female; co-twin Turner stigmata</td>
</tr>
<tr>
<td>Frasier, Bashore, and Mosier (1961, 1964)</td>
<td>1</td>
<td>MZ</td>
<td>Blood groups</td>
<td>Both twins normal female external appearance; bilateral streak gonads with gonadoblastoma</td>
</tr>
<tr>
<td>Turpin, Lejeune, Lafourcade, Chigot, and Salmon (1961)</td>
<td>1</td>
<td>MZ</td>
<td>Reciprocal skin graft; blood groups</td>
<td>Twin 1 phenotypically normal male; co-twin typical stigmata: histologically streak gonads</td>
</tr>
<tr>
<td>Turner and Zanartu (1962)</td>
<td>1</td>
<td>MZ</td>
<td>Blood groups</td>
<td>Both twins typical stigmata: histologically streak gonads</td>
</tr>
<tr>
<td>de la Chapelle (1962)</td>
<td>1</td>
<td>DZ</td>
<td></td>
<td>Twin 1 said to have been normal male; co-twin Turner stigmata, abnormal kidneys</td>
</tr>
<tr>
<td>Dent and Edwards (1963)</td>
<td>1</td>
<td>MZ</td>
<td>Blood and serum groups; palm prints</td>
<td>Twin 1 normal male; co-twin dwarf with amenorrhoea</td>
</tr>
<tr>
<td>Lindsten, Fracarro, Ikos, Kaiser, Klingler, and Luft (1963)</td>
<td>1</td>
<td></td>
<td>Blood groups</td>
<td>Twin 1 normal female; co-twin short with primary amenorrhoea</td>
</tr>
<tr>
<td>Mikkelson, Freland, and Ellebjerg (1963)</td>
<td>1</td>
<td>MZ</td>
<td>Blood groups</td>
<td>Twin 1 normal female; co-twin Turner stigmata—necropsy normal ovaries</td>
</tr>
<tr>
<td>Almqvist, Lindsten, and Lindwall (1963)</td>
<td>1</td>
<td>DZ</td>
<td>Blood groups</td>
<td>Twin 1 normal male; co-twin short with primary amenorrhoea: streak gonads</td>
</tr>
<tr>
<td>Lemli and Smith (1963)</td>
<td>1</td>
<td>MZ</td>
<td>Blood groups; palm prints</td>
<td>Both twins typical stigmata</td>
</tr>
<tr>
<td>Nance and Uchida (1964)</td>
<td>1</td>
<td>MZ</td>
<td>Monochorionic diamniotic placenta</td>
<td>Twin 1 normal female; co-twin webbed neck, arthrococphy-</td>
</tr>
<tr>
<td>Brunersche and Sullivan (1965)</td>
<td>1</td>
<td>MZ</td>
<td></td>
<td>small ovaries histologically resembling ovoides: bicornuate uterus</td>
</tr>
<tr>
<td>Shine and Corney (present case) (1966)</td>
<td>1</td>
<td>MZ</td>
<td>Blood groups; palm prints</td>
<td>Twin 1 normal female: co-twin renal and skeletal abnormalities: absent vagina—necropsy normal ovaries</td>
</tr>
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<td></td>
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</tr>
</tbody>
</table>

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**Clinical Features**

- Twin 1 normal female;
- co-twin typical stigmata
- Both twins normal female external appearance; bilateral streak gonads with gonadoblastoma
- Twin 1 phenotypically normal male; co-twin typical stigmata: histologically streak gonads
- Both twins typical stigmata: histologically streak gonads
- Twin 1 said to have been normal male; co-twin Turner stigmata, abnormal kidneys
- Twin 1 normal male; co-twin dwarf with amenorrhoea
- Male
- +ve XX Female
- +ve X iso X Female
- +ve XO/XX Female
- −ve XY Male
- −ve XO Male
- +ve XO/XX −
- +ve XO/XX −
- +ve XO/XX −
- +ve XX −
- −ve −
It was considered justifiable to regard the twins as like sexed for the determination of zygosity, as those internal genitalia that were found in the abnormal twin were female. The healthy twin was phenotypically female, sex chromatin was present in the buccal mucosal cells, and peripheral blood culture revealed a normal female karyotype with no evidence of mosaicism.

**TABLE II**

**RESULTS OF BLOOD GROUP ANALYSIS**

<table>
<thead>
<tr>
<th></th>
<th>ABO</th>
<th>MNS</th>
<th>P1</th>
<th>Rh</th>
<th>Lu*</th>
<th>K</th>
<th>Fy*</th>
<th>Xga</th>
</tr>
</thead>
<tbody>
<tr>
<td>Father</td>
<td>A1, NsNs</td>
<td>R,r</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>A1, NsNs</td>
<td>R,r</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XO twin</td>
<td>O, NsNs</td>
<td>R,r</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XX twin</td>
<td>O, NsNs</td>
<td>R,r</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Determination of Blood Groups.** Drs. Race and Sanger kindly investigated the families—blood for 8 blood group systems, with the following results (Table II).

Since both dizygotic and monozygotic female twins are expected to be Xg(a+) when the father is Xg(a+), the difference in Xg in this pedigree (Fig. 2) is not evidence of dizygosity.

**Calculation of Probability of Monozygosity.** Dermal prints were made giving a total 10 finger ridge count of 173 and 183 on the normal and co-twin, respectively.

Calculation of the dermal ridge count difference, and the blood group and sex likeness, according to the tables of Smith and Penrose (1955), gave an absolute probability of 0.9927 that the twins were monozygotic (Table III).

**TABLE III**

**CALCULATION OF THE PROBABILITY OF MONOZYGOITY**

<table>
<thead>
<tr>
<th></th>
<th>pA</th>
<th>pD</th>
<th>pA - pD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial relative probability</td>
<td>0.00733</td>
<td>0.00732</td>
<td>0.00001</td>
</tr>
<tr>
<td>Likeness in Xg pheno-type</td>
<td>0.00883</td>
<td>0.00882</td>
<td>0.00001</td>
</tr>
<tr>
<td>Likeness in X chromosome</td>
<td>0.99268</td>
<td>0.99268</td>
<td>0.00000</td>
</tr>
<tr>
<td>Relative probability ±pD</td>
<td>0.00652</td>
<td>0.00652</td>
<td>0.00000</td>
</tr>
<tr>
<td>Absolute probability ±pD</td>
<td>0.00032</td>
<td>0.00032</td>
<td>0.00000</td>
</tr>
</tbody>
</table>

**Discussion**

The finding of twins discordant for Xg phenotype, when both parents have the phenotype Xg(a+), can only be interpreted in this family as evidence that the Xg(a-) twin has lost the father’s Xg(a)-bearing chromosome, and it is of interest that in both mice and man XO daughters more often receive the single X chromosome from their mothers (Russell, 1962; Lindsten, Bowen, Lewis, McKusick, Polani, Wingate, Edwards, Hampson, Tippett, Sanger, and Race, 1963; Race 1965). The only exceptions to the usual pattern of Xg inheritance, namely that Xg(a-) fathers have Xg(a+) daughters, have been found when the daughter had an XO, an X iso X, or XY karyotype (Sanger, Race, Tippett, Gavin, Hardisty, and Dubowels, 1964). In this case the finding of normal ovaries and no testes is incompatible with an XY karyotype, and Lindsten (1963) found that patients with an X iso X karyotype had female nuclear sex. Illegitimacy might provide another exception to this rule, but the blood groups and local inquiry found no confirmation of this.

Repeated examination of 500 well-stained buccal mucosal cells taken at the age of 1 week and 4 weeks failed to reveal any normal female cells, which is good evidence that there was only one X chromosome present. Several surveys of newborn children have shown sex chromatination to be a reliable sign of chromosomal sex, e.g. Moore (1956), though within the first 3 days of life fewer cells than normal have been reported to show sex chromatin (Taylor, 1963), and it was absent in all cells from one patient; but this discrepancy was not found in a recent study of 3,367 newborn infants (Robinson.
Turner's Syndrome in Monozygotic Twins

and Puck, 1964). The baby described in this report had no sex chromatin at 1 month, by which time the reliability of nuclear sex is not disputed.

According to a recent extensive review, Turner's syndrome has considerable variation, which may be explained on the basis of mosaicism with variation in relative proportions of the cell lines, or the loss of various amounts of the sex chromosomes (Ferguson-Smith, 1965). Ferguson-Smith also states that short stature is the only constant clinical finding. Regarding the clinical features in the present case, this child is atypical and shows few of them. Renal and skeletal abnormalities were present and these were each reported in about half of Lindsten's 57 cases. The total dermal ridge count of 183, compared to the normal female count of 113 ± 58 (Holt, 1952) shows a high degree of pattern intensity which is found in Turner's syndrome (Penrose, 1963). The finding of normal ovaries must be accepted as an unusual variant and presumably indicates the presence of an XX cell line. However, the presence of functioning ovaries in Turner's syndrome is not particularly rare, as may be appreciated from the reports of XO women who have menstruated regularly (Hoffenberg and Jackson, 1957; Hutchings, 1959; Stewart, 1960; Becker, Burgert, and Albert, 1963; Lindsten, 1963; Ferguson-Smith, 1965). There is also the report of an XO woman giving birth to a normal child: she had 75 XO cells out of 92 skin and marrow cells examined, no drumsticks on her polymorphonuclear leucocytes, and no sex chromatin in the buccal mucosa (Bahner, Schwarz, Harnden, Jacobs, Hienz, and Walter, 1960). Moreover, normal ovarian tissue has been found at necropsy in a 2-week-old chromatin negative baby in whom peripheral blood cultures revealed XO cells with no evidence of mosaicism (Conen and Glass, 1963). One of the XO/XX twins with the clinical features of Turner's syndrome (Mikkelsen, Frøland, and Ellebjerg, 1963) died at the age of 4 years, and at necropsy was found to have infantile ovaries with otherwise normal ovarian stroma and numerous primordial follicles.

The family history of twinning, which is noticeable in the present pedigree and was noted by Lindsten (1963) in 21 of his 57 families, may not represent a true association, because it is difficult to establish proper controls. Also twin births, particularly dizygotic twin births, are frequently overlooked, which makes it easy to gain a false impression if the controls are not properly chosen. Similarly it is difficult to be certain of the significance of the 14 reports of Turner's syndrome in twins (Table I), since the combination would be expected by chance approximately once or twice in every 1 million pregnancies; though there have probably been many examples that were not reported. What is less likely to be an artefact is the increased frequency of monozygotic twinning in these reports, and this was also recorded by Nance and Uchida (1964) in 4 out of 34 sibships identified by the presence of a case of Turner's syndrome. They showed that the monozygotic twinning frequency was significantly more than expected on the basis of the known XO and monozygotic twinning rates and also significantly more than they found among controls. However, monozygotic twinning is not apparent in Court Brown, Harnden, Jacobs, Maclean, and Mantle's (1964) study of 66 sibships.

If monozygotic twinning is associated with Turner's syndrome, it seems reasonable to assume that there may be a common causal factor and a common time at which it operates, which is presumably at an early cleavage division, when some, if not all, monozygotic twins are thought to originate. This is consistent with the frequent finding of mosaicism which can only arise after fertilization, and with Russell's (1962) demonstration that XO mice can be most readily induced by irradiation after fertilization.

It would be relatively easy to test the hypothesis by comparing the relative frequency of monozygotic and dizygotic twinning in sibships containing a case of Turner's syndrome.

Summary

A pair of monozygotic female newborn twins is described, one of whom is a normal female in all respects, and the other had multiple abnormalities and died at 2 months. The abnormal twin was considered to have an XO karyotype on the basis of buccal smear examinations and Xg phenotype, since the father was Xg(a+) and the abnormal twin Xg(a−). At necropsy normal ovarian tissue was found, which is presumptive evidence that XX cell lines were also present. Fourteen reports of Turner's syndrome in twins are reviewed, and the evidence for an association between twinning and Turner's syndrome is discussed.

It is a pleasure to thank Dr. A. C. Stevenson for his helpful criticism and advice, and we are most grateful to Dr. Ruth Sanger and Dr. R. R. Race of the M.R.C. Blood Group Research Unit for undertaking blood group studies and for their advice in the preparation of this paper. We are also most grateful to Mr. G. Clarke and Mr. R. Edwards for cytological assistance and to Dr. Hugh Ellis for permission to publish this case. The necropsy and histological studies were performed by Dr. W. Aberne, Gibson Laboratories, Radcliffe Infirmary, Oxford.
REFERENCES


