father and G trisomy in the two mongol children, but revealed 5 cells with 47 chromosomes among 70 cells counted from the mother. In 4 of these cells the extra chromosome was from the G group, and in the remaining cell it was a C group chromosome. On these results maternal mosaicism with karyotype 46,XX,G+ was diagnosed.

In 1971 the couple elected to have a further child despite the risks involved. A male mongol was born in December 1971. His karyotype has been confirmed as 47,XY,G+.

Discussion

The difficulty of excluding chromosomal mosaicism has long been recognized, and this family re-emphasizes the need to study large numbers of cells from several tissues of both parents when two or more regular mongols are born to a couple. In this family, studies concentrated on the mother because she showed some clinical features of mongolism, but the initial investigations failed to reveal the mosaicism despite counting 59 cells from two tissues. Fortunately, appropriate genetic advice was still given.

The occurrence of another regular mongol in the family is also of interest, but his mother was 40 years old at his birth, so this may represent a chance occurrence.

Summary

A case of maternal mosaicism leading to the production of three mongol children is reported. The difficulty of detecting the trisomic cell line and the need to examine large numbers of cells is emphasized.

We thank Drs. Ann Morgan, David Pitt, and Saul Wiener for their assistance with this study; Dr. O. Margaret Garson for the bone marrow studies and confirming the trisomic state of the third child; and the Mental Health Authority for permission to publish this paper.

REFERENCES


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Dizygotic Twins with Down’s Syndrome

It is rare for both members of a twin pair to be concordant for Down’s syndrome. The reported incidence of such twins is lower than expected and it is postulated that intrauterine death of one or both members of the pair may often occur (Keay, 1958; Richards, 1971). To our knowledge, when twins have been monozygotic both have always been affected except in one case documented by de Wolff, Schärer, and Lejeune (1962). In contrast, the great majority of dizygotic twins have been discordant for Down’s syndrome. A few exceptions have been recorded in twins of the same sex considered to be dizygotic (Russell, 1933; MacKay, 1936; Jervis, 1943). Röhmer et al. (1970) reported dizygotic twins, the one 47, XX, 21+ and clinically mongoloid, the other 46, XX/47XX, 21+ and clinically nonmongoloid. We know of only one case of twins of opposite sex, both of whom were considered on clinical grounds alone to have Down’s syndrome (Nicholson and Keay, 1957). The purpose of this paper is to put on record dizygotic twins of opposite sex with unequivocal Down’s syndrome substantiated by chromosome analyses.

Case Report

The parents of the twins were not related before marriage. The mother was 39 years and the father 46 years of age when the twins were born.

The mother was one of a family of six, four brothers living and one having died in an accident. She married at the age of 19 years. The father has three brothers and one sister, all of whom are alive and well. Both parents are of average intelligence. No history of Down’s syndrome or mental subnormality was discovered on inquiry into the family history.

The mother has had 4 previous pregnancies, 2 of which resulted in normal male infants, the other 2 in first trimester miscarriages. At the time of the birth of the twins, the brothers were aged 20 and 10 years, respectively. They are of normal intellect and have good school records.

The present pregnancy was uneventful but the presence of twins was not suspected until delivery which took place at home. The female twin weighed 2·13 kg (4 lb 11 oz) at birth and at the age of 11 months weighed 7·06 kg (15 lb 9 oz). A systolic murmur could be heard over the praecordium compatible with a ventricular septal defect. The male twin weighed 2·18 kg (4 lb 13 oz) at birth and at 11 months weighed 10·8 kg (23 lb 13 oz). His cardiovascular system was clinically normal.

No immediate comment about features of Down’s syndrome was made during the neonatal period, but a growing doubt as to the normality of the female twin prompted referral, together with her brother, to a
paediatrician and then to our genetic counselling clinic for chromosome investigation. At this time, aged 9 weeks, several stigmata of Down's syndrome suggested that both twins were affected. The Fig. taken when the twins were 8 months old, supports this view, though the boy has fewer stigmata than his sister.

**Dermatoglyphs.** Inspection of the twins' palms did not reveal any 'simian' creases and two interphalangeal creases were seen on the fifth digit of each hand. All axis triradii were displaced distally and the sum of right and left add angles was 160 degrees in the female twin and 172 degrees in the male. Dermal ridge patterns showed a high incidence of ulnar loops, 90% in the female and 80% in the male. Small distal loop patterns were present in the hallucal areas of the female twin, and tibial arch patterns in the male twin.

**Cytogenetics.** Blood specimens from the twins and their parents were cultured for chromosome study. Analysis confirmed that each twin had trisomy—G Down's syndrome (Table). Cells with less than 47 chromosomes did not show consistent losses and therefore mosaicism was not suspected.

<table>
<thead>
<tr>
<th>Number of Cells with</th>
<th>Total No. of Cells Counted</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>44 45 46 47</td>
<td></td>
</tr>
<tr>
<td>Female twin</td>
<td>— 1 3 56</td>
<td>60</td>
</tr>
<tr>
<td>Male twin</td>
<td>— 1 4 56</td>
<td>61</td>
</tr>
<tr>
<td>Mother</td>
<td>1 6 53 —</td>
<td>60</td>
</tr>
<tr>
<td>Father</td>
<td>1 4 55 —</td>
<td>60</td>
</tr>
</tbody>
</table>

Chromosome analyses on both parents did not reveal any abnormality of the karyotypes. In each case one cell only from the 60 counted contained a chromosome fragment, but this was not considered significant. A further 40 cells were scored only for the number of chromosomes in Group G but none was found with an additional G chromosome. Skin specimens could not be obtained from either the twins or their parents owing to lack of parental co-operation.

**Discussion**

The chance of producing dizygous twins, both of whom have Down's syndrome, is very small. As there is no indication of mosaicism in either parent, though this cannot be entirely excluded, the most likely reason for the birth of the twins in this case would be due to a chance event which is maternal-age dependant. The random risk for a mother aged 39 giving birth to a child with Down's syndrome lies between 1/260 and 1/100 (Carter and Evans, 1961), and the empirical recurrence risk approximately double this, though this may be increased for concurrent births due to environmental factors. The chance of dizygous twins being born in this country is approximately 1/100 (Carter, 1969), but this increases with maternal age and is expected to be approximately 1 in 60 in this case. Hence in this instance for both twins to be affected by Down's syndrome the risk may be expected to be less than 1/300,000 (1/100 × 1/50 × 1/60) live births.

An alternative possibility for the birth of dizygous twins, both with the same chromosomal abnormality, may be the result of nondisjunction at first meiotic division in the female, followed by dispermous fertilization of a single ovum. Fusion of a sperm with the egg nucleus and a different sex chromosome carrying sperm with the second polar body, followed by separation of the two
Septo-optic Dysplasia with Growth Hormone Deficiency (De Morsier Syndrome)

The association of hypoplasia of the optic discs with absence of the septum pellucidum was described by De Morsier (1956). Few examples have been described outside the ophthalmological literature until recently, but it is now becoming apparent that the condition is not as rare as was once considered. It is now recognized that growth retardation is a feature of the condition, and it is the purpose of the present report to describe an example of septo-optic dysplasia with the classical features of the syndrome and an associated growth hormone deficiency in a female child.

Case Report

The patient was born after a normal pregnancy at term to an 18-year-old primipara. The birthweight was 2.84 kg. She was reported to have been jaundiced for a month after birth, but she was not seen by a paediatrician at that time. No investigations were carried out. Initially her progress was considered normal. Blindness was discovered at the age of 7 months when she was referred to hospital for the first time because she was unable to see.

Examination at this time showed a left-sided hemiplegia. There appeared to be no vision. Hearing was normal. She was unable to sit up spontaneously and her sitting balance was poor, but in spite of this she handled objects well and could play with a rattle.

Ophthalmoscopic examination under anaesthesia showed abnormal discs on both sides. On the right side the vessels all appeared on the temporal side of the disc. The disc had a deep pale cup and there was fine pigment stippling surrounding it. On the left side there was a small coloboma present, and fine pigmented disturbance surrounding the optic nerve head.

The patient was treated with regular physiotherapy, and the mother instructed to afford the child as much stimulation as possible to compensate for the lack of vision. She quickly caught up developmentally and at the age of 10 months she was sitting unsupported. She spoke at the age of 2, and walked unsupported at the age of 3. Her hemiparesis improved steadily with physiotherapy and by the time she was 2 this had disappeared completely.

Initially she appeared to grow normally and at the age of 3 years 9 months her height was 91.5 cm just at the 3rd centile. From then on she stopped growing. This was first noted when she was admitted to hospital at the age of 5½ with a fractured skull. She was then extensively investigated at the Torbay Hospital and at the Royal Devon and Exeter Hospital. Obvious causes for growth retardation due to intercurrent disease, such as chronic infection and malabsorption, were excluded, nor did there appear to be any obvious endocrine cause; there was a normal response to tetracosactrin stimulation.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Bovril (Royal Devon)</th>
<th>Bovril (G.O.S.)</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (fasting)</td>
<td>1.3</td>
<td>3.3</td>
<td>2.8 (58)</td>
</tr>
<tr>
<td>15</td>
<td>6.9</td>
<td>3.9</td>
<td>1.6 (27)</td>
</tr>
<tr>
<td>30</td>
<td>6.1</td>
<td>5.4</td>
<td>1.3 (28)</td>
</tr>
<tr>
<td>45</td>
<td>6.2</td>
<td>5.1</td>
<td>1.8 (31)</td>
</tr>
<tr>
<td>60</td>
<td>6.2</td>
<td>5.1</td>
<td>1.9 (34)</td>
</tr>
<tr>
<td>90</td>
<td>6.2</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td>6.2</td>
<td>5.1</td>
<td></td>
</tr>
<tr>
<td>150</td>
<td>3.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Bracketed figures refer to blood glucose levels (mg/100 ml).
Dizygotic twins with Down's syndrome.

D W Fielding and S Walker

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