Familial trisomy 7 mosaicism

Summary. A trisomy 7 mosaicism (46,XX/47,XX,+7) was identified by quinacrine mustard fluorescence studies in a psychiatric patient and in her daughter who also had mental illness. The aetiology of the trisomy 7 mosaicism in two generations of this family is postulated to involve an autosomal dominant gene as initially described by Zellweger and Abbo in 1965.

Even though there is a theoretical possibility of 22 autosomal trisomies, only trisomies 13, 18, and 21 are commonly found in newborns (Warkany et al, 1966; Hamerton, 1971). Autosomal trisomies such as trisomy 22 (Hsu et al, 1971; Bass et al, 1973) have been described as clinical entities but are few in number. Other trisomies do occur but are usually found only in abortion material, indicating an incompatibility with later stages of fetal development (Kuliev, 1971; Hamerton, 1971; Warkany, 1971; Hsu et al, 1972). The only exceptions to this are the autosomal trisomies which occur as a mosaic with a normal cell line. The best examples of autosomal trisomy mosaicsisms are trisomy 8 (Bijlsma et al, 1972; Caspersson et al, 1972) and trisomy 10 (Nakagome et al, 1973).

The purpose of this paper is to present two cases of the trisomy 7 mosaicism, a mother and daughter both with normal phenotypes, and to discuss the familial occurrence of the mosaicism with respect to Zellweger's and Abbo's postulate (1965) that an autosomal dominant gene may be responsible for familial mosaicism.

Materials and methods

The proposita was karyotyped in a chromosome analysis survey of patients diagnosed as having anorexia nervosa. A follow-up interview done at the time a blood specimen was obtained for chromosome studies revealed that she fulfilled the criteria for hysteria (Feighner et al, 1972) and not that of anorexia nervosa. It was obvious from the interview information that two of the proposita's children and several other of her first-degree relatives had a psychiatric illness (Fig. 1). When her karyotype was found to be abnormal, we then interviewed and physically examined her husband and all available first-degree relatives, her four children.

Chromosome studies

Preparation of chromosome spreads. Peripheral blood leucocytes were cultured according to a modification of the method of Moorhead et al (1960). Following the procedure of Hungerford (1965), whole heparinized venous blood was added to TC-199 medium supplemented with fetal calf serum, antibiotics and PHA. After 72 h of incubation, the cells were arrested in metaphase with colchicine and harvested by gentle centrifugation. Hypotonic treatment was carried out in a solution of 0.4% sodium citrate and 0.4% potassium chloride (1:1, v:v). The cells were fixed with a mixture of glacial acetic acid/methanol (1:3, v:v), spread on the slides, and air-dried.

Staining and karyotyping. Giemsa-stained chromosome spreads were used for routine counting and standard karyotyping. In those cases where aneuploidy was found, additional karyotyping was performed on chromosome spreads stained with a 0.005% solution of quinacrine mustard (QM) (Polysciences, Lot 6-41-3) in MacIlvaines's buffer pH 7 (Caspersson et al, 1971). The spreads were then mounted in fresh buffer and ex-
examined and photographed in a fluorescence microscope. The karyotypes were done according to the Paris Conference (1971).

**Sex-chromatin test.** Buccal mucosa smears were taken from both right and left sides, fixed in a mixture of ether/ethanol (1:1, v:v), stained with carbol fuchsin and examined in the microscope. Only those cells with classical Barr bodies adjacent to the nuclear membrane were counted as positive. All other cells were considered negative for Barr bodies.

**TABLE I**

**CYTOGENETIC ANALYSIS***

<table>
<thead>
<tr>
<th>Family Members (age)</th>
<th>Sex Chromatin in Buccal Mucosa Cells</th>
<th>Chromosome Analysis of Peripheral Blood Leucocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td></td>
<td>Present (%)</td>
<td>Absent (%)</td>
</tr>
<tr>
<td>Father (34)</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>Mother (34)</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>Male sib (16)</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Female sib (15)</td>
<td>28</td>
<td>72</td>
</tr>
<tr>
<td>Female sib (12)</td>
<td>30</td>
<td>70</td>
</tr>
<tr>
<td>Male sib (10)</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>

* Numbers in parentheses refer to the number of cells karyotyped.
† Number of buccal mucosa cells analysed.
‡ The karyotypes of all cells with 45 chromosomes or less showed the loss was random.
** The cell count is a combined count of both the standard Giemsa and quinacrine mustard methods.

![Fig. 2. Fluorescent karyotype of 12-year-old female sib with trisomy 7 (arrow) mosaicism.](http://jmg.bmj.com/.../hg.png)
Results and discussion

Sex-chromatin studies were conducted on buccal mucosa smears from the mother and her four children. All Barr body counts were normal (Table I).

Chromosome analyses were carried out on cultured peripheral blood leucocytes of all six members of the family. The results of the analyses are summarized in Table I and Figs. 2 and 3. A trisomy 7 cell line (47,XX,+7) was found in the mother and one of her daughters. Both the mother and daughter were mosaic (46,XX/47,XX,+7) with the trisomy 7 cell line constituting 14% and 9%, respectively, of the cells analysed. The father and the other three children had normal karyotypes. All family members, including the two trisomy 7 mosaics, were phenotypically normal.

The fact that the trisomy 7 mosaics did not lead to marked physical abnormalities could be explained on the basis of cellular distribution of the trisomy condition. However, the phenotypic expression (or the lack of it) of a chromosomal abnormality may be due to other unknown factors. For example, Zackai and Breg (1973) recently reported two cases of ring chromosome 7 with vastly different phenotypic expression. One individual was severely retarded and had multiple birth defects, but the other individual was only short in stature.

Zellweger (1964) has pointed out that the occurrence of familial aneuploidy is rare and that familial mosaicism is extremely rare (Kiousoglou et al, 1964; Zellweger and Abbo, 1965). Borges et al (1964) have suggested that different chromosomal anomalies caused by non-disjunction at meiosis and/or mitoses may be under genetic control. Since familial mosaicism, in particular, is inconsistent with the usual concepts of how mosaicism occurs, Zellweger and Abbo (1965) postulated that an autosomal dominant gene may be responsible for familial mosaicism. As a case in point, they presented a family with a balanced D/D translocation mosaicism which had been inherited for three consecutive generations. Also, the third generation (two brothers) had other chromosomal mosaics in addition to the translocations. Zdansky et al (1971) have reported a case of familial mosaicism in which a balanced C/C translocation was inherited for four consecutive generations and was always in a mosaic form with a partial C-trisomy. Thus, the postulate is a plausible explanation of the aetiology of these mosaics. The aetiology of the trisomy 7 mosaicism in two generations of the family analysed in this report could also involve an autosomal dominant gene.

Although a genetic basis has been considered for the associations of antisocial personalities, hysteria, and alcoholism occurring in first-degree relatives (Guze et al, 1967), no consistent chromosomal aberrations have been found in those diagnoses. Therefore, the trisomy 7 mosaicism we reported is most likely unrelated to the psychiatric illnesses of the mother and daughter.

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