and that the ring chromosome was most likely formed from it. Examination of the C group chromosomes suggested that the ring could have been formed from a larger member, such as a number 7 chromosome. The autoradiographic results, which show a late-labelling, normal appearing X chromosome, indicate that the ring chromosome is not derived from the inactivated X chromosome.

Sometimes the phenotypic findings in a patient are helpful in identifying an affected chromosome. The nonspecific findings in our patient are not helpful in this regard. Comparison of both the phenotypic and the chromosomal findings in our patient with those from the literature indicate that microcephaly and mental and physical retardation is a common pattern in these patients (Turner et al., 1962; Atkins et al., 1966; Bueno, Del Amo, and Hermida, 1969; Gacs, Schuler, and Selleyei, 1970). The lack of a common phenotype is not surprising and could be due to involvement of different C group chromosomes or alteration of different parts of the same chromosome in the formation of the ring structure. Further, the effect of instability of the ring chromosome as in our patient, is not known, but could possibly also have a phenotypic effect.

Summary

A 3-month-old mentally and physically retarded girl with multiple congenital defects was found to have a ring C chromosome in lymphocytes and bone marrow cells. Autoradiography of lymphocytes suggests a normal late-labelling X is present but do not further identify the ring chromosome which appears to be one of the longer autosomes of the C group. Comparison with previously reported patients with ring C chromosomes does not show a close similarity with any of these.

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References


Double Aneuploidy (47,XX,21+45,X) Arising Through Simultaneous Double Non-disjunction

The occurrence of double aneuploidy, ie, the existence of 2 chromosomal abnormalities in the same individual, is a relatively rare phenomenon. Double autosomal trisomy has been reported in combinations of groups D and G (Gustavson et al., 1962; Becker, Burke, and Albert, 1963; Koch, Santamouris, and Ulbrich, 1967; Zellweger and Abbo, 1967; Porter, Petersen, and Brown, 1969); E and G (Gagnon et al., 1961; Hsu et al., 1965; Marks, Wiggins, and Spector, 1967); D and E (Schmidt et al., 1967; Garson et al., 1969); 17 and 18 (Korányi and László, 1969); and tetrasomy D (Dhadian, 1970). In addition, structural rearrangements of the autosomes coexisting with autosomal trisome have been noted (Petit et al., 1968; Subrt and Prchlikova, 1969; Miller et al., 1970). Mixed sex-chromosomal and autosomal double aneuploidy has been of the types 48,XXX,18+ (Uchida and Bowman, 1961; Uchida et al., 1962; Ricci and Borgatti, 1963; Haas and Lewis, 1966; Engel et al., 1967); 48,XXX,21+ (Day et al., 1963); 48,XXY,13+ (Pergament and Kadotani, 1965); 48,XXY,21+ (Ford et al., 1959; Hustinx et al., 1961/62; Punnet and DieGeorge, 1967); 48,XXY,18+ (Cohen and Bumbalo, 1967); 46,XXY,D−D−,t(Dq,Dq)+ (Tiepolo et al., 1967); 48,XXY,21+ (Verreesen and van den Berge, 1965; Uchida, Ray, and Duncan, 1966); 46,X,13+/47,XX,13+ (France et al., 1967); 44,X,D−D−,t(Dq,Dq)+/45,XX,D−D−,t(Dq,Dq)+ (Stahl et al., 1966); and 46,X,21+/47,XX,21+ (Root et al., 1964; Candela et al., 1966; Duillo and Serra, 1969). In almost all these instances, both chromosomal anomalies were observed in the same cell. The following report describes a unique case of double aneuploidy which most likely arose as a result of two simultaneous postzygotic non-disjunctional events within a single cell leading to two leucocyte stem lines: 47,XX,21+ and 45,X.

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Case Report

The patient was a newborn female who was referred to the Division of Human Genetics of the State University of New York at Buffalo for cytogenetic studies because of physical features consistent with Down's syndrome. Physical examinations in the newborn period and at 6 months of age revealed an apparently typical mongoloid infant. Her height and weight were between the 50th and 75th centiles, but her head circumference was below the 3rd centile (39.5 cm). She had a typical flattened mongoloid facies with bilateral epicanthal folds, Brushfield's spots, and upward slanting of the eyes; the bridge of the nose was flattened and the tongue large; there was brachycephaly with a flattened occiput; the ears were small with overfolding of the upper helix. The chest was unremarkable and there were no heart murmurs. A small umbilical hernia was present, as were bilateral simian creases and incurving of both 5th fingers. The hands and feet were otherwise normal and no dorsal oedema or any other detectable features of Turner's syndrome were present either at birth or at repeat examination 6 months later. The infant was not hypotonic and seemed unusually alert and active.

Cytogenetic Studies

Buccal smears from the patient were fixed in 95% ethanol and stained with cresyl echt violet. Chromosome analysis was performed on leucocytes of the proposita and her parents, cultured by micromethod (Chromosome Medium 1A-Grand Island Biological Company, Grand Island, New York). Harvest of cells and slide preparation were accomplished by a slight modification of the method of Moorhead et al (1960). In addition, fibroblasts derived from skin biopsies of the proposita were studied. Autoradiography was performed following the method of Schmid (1963).

Results

The karyotypes of both parents were normal, both numerically and morphologically. The first leucocyte culture of the patient revealed 2 stem lines: approximately 50% of the cells were typical of Down's syndrome (47,XX,21+), while the remaining cells had a modal number of 45 chromosomes with a C group chromosome missing (Table I). These results were confirmed by a repeat leucocyte culture. Analysis of 7 cells with 46 chromosomes indicated random loss. In marked contrast to the leucocyte cultures, analysis of 100 metaphases from the fibroblast cultures indicated a modal number of 47, with a karyotype consistent with 47,XX,21+. The nonmodal cells evidenced random loss. Sex chromatin determination of buccal mucosal cells and fibroblasts revealed a normal female pattern (18% singly positive cells).

 Autoradiographic analysis of lymphocytes confirmed that the missing C group chromosome was an X chromosome. Of 46 cells analysed, 26 showed a definite late replicating element. All of these had 47 chromosomes, including 16 C group elements. On the other hand, of the 20 remaining cells with sufficient silver grains to indicate isotopic incorporation, none showed a late replicating element and all possessed 45 chromosomes, with one C group member missing.

Comment

The patient in this report represents a unique situation. Two distinct stem lines of cells, 47,XX, 21+ and 45,X, were present in the leucocytes in equal proportions and no cell contained both abnormalities. Those few leucocytes with 46 chromosomes all possessed the extra No. 21 and gave evidence of random loss from other chromosomal groups. However, in contrast cultured skin fibroblasts yielded only the 47,XX,21+ karyotype. These findings can be best explained as a result of either chimeraism or mosaicism. The possibility of chimeraism could not be investigated since the family was unavailable for further study of blood groups. The best interpretation of the findings on the basis of mosaicism would necessitate 3 non-disjunctional events. The first non-disjunction would be prezygotic in nature, involving chromosome No. 21 and leading to a fetus with typical Down's syndrome. The second event, involving the simultaneous loss of an X-chromosome as well as the extra No. 21, most probably arose in a precursor cell of the lymphocytic series due to double non-disjunction or double anaphase lag (or one of each occurrence). In either case, it must have been a simultaneous loss; otherwise a third stem line of cells with 46 chromosomes, including one or the other chromosome (21 or X) would be present. To our knowledge, this case represents the first instance in which a double cytogenetic error has occurred, probably within a single cell of the lymphocytic series, yielding a double aneuploid.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Chromosome Number</th>
<th>Total No. of Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>45</td>
<td>46</td>
</tr>
<tr>
<td>Peripheral blood</td>
<td>47 (13)*</td>
<td>39 (10)</td>
</tr>
<tr>
<td>Total</td>
<td>86 (23)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Skin fibroblasts</td>
<td>10 (10)</td>
<td>90 (15)</td>
</tr>
</tbody>
</table>

* Figures in parentheses indicate cells microscopically and/or photographically analysed.
condition. The clinical prognosis of this patient, vis à vis the manifestations of Turner’s syndrome, is uncertain since the 45,X karyotype may or may not be restricted of the blood cells.

Summary

A patient, clinically typical of Down’s syndrome, is reported. Cytogenetic investigation of leuco
cyte preparations revealed two stem lines of cells, 47,XX,21+ and 45,X in equal proportions. Autoradiography indicated that the missing element in the 45 chromosome line was an X chromosome. Fibroblast cultures demonstrated the 47,XX,21+ karyotype only. The most likely interpretation of this finding is double non-disjunction within a single cell.

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REFERENCES