they were present in the peripheral blood of the mother, they either did not survive for more than 4 weeks, or at least they disappeared from the circulation. They were not selected out in a long term leucocyte culture. The latter fact however is not surprising as we have been unable to detect the marker chromosome specific of the leukaemic cells in established long term leucocyte cultures in 12 patients with Ph1 positive CML and in 2 other patients with acute leukaemia (H. van den Berghe, unpublished data).

Summary

A C/B translocation has been found in the leukaemic cells of a non-malformed female newborn with acute congenital leukaemia.

The authors are very much indebted to Dr de Waele, paediatrician, Aalst, Belgium, for enabling us to study this case, to P. Fiallows for reviewing the manuscript, and to the staff of the Department for their invaluable help.

This work was aided by contract no. 20.122, FWGO, Belgium.

H. VAN DEN BERGHE,* J. P. FRYNS,† and H. VERRESEN‡

Ring F Chromosome Mosaicism (46,XY,20r/46,XY) in an Epileptic Child without Apparent Haematological Disease

Case Report

This boy was born 9 March 1960 when the father was 27 and the mother 25 years old. Delivery was spontaneous, normal, and full term following a pregnancy which was uncomplicated except for an iron-deficiency anaemia requiring intravenous iron treatment in the 3rd trimester. Birth weight was 3402 g.

At age 11 the propositus was referred to the Regional Psychiatric Service for Children and Young People because of deteriorating behaviour associated with poor control of epilepsy. He had been epileptic since the age of 4; there was no preceding history of head injury or other cerebral insult.

On examination his weight was 32.5 kg and his height 135.5 cm. Facial appearance was unremarkable except for bilateral epicanthus. There was no abnormality in the shape or size of the skull and no apparent skeletal abnormality. Hypertrophy of the gums was attributed to medication with phenytoin. The cardiovascular and respiratory systems were normal; there were no abdominal masses. On examination of the central nervous system he was dull and slow. Epileptic phenomena consisted mostly of temporal lobe attacks, with episodes of mood abnormality and automatic behaviour accompanied by varying degrees of alteration of consciousness; there were a lesser number of minor seizures with twitching of the upper limbs. There was no hyperkinesis. Intellectual assessment on the Wechsler Intelligence Scale for Children gave scores of 77 (full-scale IQ), 80 (verbal IQ), and 80 (performance IQ); there were discrepancies between subtest scores on the verbal scale, reflecting poor educational attainment.

Cerebrospinal fluid examination and amino-acid chromatography were normal. Electroencephalography demonstrated extensive bilateral abnormality. No intracranial abnormality was demonstrated on skull radiography, air encephalography, or carotid angiography.

Family History. The patient was the 4th child in a sibship of 6 consisting of 1 female and 5 males; there were no other recognized pregnancies. The father died before this investigation in a road traffic accident but all other first-degree relatives are alive and well. There was no family history of epilepsy or psychiatric disorder.

Dermatoglyphs. The 5th digits on each hand were short but showed 2 flexion creases. There was an unilateral simian crease on the left palm. Ulnar loop patterns were present on all 10 fingers. The total ridge count

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was low at 120. The palmar triradius was situated at r° in both hands. Atd angles were 63° (left) and 71° (right).

**Haematological Investigations.** Haemoglobin was 12.7 g/100 ml and the white cell count 8200/mm³. On differential white cell count there was an eosinophilia of approximately 14% (1148/mm³) which was regarded as a toxic effect of long-term anticonvulsant medication.

**Cytogenetics.** The chromosomes of cells from lymphocyte cultures and a fibroblast culture from the skin were examined. No dividing cells were found in lymphocyte cultures without phytohaemagglutinin but a ring chromosome replacing a member of the F group was present in 43% and 60% of cells in stimulated cultures harvested at 48 and 72 hours respectively (Table I). A few cells were present in which the ring was enlarged or duplicated (Fig. 1) indicating instability which is usual for rings. The ring chromosome was also present in 3 cells from a skin culture but as it was possible to examine only 10 cells the lesser proportion of affected fibroblasts cannot be considered significant.

Using the quinacrine fluorescence technique (Caspersson, Zech, and Johansson, 1970) it was shown that the chromosome replaced was No. 20. Further, assuming that the quinacrine staining characteristics of chromosomes are not altered in the formation of rings, this ring was composed predominantly of material from the brighter arm of the chromosome. This was also true for the enlarged rings.

The chromosomes of cells from the mother, sister, and 2 of the brothers had no detectable constitutional abnormality. No other family members were available for study.

**Blood Group Investigation** (MRC Blood Group Unit). The blood groups of the family members examined are shown in Table II. No red cell mosaicism or abnormality of inheritance was detected.

**Discussion**

Constitutional ring chromosomes have been reported for most of the chromosome groups but not apparently for the F group. Even duplications or deletions involving a chromosome in this group are rare. A phenotypically normal female with a small acrocentric chromosome replacing a member of the F group was reported by Sparkes, Carrel, and Wright (1968). She had a poor reproductive history and her 3 surviving children were all mentally retarded, of similar facial appearance, and had a large number of digital arches. It was tentatively suggested that the mother had a balanced translocation and the children, whose chromosomes were indistinguishable from normal, had partial trisomy of an F group chromosome. A child with multiple malformations including congenital heart disease, low stature and weight, with right cryptorchidism and bony abnormalities was found by Loiodice et al (1970) to have a deletion from the short arms of chromosome 20.

### Table I

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Time in Culture</th>
<th>Ring Present</th>
<th>Ring Absent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>48 hr</td>
<td>13</td>
<td>17</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>72 hr</td>
<td>18</td>
<td>12</td>
<td>30</td>
</tr>
<tr>
<td>Skin</td>
<td>19 dy</td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
</tbody>
</table>

Fig. 1. Partial karyotypes. F group chromosomes from 4 cells with rings present. (a) Single small ring; (b) single enlarged ring; (c) and (d) ring duplicated.

### Table II

RED CELL ANTIGENS

<table>
<thead>
<tr>
<th></th>
<th>ABO</th>
<th>MNSs</th>
<th>P₁</th>
<th>Rh</th>
<th>Lu</th>
<th>K</th>
<th>Le</th>
<th>Fy</th>
<th>Jk</th>
<th>Xg</th>
<th>Do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propositus</td>
<td>O</td>
<td>MsNs</td>
<td>+</td>
<td>R₁r</td>
<td>a-</td>
<td>+</td>
<td>a+b</td>
<td>a+b</td>
<td>a+b-</td>
<td>a-</td>
<td>a-</td>
</tr>
<tr>
<td>Mother</td>
<td>O</td>
<td>MsNs</td>
<td>+</td>
<td>R₁r</td>
<td>a-</td>
<td>+</td>
<td>a+b</td>
<td>a+b</td>
<td>a+b-</td>
<td>a-</td>
<td>a-</td>
</tr>
<tr>
<td>Sister</td>
<td>O</td>
<td>MsMs</td>
<td>+</td>
<td>rr</td>
<td>a-</td>
<td>+</td>
<td>a+b</td>
<td>a+b</td>
<td>a+b+</td>
<td>a+</td>
<td>a-</td>
</tr>
<tr>
<td>Brother</td>
<td>A₁</td>
<td>MsNs</td>
<td>+</td>
<td>rr</td>
<td>a-</td>
<td>+</td>
<td>a-</td>
<td>a-</td>
<td>a+b-</td>
<td>a-</td>
<td>a-</td>
</tr>
<tr>
<td>Brother</td>
<td>O</td>
<td>MsNs</td>
<td>+</td>
<td>R₁r</td>
<td>a-</td>
<td>+</td>
<td>a+b</td>
<td>a+b</td>
<td>a+b+</td>
<td>a+</td>
<td>a-</td>
</tr>
</tbody>
</table>
His clinically normal father, however, had an indistinguishable chromosome malformation and there was also parental consanguinity. An adult male with a deletion from a chromosome considered to be 19 on the criterion of size had microcephaly, muscular hypotonia, ankylosis of both knees, and bilateral cataracts accompanied by severe behavioural disorders and mental retardation (Genest, Bouchard, and Poty, 1971). Recently, a male, aged 69 years, with mental retardation, cardiovascular disease, cervical spondylosis, degenerative osteoarthropathy, a hydrocele, microcephaly, a flat occiput, and slanting eyes with epicantic folds was found to have a long arm deletion of an F group chromosome (Ahmed, 1972).

Abnormality apparently restricted to a chromosome in the F group has been found in some cells from the marrow of patients with sideroblastic anaemia (de Grouchy et al, 1966; Goodall and Robertson, 1970) as well as in cases of polycythaemia vera (Millard et al, 1968) and acute granulocytic leukaemia (Kiossoglou, Mitus, and Dameshek, 1965). A ring chromosome formed from a member of this group has been observed in this laboratory in a clone of cells from a patient with acute leukaemia but other abnormal chromosomes were also present as was the case for the F group anomaly reported in a case of myelofibrosis (Goodman et al, 1968). It has been suggested that genes relevant to haematopoiesis reside on an F group chromosome (de Grouchy et al, 1966) but no abnormality other than an eosinophilia, which is probably a response to drug therapy, was found in this patient.

We have been able to show, by the fluorescence banding technique, that the chromosome affected in this patient is No. 20 (following the convention of Caspersson et al [1970]) and that material has probably been lost from the long arms of the chromosome. Chromosomes 19 and 20 are difficult to distinguish by measurement and useful comparisons of the chromosome material involved in the various conditions must await reports of banding studies. Very recently Reeves, Lobb, and Lawler (1972) have reported that the deletion found in cases of polycythaemia vera is from the long arm of chromosome 20. It may be that in such cases the chromosome anomaly is a manifestation, rather than a cause, of the disease. At the present time there is no evidence of this disease in our patient.

Ring chromosomes can be formed after fertilization and a number of other cases have been reported in which there is a normal cell line in addition to the ring bearing line (Lucas et al, 1963/1964; Steele et al, 1966; Faed, Stewart, and Keay, 1969) although it is surprising that cells with an unstable abnormality maintain themselves in competition with normal ones. It is possible that cells lost in vivo are replaced by the multiplication of neighbouring cells which have a good chance of belonging to the same clone. On the other hand, what evidence there is on the behaviour of such unstable cells in fibroblast cultures (Faed et al, 1969) shows that they may persist even under conditions in which growth is not restricted. In our patient the number of ring-bearing cells in the lymphocyte cultures rose from 43% to 60% between 48 and 72 hr indicating a vigorous rate of growth of the abnormal cells. It may be that in such mosaic situations only rings which carry with them an incidental compensating increase in growth rate survive to be recognized.

Summary

A boy with epilepsy and associated behavioural disorder has been found to have a ring replacing chromosome 20 in a large percentage of his cells. The patient is not severely mentally defective and has no apparent haematological disorder.

We wish to thank Dr Helen S. Mathewson for permission to study the patient in her charge; Dr Janet M. Donald for examining the palm prints; Dr Ruth Sanger for the blood group results, and Miss Mary Hamilton for technical assistance.

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Cytogenetics Laboratory, Department of Pathology and Department of Psychiatry, University of Dundee

REFERENCES


Bone Marrow Chromosomes in Fanconi’s Anaemia

Patients with the autosomal recessive syndrome, Fanconi’s anaemia (FA), exhibit a high frequency of chromosome breakage and rearrangement in their cultured lymphocytes and skin fibroblasts (Swift and Hirschhorn, 1966). However, there is little published data on the aberration frequency in direct bone marrow preparations: in a recent review, bone marrow from 3 FA patients were reported to show no chromosome breaks while in 4 other cases 10% aberrant metaphases were found (Schroeder and Kurth, 1971). Bone marrow chromosome preparations differ significantly from those of lymphocytes in that the relatively short incubation time of marrow cells in vitro (approximately 2 hours) includes only a small fraction of a single cell cycle. Therefore findings in the marrow cells are important because it is likely that these cells synthesized their DNA within the living patient. In contrast lymphocytes undergo one to two entire cell cycles in vitro (48-72 hr) before chromosome analysis.

Case Report

We have studied a patient with Fanconi’s anaemia whose clinical course has been described previously (Pochedly et al., 1971).

The propositus, an 8-year-old Negro male, was of subnormal size and weight for his age with a normocytic, normochromic anaemia and pancytopenia. Skeletal anomalies included small head circumference, Sprengel’s deformity, Klippel-Feil anomaly, and short thumbs with flat thenar eminences. There was renal ectopia with both kidneys on the right side. Unusual features included growth hormone deficiencies and a marked elevation of haemoglobin F.

Chromosome Studies

Chromosome studies were done on direct bone marrow preparations following incubation of 1½ hr with vincleucoblastine, on peripheral blood lymphocytes incubated with phytohaemagglutinin for 72 hr in vitro, and on skin fibroblasts cultivated in vitro for 7 weeks. The percentage of dividing cells (Table I) containing significant structural damage comprised 10% of the bone marrow cells, 26% of the fibroblasts, and 60% of the lymphocytes. There were, therefore, striking differences between populations of cells derived from a single individual.

Gaps, which were not recorded in the table of aberrations, were found in 4 marrow metaphases, 11 lymphocytes, and 7 of the cultured fibroblasts. Both gaps and breaks, chromatid and chromosomal, appeared to be distributed randomly within the chromosome groups with the exception that group A may have had slightly more than its share of breaks. No predilection for specific chromosomes or loci within chromosomes, such as points of secondary constriction, was apparent.

In this laboratory we have not obtained a series of marrow preparations from normal controls. Of 300 bone marrow cells from 15 patients, mainly suffering from leukaemia, 17 had chromatid or

Received 8 May 1972.

<table>
<thead>
<tr>
<th>TABLE I</th>
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<tbody>
<tr>
<td>CHROMOSOME ANALYSIS</td>
</tr>
<tr>
<td>Number of Cells</td>
</tr>
<tr>
<td>Examined</td>
</tr>
<tr>
<td>Bone marrow</td>
</tr>
<tr>
<td>Lymphocytes</td>
</tr>
<tr>
<td>Skin fibroblasts</td>
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