Case Reports

Journal of Medical Genetics (1972).  9, 468–484.

Congenital Leukaemia with 46,XX,t(Bq+,Cq−) Cells

Congenital leukaemia is a very rare condition. The symptoms are either present at birth (congenital type) or become evident within 1 month after birth (neonatal type). Cytologically 3 main varieties exist: myeloid, histiomyelocytic, and lymphoid. In contrast to childhood leukaemia, the lymphoid type is much less prevalent.

Simultaneous occurrence of congenital leukaemia and mongolism had already been reported before chromosome studies in man were available (Schunt and Lehman, 1954). Beside this now well established relationship, congenital leukaemia has also been found in Turner's syndrome (Pridie and Dimitrescu-Pirvu, 1961) and in trisomy D (Schade, Schoeller, and Schultz, 1962).

Case Report

The proposita, a newborn female, was the 4th child born to healthy parents. The 3 previous children, all boys, are normal. There have been no abortions. At birth the mother was 30 and the father 32 years old.

Pregnancy was uneventful, except for asymptomatic rubella during the 8th month of pregnancy, at which time 2 of the 3 sibs were also ill with the same disorder. Rubella antibody titres in both the proposita and her mother were 1024 haemagglutination inhibition units on 2 different occasions (the 5th and 7th day after birth).

Delivery was at term, spontaneous, and without complications. Birth weight was 3200 g, length 50 cm, head circumference 35 cm. No external malformations were noted. Jaundice was present at birth as well as a few petichiae. The spleen was considerably enlarged and of very firm consistency. Liver and lymph nodes appeared normal.

Peripheral blood examination on the day of birth showed a haemoglobin of 19.2 g%, haematocrit was 56%, the leucocyte count was 55,100 of which the large majority were myeloblasts and erythroblasts, platelet count was 14,000, and normal reticulocytes 34%.

Direct Coombs reaction was negative. The child was breast fed and drank well. Her general condition initially was very satisfactory but deteriorated rapidly. Jaundice and subcutaneous haemorrhages became more apparent, the nucleated cell count increased very rapidly to 128,000 on the 8th day, and death occurred on the 12th day after birth, the immediate cause of death being ascribed to meningeal bleeding. No treatment was given. Permission to perform a necropsy was not granted. One day before death a 0·2 ml heparinized blood sample was brought to the laboratory and only one culture, without using phytohaemagglutinin (PHA), could be set up. We had no opportunity to study skin fibroblasts or peripheral lymphocytes, as the child was dead by the time we asked for additional investigations.

Cells were harvested for chromosome analysis after 2, 3, 5, 7, and 9 days of culture and a total of 71 cells could be examined from the last 3 cultures. There were 4 cells with 44 chromosomes, 4 with 45 chromosomes, and 63 with 46 chromosomes. A C/B translocation was found in all the cells (Fig. 1).

Karyotypes of the father and the mother, examined 4 weeks after the birth of the child, appear normal. Six hundred and fifty-one of the mother's cells from lymphocyte cultures have been examined and none had a translocation. No metaphases were detected in cultures of the mother’s blood in the absence of PHA (after 24, 48, 72, and 96 hours and 6 and 9 days). A long term leucocyte culture of the mother examined after 9 weeks of culture showed only a normal 46,XX karyotype in 55 cells. There is no evidence of leukaemia in the mother 12 months after the birth of the child.

Discussion

Since PHA was not added to the culture of the proposita's cells, it is very likely that only leukaemic cells were in metaphase. Thus, the leukaemic cells are considered to have a C/B translocation. Nothing is known about the normal cells of this child, except that the translocation, if it was present in the normal cells, was not inherited from one of the parents.

There are some previous reports on chromosome studies in patients with congenital leukaemia, but they are mainly in patients with Down's syndrome. Patients with congenital leukaemia and Down's syndrome almost always had hyperdiploid lines, often with selective endoreduplication of a G− or other chromosome (Conen and Erkman, 1966). There are very few reports of chromosomal findings in patients with congenital leukaemia who do not have Down's syndrome. Abnormal karyotypes in malignant cells such as 46,XY,3p− (Zussman, Khan, and Shayesteh, 1967), 46,XX,D+,16−

Received 21 February 1972.
Case Reports

(Bauke, Cremer, and Heimpel, 1970), and pseudodiploid and hyperdiploid cells (Wagner, Tonz, and Greyerz-Gloor, 1968) have been found in 3 cases presumed to have congenital myeloid leukaemia. It is unfortunate, for perfectly understandable reasons, that children with congenital leukaemia and their parents are seldom extensively investigated, since they offer unique possibilities for the study of fundamental problems in oncogenesis and tumour immunity.

The possible role of chromosomal anomalies in leukaemogenesis has been reviewed by Miller (1966). It seems likely that congenital leukaemia arises more frequently in fetuses with constitutional chromosomal anomalies. In addition to Down’s syndrome, the examples cited above of the occurrence of this rare disorder in relatively rare conditions such as Turner’s syndrome and 13-trisomy, and possibly the present case may be an illustration of this tendency. The analysis of more cases will show whether congenital leukaemia is as prevalent in other chromosomal syndromes as it is in Down’s syndrome. In later life, leukaemia and lymphoma may occur with slightly increased frequency in Klinefelter’s syndrome (Borges, Nicklas, and Hamm, 1966). The latter condition being inconspicuous in newborns, it may well be that congenital leukaemia does also occur in newborns with this syndrome.

Fetal lymphocytes pass the placental barrier (de Grouchy and Trebuchet, 1971) and this raises the possibility that maternal cells also enter the fetus and that the abnormal cell lines in some patients with congenital leukaemia may be maternal in origin. A detailed analysis of a battery of genetic markers of the leukaemic and normal cells of the affected child and of the mother could solve this problem in those cases where the sex chromosome pattern of the leukaemic cells does not exclude the possibility of their maternal origin, but unfortunately it was not possible to study this in our patient.

If leukaemic cells entered the maternal circulation, we were not able to detect them. If at some time

![Fig. 1. Karyotype of the proposita.](image-url)
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 Wael, paediatrician, Aalst, Belgium, for enabling us to study this case, to P. Fialkow 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

References


* Division of Human Genetics, Department of Human Biology, University of Leuven, Belgium.
† Department of Pediatrics, Academisch Ziekenhuis, University of Leuven, Belgium.
‡ Bevoegd Navorser NFWO.

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 hyperkinesia. 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 a unilateral simian crease on the left palm. Ulnar loop patterns were present on all 10 fingers. The total ridge count

Received 6 March 1972.