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 (Pochelly et al., 1971).

The propositus, an 8-year-old Negro male, was of subnormal size and weight for his age with a normocytic, normochromatic 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 vincaleucoblastine, 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.

| TABLE I
<table>
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<tr>
<th>CHROMOSOME ANALYSIS</th>
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<tr>
<td>Number of Cells</td>
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<td>Bone marrow</td>
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<td>Lymphocytes</td>
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<td>Skin fibroblasts</td>
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Case Reports

Pochedly, C., Sandberg, M. Inherited metabolic anaemia. Fibroblast patient with difference for the increase marrow with gotes and nature dated if have not respectively dence of chromosome expected proportion 0
Berry, control recent chromosome aberrations many of whom cells than breaks. 474 cancer and efficiency. British Journal Haematology, 55% of this be been found incidences of chromosome aberrations of many of whom cells than breaks. (Swift, 1971).

Conclusion

The FA gene is of great interest because of its association with cancer and leukaemia in homozygotes and heterozygotes (Swift, 1971). If the bone marrow cells from a patient with Fanconi’s anaemia showed a lower aberration frequency than that of either lymphocyte or fibroblast cultures from the same patient. This difference between the aberration frequency in vivo and in vitro may provide a clue to the nature of the inherited metabolic defect underlying Fanconi’s anaemia.

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REFERENCES


Fanconi’s Anaemia: Report of a Patient with Significant Chromosomal Abnormalities in Bone Marrow Cells

In Fanconi’s anaemia, the presence of frequent chromosomal aberrations in cultured peripheral lymphocytes is now an established phenomenon. In fact, a number of authors (Bloom et al, 1966; Swift and Hirschhorn, 1966; Hirschman et al, 1969), suggest its demonstration as a valuable aid in establishing diagnosis in doubtful cases. On the other hand, very few instances of the above disease have been encountered in which similar changes were seen in bone marrow cells. The following communication describes one such patient.

Methods

Routine haematological investigations were carried out on blood and bone marrow aspirates according to standard methods.

Chromosome studies were performed on a peripheral leucocyte culture following the method of Moorhead et al (1960). One hundred consecutive metaphases were examined in detail. In addition, a bone marrow specimen obtained by sternal puncture was prepared for karyotyping using a slight modification of the technique of Tjio and Whang (1962). Ninety suitable spreads were photomicrographed and analysed.

Case Report

The patient, an 11-year-old male, was first seen at the paediatric service at the American University Hospital in September, 1966. His symptoms dated back to the age of 4 years, when he started having repeated attacks of easy bruising and bleeding from various sites (nose, urinary tract, rectum, and retina). Meanwhile he was noticed to develop progressive pallor which was not commensurate with the amount of blood loss. There was no history of exposure to drugs or bone marrow toxins.

The family history disclosed consanguinity in the

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