42. Two Cases of Acute Myeloblastic Leukemia Associated with a 9/22 Translocation

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Abnormally small G-group chromosomes morphologically indistinguishable from the Ph¹-chromosome of chronic myelogenous leukemia (CML) have been reported to occur in various conditions of blood disorders other than CML (Hossfeld et al. 1971). However, the origin and significance of those Ph¹-like chromosomes have remained uncertain due to technical limitations. Recent chromosome banding studies demonstrated that the Ph¹-chromosome was represented by a chromosome 22 with partial deletion of the long arm (Caspersson et al. 1970a), and that the deleted segment was translocated to the long arm of a chromosome 9 (Rowley 1973), although some exceptions were present in which the translocation occurred onto other chromosomes (Hayata et al. 1973, Gahrton et al. 1974, Ishihara et al. 1974), or it was undetected (Mitelman 1974). Thus, it became pertinent to reevaluate exact origin of the above mentioned Ph¹-like chromosomes.

We describe here two cases of acute myeloblastic leukemia (AML) which were associated with a (9q+; 22q−) translocation identified by banding analyses.

Case report. Case 1 (No. 209, Y. H.) was a 17-year-old female who developed fatigability with high fever and anemia, in the middle of February, 1972. A blood smear made on February 23 revealed a high white cell count over 25,000 with 74% blasts, mostly of monocytoid cells, 18% lymphocytes and 8% neutrophils. The red cell count was 185×10⁴, and platelets 23.8×10³. Bone marrow aspirates taken on May 15 and 23, after repeated blood transfusions and steroid therapy, exhibited total cell counts of 8,000 and 126,000, respectively, which were represented by 17% and 26% of highly pleomorphic

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leukemic blasts, with PAS-negative and peroxidase-positive (40\%) reactions. The megakaryocyte count was within a normal range (94/mm$^3$). The alkaline phosphatase activity of mature neutrophils (NAP) was also normal (rate 80\%, score 228), which later showed a decrease (rate 47, score 113, June 12). The number of platelets increased up to 230\times 10^3 during remission which lasted for about 3 months (April to June). The patient died on November 26 (life span 9 months) following an inevitable relapse beginning in the end of August (WBC 38,000, 55\% blasts in marrow). She was diagnosed as AML with an atypical clinical course in the therapeutic response and prognosis.

Case 2 (No. 265, E. K.) was a 25-year-old pregnant woman who delivered a healthy female infant on August 30, 1973. On August 10, she complained of general fatigue, anemia and severe pains on indurated breasts. The white cell count was 108,600 with 97\% myeloblasts (Aug. 20). The bone marrow showed total cell counts of 906\times 10^3 (93\% blasts, Aug. 15, 1973), 43.5\times 10^3 (44\% blasts, Sep. 28), 629\times 10^3 (98\% blasts, Nov. 20), and 498\times 10^3 (95\% blasts, Feb. 1, 1974). The peroxidase reactions were 6\% positive for blood and 7\% positive for marrow, while NAP was within a normal range (score 250). Blood samples taken at 8 different occasions, during a period from August, 1973 to March, 1974, showed WBC 1.4-220\times 10^3, RBC 132-360\times 10^4, platelets 6.8-58.5\times 10^3 and hematocrit 17-37\%.
Whenever the white cell count was higher than $100 \times 10^3$ (Aug., Nov., Jan. and Mar.), the cell population was predominated by myeloblasts (more than 95%). No complete remission was attained with extensive chemotherapy and repeated transfusions. The patient died on March 2, 1974 (life span 7 months). A diagnosis of AML was made.

Cytogenetic findings. The chromosomes were studied on direct marrow preparations (case 1, Mar. 25, 1972) and on cultured marrow and blood (3 days without PHA, case 2, Aug. 21, 1973). The slides were air-dried and stained with conventional Giemsa as well as with Q- and G-banding methods after Caspersson et al. (1970b) and Seabright (1971).

The Ph$^1$-chromosome was observed in 85% (17/20) of cells in case 1, and 100% (20/20 for marrow, 8/8 for blood) in case 2 (Fig. 1). A consistent karyotype of 46, XX, t(9q+; 22q−) was established in both cases, on the basis of 10 Q-band and 6 G-band metaphases.

Fig. 2. Partial karyotypes representing chromosomes 9, 21 and 22. a, b, from case 2 after Q-staining. c, d, from case 1, after Q-staining (c) and G-staining (d) in the same cell.
from case 1, and 7 Q-band metaphases from case 2 (Fig. 2). PHA-
added blood cultures of the patient (case 2, Aug. 21, 1973) and her
baby (Apr. 24, 1974) showed exclusively a normal karyotype, 46, XX.

Remarks. Apparent existence of the Ph1-chromosome has been
reported in certain cases of AML without positive identification of
the said chromosome (Kissoglou et al. 1965, Hossfeld et al. 1971, etc.).
This is now better substantiated by the present banding analyses. It
has been suggested that the Ph1-positive AML may actually corre-
spond to the blastic phase of CML in which the chronic phase is too
short to be detected, or it is represented by an abortive chronic phase
(Hossfeld et al. 1971, Canellos and Whang-Peng 1972). This may be
ture for some cases, though it may not always suffice physicians and
hematologists who made the diagnosis. At the present moment, there
is no reason to believe that the Ph1-chromosome should be strictly
specific for CML. It has been shown that CML is not always as-
associated with the Ph1-chromosome; Ph1-negative cases of CML were
shown to have a normal karyotype with apparently normal banding
patterns (Rowley 1974a). There is a definite evidence that the Ph1-
chromosome is present in erythroid as well as myeloid precursors of
CML (Rastrick et al. 1968). Assuming that there are many cases of
AML with an apparently normal karyotype and that the Ph1-chromo-
some can exist in blood stem cells without appreciable hematological
abnormalities, the Ph1-chromosome in rare instances of AML may not
necessarily be causally related to the manifestation of malignancy.

Another line of evidence has been presented in experimental an-
imal tumors that a given chemical agent produced an identical chro-
some abnormality in histologically different neoplasms, i.e., leukemia
and sarcomas (Mitelman and Levan 1972). This and some other
findings have led to an inference that a certain etiological factor may
cause a common chromosomal change in different types of tumors
(Levan 1973, Rowley 1974b). Whether this can be applied to human
leukemias must await for future studies. Despite that the karyotypic
changes occurring in AML are generally diverse, their stemline karyo-
types appear to be rather distinctive and stable as compared with
those seen in the blastic phase of CML in that the karyotypic varia-
tions are much pronounced (Sandberg et al. 1968, 1971, Fitzgerald
et al. 1973, Hossfeld 1974). It should be mentioned that our AML
cases showed no karyotypic deviations other than the 9/22 transloca-
tion.

Summary. Two cases of acute myeloblastic leukemia are de-
scribed, in which a consistent chromosome abnormality showing a
(9q+; 22q−) translocation was detected by banding analyses.

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