A Case of Acute Myeloblastic Leukemia With Ph' Chromosome Showing Translocation 9q+ ;22q–

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Cytogenetic studies of the bone marrow delphi...and peripheral blood with the quinacrine fluorescence banding technique in a patient with the clinical diagnosis of acute myeloblastic leukemia revealed the Philadelphia chromosome due to a translocation between chromosomes 22 and 9. He had been exposed to the atomic bomb in Hiroshima, and some hours after the exposure he wandered into the hypocenter.

Recently, quinacrine fluorescence banding analyses have demonstrated that the Philadelphia chromosome (Ph') is a No. 22 missing a portion of its long arm which is translocated to the long arm of a chromosome 9. The translocation may occur between chromosome 22 and a chromosome other than No. 9. The presence of the Ph' has been reported in diseases other than chronic granulocytic leukemia (CGL), i.e., acute myeloblastic leukemia (AML) and erythroleukemia. This paper describes an AML patient who had been exposed to the atomic bomb in Hiroshima. A chromosome study has shown a Ph' with a translocation between chromosomes 22 and 9.

CASE REPORT

A 51-yr-old Japanese male bank clerk was admitted to Kawatetsu General Hospital, Chiba, on April 22, 1974, with complaints of general malaise and purpura of 1 mo duration. On August 6, 1945, he was exposed to the atomic bomb in Hiroshima at a distance of 4.8 km from the hypocenter of explosion, and some hours later he entered the hypocenter and wandered for half a day.

The Health Handbook of Atomic Bomb Explosion Sufferers* was issued to him in November 1963, and thereafter he received screening examinations twice a year until July 1973. The record showed no abnormal physical findings nor anemia, and the white cell count ranged from 4.0 to 7.0 x 10^9/liter.

On admission, his temperature was 37.4°C and blood pressure was 110-70 mmHg. The visible mucosa was somewhat anemic, but there was no lymphadenopathy or hepatosplenomegaly. His extremities were dotted with petechiae. Chest X-ray and electrocardiogram disclosed no abnormalities. Hematologic studies showed the following: hemoglobin, 8.5 g/dl; erythrocytes, 2.9 x 10^12/liter; hematocrit, 27%; platelets, 20 x 10^9/liter; and white count, 234 x 10^9/liter with 88% myeloblasts, 1% bands, 1% segments, and 10% lymphocytes. In a bone marrow aspirate, the nucleated cell count was 58 x 10^9/cu mm with 90.5% myeloblasts, 0.5% promyelocytes, 0.5% myelocytes, 0.5% metamyelocytes, 0.5% segmented neutrophils, 6.0% lymphocytes, 1.0% erythroblasts, and 0.5% reticulum cells. The myeloblasts were all leukemic cells (Fig. 1). Peroxidase reaction was negative, and alkaline phosphatase activity of neutrophils (NAP) was 374 by the method of Tomonaga et al. (normal, 170-330). The absolute count of basophils was zero and...
that of eosinophils was $2 \times 10^7$/liter. Blood chemistries were within normal limits, except for serum lactic acid dehydrogenase, which was 550 IU. The C-reactive protein was positive, serum iron 65 μg/dl, and serum vitamin B$_{12}$ 760 ng/liter.

Treatment was started with 80 mg of prednisolone, 40 mg of cytosine arabinoside, and 100 mg of 6-mercaptopurine. Although incomplete remission was induced twice during the hospital course,
he died on September 22, 1974, from bleeding in the lung. At autopsy, his spleen was 40 g in weight and the liver showed fatty metamorphosis. Pathologic diagnosis was AML.

CHROMOSOMAL STUDY

The first analysis of chromosomes was performed on April 23, 1974, before the start of treatment, using a 24-hr culture of peripheral cells prepared without phytohemagglutinin. On May 24, 1974, 1 mo after initiation of treatment, the second analysis was made from a direct sternal marrow preparation. Both were stained by the quinacrine fluorescence banding technique.

Of the 32 peripheral leukemic cells, 31 had the Ph' chromosome, and 4 of them showed double Ph'. The mode was 46 and 47 with a karyotype of 46,XY,Ph' (11 cells); 47,XY,+17,Ph' (13 cells); 47,XY,Ph',+Ph' (4 cells).

All of the 50 marrow cells studied possessed the Ph', of which 41 had a double Ph' with the mode of 47. The karyotype was 46,XY,Ph' (9 cells); 47,XY,Ph',+Ph' (36 cells). The cells containing the Ph' chromosome showed the translocation (9q+:22q-). (See Fig. 2.)

DISCUSSION

There have been a number of chromosome studies in AML, but no specific changes of chromosomes have been identified. It has been established that the Ph' is relatively specific for CGL, but sporadic cases of Ph'-positive AML have also been reported.

Two explanations may be possible for Ph'-positive AML. One is that these cases are not AML but are what Mastrangelo et al. call “abortive CGL,” preceded by a blastic phase indistinguishable in all respects from AML. The other explanation is that the Ph' chromosome may also occur in diseases other than CGL and related conditions. Hossfeld et al. maintain that the Ph' chromosome is not strictly specific for CGL and that varying clinical manifestations may be determined by the level of cellular differentiation at which the induction of Ph' takes place. Kiossoglou et al. has wondered if chromosome changes, such as single or double Ph' and other abnormalities, are of any significance in the pathogenesis, and if they are only an epiphenomenon of the neoplastic process. Finally, he suggests that mere genetic disbalance, irrespective of chromosomes involved, may predispose to an acute neoplastic process or blast transformation of CGL.

In our case the Health Handbook for Atomic Bomb Explosion Sufferers recorded no hemorrhagic tendency, no anemia, and a normal leukocyte count. There was no hepatosplenomegaly from November 1963 to the time he died. The onset was very abrupt, the NAP score was not decreased, the basophil count was very low and the serum B12 was normal. These data are compatible only with the diagnosis of AML.

Another question in this case is whether or not the patient’s chromosomal abnormality was related to the atomic bomb exposure. His radiation dose was estimated at approximately 6 rads. Among the individuals who were proximally exposed to the atomic bomb (within 1500 m from the hypocenter), more CGL occurred in Hiroshima than in Nagasaki; this finding is thought to be due to a heavier neutron bombardment in Hiroshima. There has been no statistical difference in the frequency and type of leukemia that occurred between the distally exposed people, like the present case, and the nonexposed. Kamada et al. could not demonstrate any specific chromosomal aberration for atomic bomb-induced leukemia. It cannot, therefore, be decided if his AML was necessarily related to the atomic bomb.
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REFERENCES

A case of acute myeloblastic leukemia with Ph1 chromosome showing translocation 9q+;22q-

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