Patho-molecular analysis of leukemias among A-bomb survivors

S-II-2 Epidemiology and Pathology of Atomic Bomb Irradiation-induced Leukemia

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The epidemiological evidence for increased risk of leukemia has been provided since 1950 by the joint LSS Study by RERF (former ABCC) and Hiroshima & Nagasaki Universities with a cohort of approximately 120,000 survivors. 231 cases registered between 1950 to 1980 were analysed based on French-American-British (FAB) classification. Major three types of human leukemia, namely acute lymphocytic leukemia (ALL) especially among children, chronic myeloid leukemia and acute myeloid leukemia (AML) especially among adults, showed statistically significant increase in relative risk (RR) and absolute risk (AR). The RR was high in order of ALL > CML > AML, and the AR in order of AML > CML > ALL. Recent analysis also revealed that myelodysplatic syndrome (MDS) was induced in proportion to exposure dose. In contrast to atomic bomb-related leukemia which apparently involves CML, the so-called secondary leukemia which is induced by anti-cancer drugs involves only several subtypes of AML. Thus our study indicates a close relationship between radiation and hematopoietic stem cell injury and subsequent transformation which leads to induction of leukemia in human beings.

S-II-3 Chromosomal and Molecular Biological Changes in Atomic Bomb Radiation-related Leukemias, which were different from those in de novo Leukemias

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Out of 363 acute myelocytic leukemia (AML) and myelodysplastic syndrome (MDS) patients analysed from 1962 to 1994, 88 AML patients were used for present study. No FAB M3 patients and complexity of chromosome aberration were observed in the heavily exposed group (2Gy). Unbalanced translocations of chromosomes 5 and 7, and deletions of chromosomes 11 and 20 were predominantly observed in the patients. No patients with 8:21, 15:17 and 11q23 translocations were found in the heavily exposed group. Microsatellite and minisatellite instabilities were detected in 10 of 14 atomic bomb leukemias. Thus, atomic bomb related AML patients had different cytogenetical and molecular biological features from those in de novo AML. Experiments with human B cell lines established from a and γ rays irradiated lymphocytes also showed that irradiated cell lines developed higher genetic instability, in which low amount of expressions of Ku 70, p53 and TRF 1 telomere proteins were observed. Resolution of the molecular mechanism for developing radiation-induced genetic instability is important for the study on atomic bomb leukemias.