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Atomic Bomb and Leukemia

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CML, threshold/FAB classification/atypical leukemia/chromosome

Characteristic features of the leukemia among atomic bomb survivors were studied. Dose estimates of atomic bomb radiation were based on T65D, but the new dosimetry system DS86 was used for some analyses. The ratio of a single leukemia type to all leukemias was highest for CML in Hiroshima, and the occurrence of CML was thought to be most characteristic to atomic bomb radiation induced leukemia. The threshold of CML occurrence in Hiroshima is likely to be between 0.5~0.09 Gy. However, the threshold of acute leukemia appears to be nearly 1 Gy. In the distribution of AML subtypes by FAB classification, there was no M3 case in 1 Gy or more group, although several atypical AML cases of survivors were observed. Although aplastic anemia has not increased as a late effect of the atomic bomb radiation exposure, many atypical leukemia or other myeloproliferative diseases who had been diagnosed as aplastic anemia or its related diseases have been experienced among atomic bomb survivors. Chromosome study was conducted using colony forming cells induced by hemopoietic stem cells of peripheral blood of proximal survivors. Same chromosome aberrations were observed in colony forming cells and peripheral T-cells in several atomic bomb survivors.

INTRODUCTION

The leukemias that occurred among atomic bomb survivors are one of the important model of the radiation induced human leukemia. There are some differences among the atomic bomb induced leukemia, so-called secondary leukemia and de novo leukemia. We shall describe some characteristic features of the leukemias which were probably induced by atomic bomb radiation. The effect of atomic bomb radiation on human body was mainly due to simple whole body irradiation.

The bone marrow of proximally exposed survivors became aplastic by heavy dose of radiation, however, the reproduction of new blood cells in the bone marrow was already seen in proximally exposed persons who died about 2 months after the bomb. The leukemia occurred among those exposed persons whose blood cells had recovered to a normal count after the bomb.

LEUKEMIA AMONG ATOMIC BOMB SURVIVORS

Leukemia cases among atomic bomb survivors increased gradually from 1946, and the peak of occurrence was observed 6 years after the bomb.

Fig. 1 shows the number of cases and types of leukemia in Hiroshima and Nagasaki among those who received 0.01 Gy or more.

There are some differences in leukemia type between the two cities. The ratio of chronic myelogenous leukemia (CML) to all leukemia is significantly higher in Hiroshima than in Nagasaki. The risk of all types of leukemia increases with dose in both cities, except for Nagasaki survivors who received less than 1 Gy Kerma total dose (average marrow dose). This difference between two cities is clearly observed in CML incidence, but not so clear in acute leukemia. Accordingly, this difference seems to be due to the difference in CML incidence between the two cities. Another important point of atomic bomb induced leukemia is that leukemogenic risk has been higher among the survivors who were younger at atomic bomb in earlier stage. This tendency is most clear in CML cases.

The threshold of acute leukemia and CML was reviewed using the leukemia samples of Hiroshima.

The features of CML in Hiroshima are most characteristic to atomic bomb radiation induced leukemia. This increased incidence of CML is much different from so-called secondary leukemia.

The peak of the occurrence of CML was observed 6 years after the bomb also in the below 1 Gy group as in the 1 Gy or more group. Accordingly, there might be radiation effect to induce CML occurrence in the below 1 Gy group also.

Fig. 2 shows the percentage of cumulative CML cases in each year from 1946 to 1980.

The shape of occurrence curve is the same in the 0.5 Gy or more and 0.1~0.49 Gy

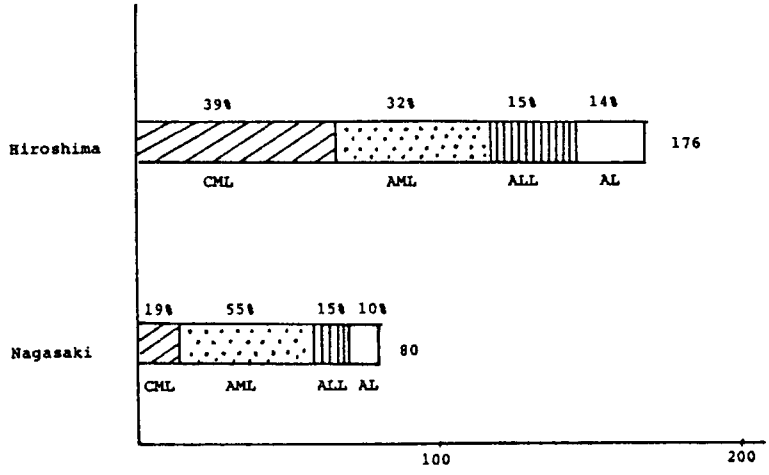

Fig. 1. Cases and type of leukemia among atomic bomb survivors who received 0.01 Gy or more (1945–1975)

groups, but different in the below 0.09 Gy group. Therefore, it is suggested that the threshold of CML occurrence is between 0.5 and 0.09 Gy.

On the other hand, the shape of acute leukemia in the 0.1~0.49 Gy group was similar to that in the below 0.09 Gy group as shown in Fig. 3.

When acute leukemia cases in Hiroshima are divided into two groups by exposure dose (1 Gy or more than below 1 Gy), there is no peak of occurrence unlike CML in the lower dose group. These findings suggest that the threshold of acute leukemia occurrence may be near 1 Gy.

Therefore, it was suspected that the characteristic feature of A-bomb induced acute leukemia might be in the cases who received 1 Gy or more.

Recently, blood samples of leukemia cases among atomic bomb survivors have been

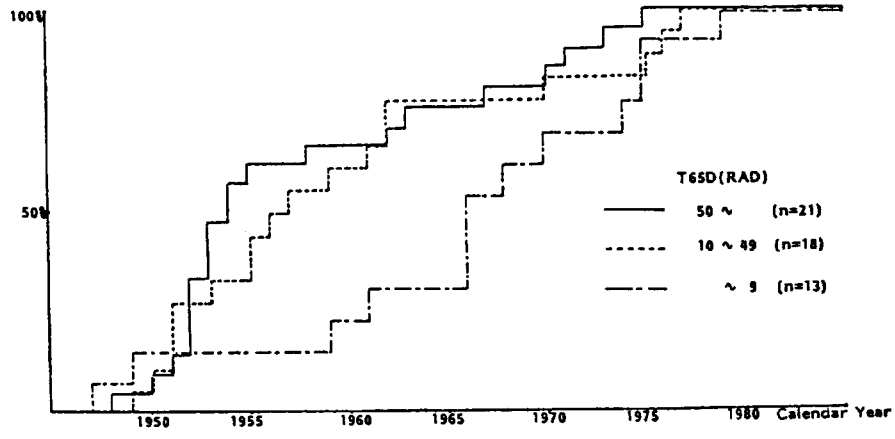

Fig. 2. Cumulative Cases of Chronic Myelogenous Leukemia by Radiation Dose
–Hiroshima–

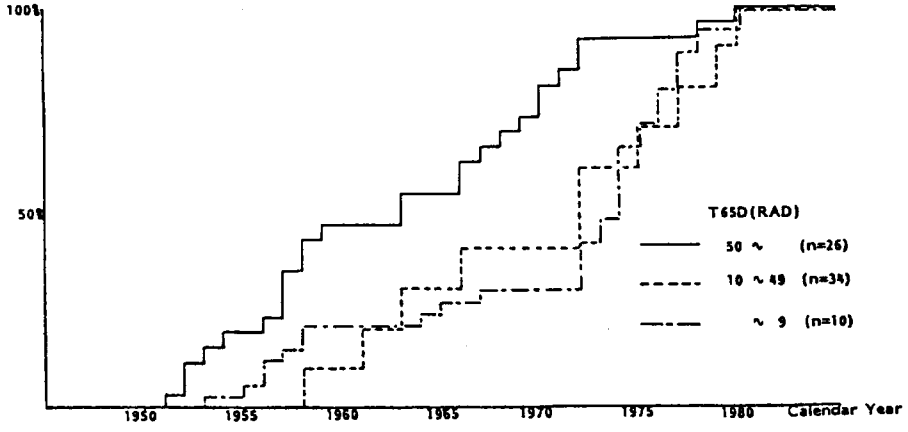

Fig. 3. Cumulative Cases of Acute Myeloid Leukemia by Radiation Dose
–Hiroshima–

reviewed by FAB (French-American-British) classification. The review has been completed for about 65% of the cases.

As shown in Table 1, ALL and MDS increased compared with the control group in 1 Gy or more group. CML increased in 1 Gy or more and 0.01~0.99 Gy groups. In the distribution by age at bomb, the ratio of AML and ALL of below 15 years of age was biggest. In the distribution of AML subtypes, there was no M3 case in 1 Gy or more group. (Tab. 2)

Risk of CML and ALL were higher than AML or other type leukemia by the study using the DS86 new dosis.

Soon after the bomb, many survivors died of bone marrow aplasia due to direct effect of the atomic bomb radiation. However, bone marrow of the survivors who could survive from the initial damage of radiation recovered to almost normal appearance within 1 year. We have studied the incidence of aplastic anemia among atomic bomb survivors since 5 years after the bomb. We could not find any increase of aplastic anemia as a late effect of the atomic radiation exposure. However, many atypical leukemia or other myelopreliferative diseases who had been diagnosed as aplastic anemia or refractory anemia in their first stage

Table 1. Leukemia Types by FAB Classification and Radiation Dose (Both Cities Combined)

	T65D		
	0 Gy	0.01–0.99 Gy	>1 Gy
AML	120 (65.9%)	49 (45.8%)	33 (31.7%)
ALL	20 (11.0%)	15 (14.0%)	27 (26.0%)
MDS	10 (5.5%)	4 (3.7%)	13 (12.5%)
CML	32 (17.6%)	39 (36.5%)	31 (29.8%)
Total	182 (100%)	107 (100%)	104 (100%)

Table 2. Distribution of AML Subtypes by FAB Classification (Atomic Bomb Survivors)

	T65D		
	0 Gy	0.01–0.99 Gy	>1 Gy
M1	33	11	12
M2	30	12	7
M3	16	9	0
M4	20	8	6
M5	10	1	1
M6	8	2	1
Total	117	43	27

Table 3. Incidence of aplastic anemia and atypical leukemia (aplastic anemia like) among atomic bomb survivors belonging LSS sample Oct, 1950-Dec 1973

Items	T65 total dose (rad)						
	NIC*	<1	1–49	50–99	>=100	No estimate	total
	Hiroshima and Nagasaki						
(1) No. of subjects	26,542	34,682	35,059	4,034	6,046	2,511	108,874
(2) Person years	525,265	711,625	721,690	83,050	125,204	50,624	2,217,457
(3) No. of aplastic anemia	8	10	16	0	2	0	36
(4) No. of atypical leukemia	0	1	2	0	3	0	6
(5) Crude annual incidence rate:aplastic anemia (3)/(2)×10^5	1.52	1.41	2.22	0.00	1.60	0.00	1.62
(6) Relative risk	1.1	1.0	1.6	—	1.1	—	—
(7) Crude annual incidence rate:atypical leukemia (4)/(2)×10^5	—	0.41	0.28	0.00	2.40	0.00	0·27
(8) Relative risk	—	1.0	2.0	—	17.1	—	—

NIC: not in city
LSS: life span study of RERF

has been experienced. This table shows that the incidence of such cases in 1 Gy or more group was 17 times as high as that in less than 0.01 Group, using LSS sample. (Tab. 3)

CHROMOSOME STUDY

Finally, we would like to describe the chromosome aberrations in atomic bomb survivors.

Even now, significantly increased chromosome aberrations due to atomic bomb radiation are recognized in peripheral blood T-cells and bone marrow cells in proximally exposed atomic bomb survivors. Chromosome study was performed using colony forming cells induced by hemopoietic stem cells of peripheral blood of proximally exposed survivors whose chromosome aberrations were confirmed in peripheral blood T-cells.

Granulocyte colonies and erythroid colonies were formed. The same chromosome aberrations in colony forming cells and peripheral T-cell were observed in several survivors. This also suggests that atomic bomb radiation affected hemopoietic stem cells and these cells differentiated to peripheral T-cells.

CONCLUSION

1) There were some qualitative differences in leukemia type among atomic bomb

survivors between Hiroshima and Nagasaki.

2) The risk of chronic myelogenous leukemia was higher in Hiroshima than in Nagasaki. This increase of CML may be the different feature of atomic bomb survivors' leukemia from the so-called secondary leukemia.

3) There was no remarkable difference in feature between the leukemia of atomic bomb survivors and de novo leukemia, although several non-typical cases have been observed.

4) The incidence of atypical leukemia or other myeloproliferative diseases who had been diagnosed as aplastic anemia or related diseases at initial stage has increased among atomic bomb survivors.

5) In 1 Gy or more group, ALL and MDS increased compared to the control group, and there was no M3 case in the distribution of AML subtypes (FAB classification).

6) The threshold of CML occurrence in Hiroshima might be between 0·5~0.09 Gy, and that of acute leukemia near 1 Gy.

7) Same chromosome aberrations were observed in colony forming cells induced from stem cells as well as in the peripheral T-cells.

It was suggested the intial leukemogenic effects of atomic bomb radiation in hemopoietic stem cells.

ACKNOWLEDGMENTS

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