II. BIOLOGICAL EFFECTS

Multiple Myeloma among Atomic Bomb Survivors

MICHITO ICHIMARU AND KIYOHICO MABUCHI

Radiation Effects Research Foundation

Multiple myeloma/Life span study/Dose effect

Multiple myeloma (MM) is a malignant tumor of B-cell lineage. Whether this disease occurs as a result of radiation exposure is of interest because B-cell chronic lymphocytic leukemia (CLL), another type of malignancy of B-cell lineage, has not been shown to be increased among atomic bomb survivors and other irradiated populations. An excess frequency of MM has been found in some of the irradiated populations, including U.S. radiologists¹⁾, Hanford workers^{2,3)}, thorotrast patients⁴⁾, radium-dial painters⁵⁾ and others⁶⁾.

An increase of MM in the atomic bomb survivors had not been observed until 15 years after the bombing⁷⁾. During 1963-65, we observed several cases of MM among the atomic bomb survivors^{8,9)} and suspected that the occurrence of MM could be influenced by atomic bomb radiation. This led to the conduct of a specific investigation on this malignancy in the Life Span Study (LSS) population in 1982. In this study, clinical data on M-protein and bone changes, hematological and bone marrow findings were reviewed to confirm diagnosis for patients who were suspected to have MM. A total of 29 cases of MM was identified among 109,000 individuals in the LSS sample. Data on these cases were analyzed using bone marrow dose based on T65D¹⁰⁾. Increased risk of MM in the high dose group (0.5 Gy or more) was apparent after 1965 (Figure 1), suggesting a prolonged latency period for radiation-induced MM. By age at time of bomb (ATB), the dose effect was most evident in those aged between 40–59 years ATB, followed by those aged 20–39 ATB. However, there was no increase of MM in high dose group among those aged 60 years or older and age 0–19 years ATB (Fig. 2).

More recently, an attempt was made to update the MM series in the LSS cohort through 1985, which resulted in the identification of over 80 cases¹²⁾. A significant dose-response relationship was found between DS86 bone marrow dose and the incidence of MM. There still was no significant dose effect among those who were young ATB¹¹⁾. Since MM is predominantly a disease of elderly persons, a further follow-up was deemed necessary to characterize the risk among those who were exposed at young ages and thus who still have not entered the age groups in which the high background incidence of MM is expected.

B-cell chronic lymphocytic leukemia (CLL) and MM are both proliferative disease of B-cell lineage. However, they are different in that the former cells show the morphology of mature

Fig. 1. Cumulative hazard rates for atomic bomb survivors and controls (aged 20–59 yr ATB) in the LSS sample, Oct. 1950–Dec. 1976, Hiroshima and Nagasaki. The controls, selected in Oct. 1950, were individuals who had received <1 rad radiation or were NIC ATB. NIC: not in city

lymphocytes and are considered to proliferate in the periphery whereas the latter cells generally appear as young cells such as nucleolus and proliferate basically in the bone marrow. As stated earlier, B-cell derived CLL has not been shown to be induced by radiation exposure. There is also no definite evidence on increased incidence of T-non-Hodgkin's lymphoma or adult T-cell leukemia, which are malignant lymphoma of differentiated T-lymphocytes among atomic bomb survivors. On the other hand, a recent theory states that MM results from abnormality of hemopoietic stem cells¹²⁾. Because many types of leukemia derived from stem cells of the bone marrow are associated with radiation exposure, it is biologically reasonable that MM occurs as a result of exposure to radiation, and further efforts would be worthwhile to define more precisely the nature and magnitude of the risk of MM in the atomic bomb survivors.

REFERENCES

1. Lewis, E.B. (1963) Leukemia, multiple myeloma and aplastic anemia in American radiologists. *Science* **42**: 1492-1494.

Fig. 2. Crude annual incidence rate of multiple myeloma (by age ATB and total marrow dose) for atomic bomb survivors and controls in the LSS sample, Oct. 1950–Dec. 1976, Hiroshima and Nagasaki.

- Mancuso, T.F., Stewart, A. and Kneale, G. (1977) Radiation exposure of Hanford workers dying from cancer and other causes. *Health Phys.* **33**: 369-385.
- Gilbert, E.S. and Marks, S. (1979) An analysis of the mortality of workers in a nuclear facility. *Radiat. Res.* **79**: 122-148.
- Faber, M. (1978) Malignancies in Danish thorotrast patients. *Health Phys.* **35**: 153-158.
- Poledenak, A.P., Stehney, A.F. and Rowland, R.E. (1978) Mortality among women first employed before 1930 in the U.S. radium dial painting industry. A group ascertained from employment lists. *Am. J. Epidemiol.* **107**: 179-195.
- Cuzick, J. (1981) Radiation-induced myelomatosis. *N. Engl. J. Med.* **304**: 204-210.
- Nishiyama, H., Anderson, R.E., Ishimaru, T., Ishida, K., Ii, Y. and Okabe, N. (1973) The incidence of malignant lymphoma and multiple myeloma in Hiroshima and Nagasaki atomic bomb survivors 1945-65. *Cancer* **32**: 1301-1309.
- Ichimaru, M., Yasui, S. and Otsuru, S. (1963) Twelve cases of multiple myeloma in Nagasaki (7 cases from atomic bomb survivors). *Nagasaki Med. J.* **38**: 109-113.
- Ichimaru, M., Yasui, S., Danno, H. et al. (1965) Additional two cases of multiple myeloma in atomic bomb survivors. *Nagasaki Med. J.* **40**: 608-611.
- Ichimaru, M., Ishimaru, T., Mikami, M. and Matsunaga, M. (1982) Multiple myeloma among atomic bomb survivors in Hiroshima and Nagasaki, 1950-76: Relationship to radiation dose absorbed by marrow. *J. Natl. Cancer Inst.* **69**: 323-328.

11. Mabuchi, K. and Ichimaru, M. (1990) Recent findings on multiple myeloma among A-bomb survivors, preliminary data. Presented at the 31st meeting on research on late effects of atomic bomb radiation, June 3, Nagasaki.
12. Barlogie, B., Epstein, J., Selvanayagam, P. and Alexanian, R. (1989) Plasma cell myeloma – new biological insights and advances in therapy. *Blood* **70**: 865-879.