Acta Med. Nagasaki 30 : 249−255

Multiple Myeloma of Atomic Bomb Survivors
—Autopsy Cases in the Nagasaki District (1946−1980)—

Masao KISHIKAWA[1], Yoshihide TAKAKI[1],
Mika IKEYAMA[1], Masachika ISEKI[1],
Hisayoshi KONDO[2] and Issei NISHIMORI[1]

Department of Pathology[1] and Department of Statistics[2],
Scientific Data Center of Atomic Bomb Disaster,
Nagasaki University School of Medicine,
Nagasaki, Japan

Received for publication, June 28, 1985

The present investigation was carried out with particular stress placed on the relationship between the autopsy cases of multiple myeolma in the Nagasaki district and exposure to the Atomic Bomb. A total of 10372 autopsy cases, all patients who had been born before the time of the Atomic Bomb explosion, were examined.

Only 58 autopsy cases (0.6%) of multiple myeloma were detected up to 1980. There was no autopsy case of multiple myeloma which had been exposed within 1 km from the hypocenter. The patients who were within 1−2 km and over 2 km from the hypocenter at the time of the Atomic Bomb explosion were composed of 5 cases (0.6%) and 16 cases(0.5%), respectively. The group of non-exposed persons was composed of 36 cases(0.6%). In the patients who were within 1−2 km at the time of the Atomic Bomb explosion, the first 20 years (1945−1965), there was no autopsy case of multiple myeloma, although during the subsequent 15 years (1966−1980) there were 5 autopsy cases (1.2%). In control group, however, multiple myeloma during the first 20 years was 13 cases (0.5%), and it was 24 cases (0.6%) in the subsequent 15 years.

It is possible that the frequency of multiple myeloma in exposed persons has increased in recent years. However, the proportions of myeloma among all autopsy cases during the 1946−1965 period and the 1966−1980 period showed no significant differences with other groups.

INTRODUCTION

In our laboratory, histopathological studies have been continued to clarify the relationship between the Atomic Bomb (AB) exposure and various diseases. The results obtained have already been reported several times[2)3)]. In one of these reports on hemato-

岸川 正大, 高木 芳秀, 池山 美香, 井関 充及, 近藤 久義, 西森 一正

logical diseases, it was mentioned that there was a significant difference between the two groups, i.e. the AB-exposed group and non-exposed group, but this report concerned only the morbidity of leukemia occurring during a relatively early stage after exposure[3].

Of the blood and lymph node lesions studied up to date, multiple myeloma has been considered to have no relation to the effect of radiation. In some papers recently published, however, it is suggested that it may be necessary to reexamine the relationship between multiple myeloma and exposure to the AB[4][5].

The present investigation was carried out with particular stress placed on the relationship between the autopsy cases of multiple myeloma in the Nagasaki district and exposure to the AB.

MATERIALS AND METHODS

The autopsy cases in this study were carried out in the following four institutions over a 35-year period from 1946 to 1980: Nagasaki University School of Medicine, the Radiation Effects Research Foundation at Nagasaki (formerly Atomic Bomb Casualty Commission), the Nagasaki Atomic Bomb Hospital of the Japan Red Cross, and the Nagasaki Municipal Hospital. All the patients born before the day of the AB were presented for investigation. They were divided into three groups (1 to 3) by the status of exposure to the AB. The patients who were within 2 km (subdivided in some analyses into two: within 1 km and 1-2 km) and over 2 km from the hypocenter at the time of the AB explosion were designated as group 1 and 2, respectively. Group 2 also consisted of the "early entrants", who entered the vicinity of the hypocenter (Urakami district) immediately after or within 2 weeks of the AB explosion and were thought to be exposed to residual radiation. The patients of the other autopsy cases (not exposed to the AB), were classified as controls (Group 3).

The 35-year period was divided equally into seven stages of five years each. Those who were exposed to the AB prenatally and the children and grand-children of the AB-exposed persons were discarded from the present investigation.

The cases of multiple myeloma were chosen from the protocol of autopsy. To compare hematological diseases with one another, the cases of leukemia, malignant lymphoma and aplastic anemia were also chosen. A statistical investigation was performed.

RESULTS

A total of 10372 autopsy cases, all patients who had been born before the time of the AB explosion, were examined. Group 1 consisted of 130 cases (within 1 km) and 653 cases (1-2 km from the hypocenter). Group 2 accounted for 3159 cases and group 3 for 6430 cases (Table 1).

Of all the cases studied, 941 cases (9.1%) were affected with four main hematological diseases (Table 2). During the first 15 years, cases of leukemia (5.2%-3.5%)

were more frequent than those of lymphoma (3.5%-1.2%), but in the recent 20 years lymphoma was more frequent than the leukemia. The cases of aplastic anemia were few and the frequency of the disease was similar to that of myeloma (Table 2). In the Nagasaki district, multiple myeloma was found in 3 autopsy cases for the first time in 1959, and only 58 autopsy cases (0.6%) of the disease were detected up to 1980. Its incidence was lower than both lymphoma and leukemia, but showed the same tendency as anatomical diagnosis of aplastic anemia (58 cases, 0.6%; Table 2). The frequency of multiple myeloma was analyzed by the distance from the hypocenter (Table 3). Group 1 consisted of 5 cases (5/783, 0.6%; Table 3), but there was no autopsy case of multiple myeloma which had been exposed within 1 km from the hypocenter (Table 6). Group 2

Table 1. Autopsy Cases in Nagasaki

Years	Number of Autopsies	Group 1		Group 2	Group 3
		0～1Km	1～2Km	2Km～, Early Entrants	Non-exposed Cases
1946 — 1950	115	3	8	20	84
1951 — 1955	602	6	25	213	358
1956 — 1960	1349	11	65	497	776
1961 — 1965	2180	35	218	607	1320
1966 — 1970	2694	30	169	780	1715
1971 — 1975	1759	31	100	534	1094
1976 — 1980	1673	14	68	508	1083
Total	10372	130	653	3159	6430

Table 2. Main Hematological Diseases

Years	Number of Autopsies	Myeloma	Leukemia	Lymphoma	Aplastic Anemia
1946 — 1950	115	0 (0%)	6 (5.2%)	4 (3.5%)	1 (0.9%)
1951 — 1955	602	0 (0)	26 (4.3)	7 (1.2)	3 (0.5)
1956 — 1960	1349	5 (0.4)	47 (3.5)	35 (2.6)	3 (0.2)
1961 — 1965	2180	13 (0.6)	72 (3.3)	82 (3.8)	9 (0.4)
1966 — 1970	2694	17 (0.6)	90 (3.3)	110 (4.1)	21 (0.8)
1971 — 1975	1759	13 (0.7)	77 (4.4)	106 (6.0)	11 (0.6)
1976 — 1980	1673	10 (0.6)	65 (3.9)	98 (5.9)	10 (0.6)
Total	10372	58 (0.6)	383 (3.7)	442 (4.3)	58 (0.6)

and group 3 were composed of 16 cases (16/3159, 0.5%) and 36 cases (36/6430, 0.6%), respectively. The differences in proportions of myeloma cases among all autopsy cases in 1946-1965 period (group 1, 0/371; group 2, 5/1337; group 3, 13/2538) and 1966-1980 years (group 1, 5/412; group 2, 11/1822; group 3, 23/3892) were analyzed by a χ^2-test that included a correction for continuity. The comparison between group 1 and group 2 showed no significant difference ($\chi^2=0.033$). There were also no significant differences in any other comparisons. Chronological comparisons in each group, the χ^2, were 2.821 (group 1), 0.416 (group 2) and 0.059 (group 3). They were not significantly different.

With regard to the age at necropsy, the 40- to 79-year age group was definitely more numerous than the other age groups. This became obvious after the 1961-1965 period group and up to the present to update (Table 4).

Table 3. Multiple Myeloma

Years	Group 1	Group 2	Group 3
1946 — 1950	0 (0%)	0 (0%)	0 (0%)
1951 — 1955	0 (0)	0 (0)	0 (0)
1956 — 1960	0 (0)	3 (0.6)	2 (0.3)
1961 — 1965	0 (0)	2 (0.3)	11 (0.8)
1966 — 1970	2 (1.0)	2 (0.3)	13 (0.8)
1971 — 1975	1 (0.8)	6 (1.1)	6 (0.5)
1976 — 1980	2 (2.4)	3 (0.6)	4 (0.4)
Total	5 (0.6)	16 (0.5)	36 (0.6)

Table 4. Age Group of Multiple Myeloma

Years	0 ～ 19	20 ～ 39	40 ～ 59	60 ～ 79	80 ～
1946 — 1950	0	0	0	0	0
1951 — 1955	0	0	0	0	0
1956 — 1960	0	0	1	4	0
1961 — 1965	0	2	5	6	0
1966 — 1970	0	1	4	12	0
1971 — 1975	0	0	4	8	1
1976 — 1980	0	0	5	4	1
Total	0	3	19	34	2

There was a slight female predominance (male : female = 9 : 12) in the exposed group, while males were more frequently affected (male : female = 23 : 13) in the control group (Table 5). This observation was made on the basis of the relationship between the status of exposure to the AB and the interval from the day of the AB to the onset of clinical signs (Table 6). The two groups of multiple myeloma were analyzed in the same manner (Table 6).

Table 5. Sex Difference of Multiple Myeloma

Status	Male	Female	Total
Group 1	3	2	5
Group 2	6	10	16
Group 3	23	13	36
Total	32	25	57

Table 6. Interval between Exposure and Onset of Clinical Symptoms

Status	Onset	11～15 (years)	16～20	21～25	26～30	31～35
Group 1	0～1Km	0	0	0	0	0
	1～2Km	0	2	1	1	1
Group 2		4	1	3	5	3
Total		4	3	4	6	4

DISCUSSION

The present investigation was carried out to include all the autopsy cases dealt with in the Nagasaki district over a 35-year period from 1946 to 1980. The cases were restricted to those who were born before or on the day of the AB explosion (Aug. 9, 1945).

The frequency of appearance of hematological diseases seems to have increased to some extent in recent years, but exhibited no significant difference[8]. A chronological study was made concerning the frequency of each hematological disease. Leukemia was higher than others in frequency of appearance in autopsy cases up to 1960. It sank below (3.3%) malignant lymphoma (3.8%) in frequency for the period from 1961 to 1965

(Table 2). Malignant lymphoma has been increasing in frequency ever since (Table 2). It was of great interest to note that T-cell lymphoma was reported by ICHIMARU *et al.* (1979)[1] to be higher in frequency in the Kyushu district than in other areas. The higher frequency of malignant lymphoma, here, might be correlated to the increasing number of autopsy cases of T-cell lymphoma. However, there was no relation between the AB exposure and the morbidity of lymphoma.

There were no autopsy cases of multiple myeloma within the first 10-year period (1945-1955). The frequency of autopsy cases of multiple myeloma was relatively similar to that of aplastic anemia (Table 2). There were no autopsy cases of multiple myeloma in which the patient was within 1 km of the hypocenter at the time of the AB explosion (Table 6). There were only 5 cases in which the patients were within 2 km of the hypocenter (Table 3, Table 6). In group 1, the first 20 years (1945-1965), there was no autopsy case of multiple myeloma, although during the subsequent 15 years (1966-1980) there were 5 autopsy cases (5/412, 1.2%; Table 1, Table 3). In group 3, however, multiple myeloma during the first 20 years was 13 cases (13/2538, 0.5%), and it was 24 cases (24/3892, 0.6%) in the subsequent 15 years (Table 1, Table 3). It is possible that the frequency of multiple myeloma in exposed persons has increased in recent years. However, the proportions of myeloma among all autopsy cases during the 1946-1965 period and the 1966-1980 period showed no significant differences with other groups. Though the statistical examinations using χ^2-test with a correction for continuity showed no significant difference in chronological years of each group, group 1 ($\chi^2 = 2.281$) displayed a mild tendency ($0.10 > p = 0.09 > 0.05$) toward on increase in myeloma during the latter 15-year period (1966-1980). Because the frequency in autopsy cases does not always display the true morbidity of the disease, a difinite conclusion concerning multiple myeloma related to the AB should not be drawn impetuously.

The independence test was carried out on the status of exposure to the AB in order to clarify the relationship between the AB exposure and the time of onset of clinical symptoms, but no significant difference could be detected.

ACKNOWLEDGEMENTS

The authors wish to express their thanks to the departments of pathology of the following institutions for cooperation in the present investigation: the Radiation Effects Research Foundation at Nagasaki, the Nagasaki Atomic Bomb Hospital of the Japan Red Cross, the Nagasaki Municipal Hospital, and the Nagasaki University School of Medicine. They are also grateful to the colleagues of the Department of Pathology, Atomic Disease Institute, Nagasaki University School of Medicine. They are indebted to Misses Y. SAKAI and A. KAIGA for their help in the preparation of data for the present investigation.

REFERENCES

1) ICHIMARU, M. *et al.*: T-cell malignant lymphoma in Nagasaki district and its problems. *Jpn. J. Clin. Oncol.* 9 (Suppl.): 337−346, 1979

2) KISHIKAWA, M. *et al.*: Pathologic and statistic analyses of the Atomic Bomb survivors within 2 km from the hypocenter in Nagasaki. *J. Hiroshima Med. Ass.* 31: 405−411, 1978 (in Japanese)

3) KISHIKAWA, M. and NISHIMORI, I.: Study of Atomic Bomb survivors -Postmortem examination in the Nagasaki district over a 32-year period- *Acta Med. Nagasaki.* 26: 38−55, 1981

4) MANCUSO, T. F. *et al.*: Radiation exposures of Hanford workers dying from cancer and other causes. *Health Physics* 33: 369−385, 1977

5) NAJARIAN, T.: Is low radiation associated with myeloma? *New Engl. J. Med.* 300: 1278, 1979