High Incidence of Meningioma among Hiroshima Atomic Bomb Survivors

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Since the atomic bomb explosions in Hiroshima and Nagasaki, high incidences of leukemia, thyroid cancer and other tumors have been reported as atomic bomb-induced tumors. We investigated the incidence of meningioma among Hiroshima atomic bomb survivors. Sixty-eight patients surgically treated for meningioma who had been within 2.0 km of the hypocenter of the explosion were identified. Six hundred and seven non-exposed patients with meningioma were also studied. Treatment dates were from 1975 to 1992. The incidences of meningioma among 68 subjects within 2.0 km and 607 non-exposed patients were 8.7 and 3.0 cases per 105 persons per year, respectively. The incidences of meningioma among the survivors of Hiroshima in 5-year intervals since 1975 were 5.3, 7.4, 10.1, and 14.9, respectively. The incidences of meningioma classified by distances from the hypocenter of 1.5–2.0 km, 1.0–1.5 km and less than 1.0 km were 6.3, 7.6 and 20.0, respectively. The incidences of meningioma classified by doses to the brain of 0–0.099 Sv, 0.1–0.99 Sv and more than 1.0 Sv were 7.7, 9.2 and 18.2, respectively. The incidence of meningioma among Hiroshima atomic bomb survivors has increased since 1975. There was a significant correlation between the incidence and the dose of radiation to the brain. The present findings strongly suggest that meningioma is one of the tumors induced by atomic bombing in Hiroshima.

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INTRODUCTION

Fifty-four years have passed since the atomic bombing of Hiroshima and Nagasaki. A number of reports relating to atomic bomb-induced tumors have appeared\(^1,2\). Acute leukemia\(^3\)–\(^5\), thyroid cancer\(^6\)–\(^8\), breast cancer\(^9\), lung cancer\(^10\), gastric cancer\(^11,12\), colon cancer\(^13\) and skin cancer\(^14\) have increased in incidence, relating to the exposure doses from the atomic bomb. Furthermore, multiple myeloma, esophageal cancer, salivary gland cancer, urinary tract cancer, ovarian cancer and malignant lymphoma are thought to be possible tumors whose incidence has increased since the atomic bombing. Recently, a high incidence of meningioma among Nagasaki atomic bomb survivors relating to distance from the hypocenter was reported\(^15,16\). We investigated the incidence of meningioma among Hiroshima atomic bomb survivors in relation to the radiation doses to the brain, as well as the relation between the distance from the hypocenter and histological subtype of meningioma. These findings may help to elucidate the late effects of radiation, not only in the atomic bomb survivors, but also in patients treated with radiation.

MATERIALS AND METHODS

Patients with meningioma among Hiroshima atomic bomb survivors and non-exposed patients

Information on 774 patients with meningioma who had been surgically treated in Hiroshima from 1975 to 1992 was collected from the database of the Hiroshima Tumor Registry. The database of the International Radiation Center, Hiroshima University, was also used for collecting information on shielding conditions, estimated distance from the hypocenter and radiation doses to the brain of the atomic bomb survivors. The latter database revealed that 68 of the 774 patients were exposed within 2.0 km from the hypocenter, 27 were “Early Entrants” who entered the city soon after the blast, 72 were “Others” who had been more than 2.0 km away from the hypocenter and 607 were non-exposed patients.

Population of exposed and non-exposed people

Numbers of the atomic bomb survivors and the non-exposed people in Hiroshima were obtained from the database of the International Radiation Center, Hiroshima University, and the Annual Report of Dynamic Statistics of the Population in Hiroshima. The cumulated numbers of exposed people within 2.0 km and non-exposed people during the 18 year period from 1975 to 1992 were 778,355 (Table1)\(^17\) and 20,219,093, respectively. The cumulated number of non-exposed people was calculated by subtracting the number of atomic bomb survivors in Hiroshima prefecture which includes directly exposed (within 2.0 km), Early entrants and Others, 2,989,828, from the Hiroshima population born before 1945 which was 23,208,921.

Incidence of meningioma and data analysis

The incidences of meningioma were calculated from several view points, such as latency period, distance from the hypocenter and DS86\(^18\) brain dose (Sv). The significance of the statis-
tical differences among the groups was assessed by chi-square test or Student’s t test. Ninety-five percent confidence intervals were also calculated to analyze these data.

**Histological subtypes of meningioma**

Histological subtypes of meningioma had been recorded in the database of the Hiroshima Tumor Registry. Some patients were operated on 2 or more times because of relapse or tumors in multiple regions. Therefore, in this study, histological subtypes recorded at the first operation were used for analysis.

**RESULTS**

**Incidence of meningioma**

The incidences of meningioma over 18 years among the exposed and non-exposed popula-
tions were 8.7 and 3.0 cases per $10^5$ persons per year, respectively. Chi-square test revealed that the incidence of meningioma among the exposed was significantly higher than that of the non-exposed ($p < 0.005$). The incidences of meningioma over 18 years among Early Entrants and Others were 2.9 and 5.5. In the present analysis, the patients among Early Entrants and Others were excluded from atomic bomb survivors. Because of later acquisition of certification as an “atomic bomb survivors”, the populations of Early Entrants and Others have been estimated inaccurately.

**Incidence of meningioma in relation to latency period since the atomic bombing**

To investigate the incidence of meningioma and the latency period, the subjects were divided into 4 groups representing 5 year intervals since 1975 (1975–1979, 1980–1984, 1985–1989 and 1990–1992). The incidences of meningioma among the exposed in each period were 5.3, 7.4, 10.1 and 14.9 cases per $10^5$ persons per year, respectively (Fig. 1). In contrast, the incidences among the non-exposed group during the same periods were 1.0, 2.8, 4.3 and 5.6. The incidence of meningioma among the exposed group was significantly higher than that of the non-exposed group in all 4 periods, analyzed by chi-square test ($p < 0.001$). The incidence of meningioma among the atomic bomb survivors was already high in 1975 and gradually increased.

**Incidence of meningioma in relation to distance from the hypocenter**

The incidences of meningioma among the exposed patients at distances of 1.5–2.0 km, 1.0–1.5 km and less than 1.0 km were 6.3, 7.6 and 20.0 cases per $10^5$ persons per year, respectively. Chi-square test revealed that the incidence in each of the 3 groups was significantly higher than that of the non-exposed group ($p < 0.005$) (Fig. 2). The relation between the incidence and the
Fig. 2. Incidence of meningioma as a function of distance from the hypocenter. Patients exposed within 2.0 km were divided into 3 groups based on distance from the hypocenter. Bars indicate 95% confidence intervals. Asterisk (*) means that the incidence is significantly higher than that of non-exposed group (p < 0.005).

Fig. 3. Relationship between the incidence of meningioma and the distance from the hypocenter, in 5-year intervals since 1975.

distance, in 5-year intervals starting at 1975, is shown in Fig. 3. During 1990–1992, the incidence of meningioma among the patients exposed within 1.0 km was 36.3.

**Incidence of meningioma in relation to doses of radiation exposure to the brain**

Exposure doses to the brain had been calculated in 30 patients out of the 68 exposed within 2.0 km, based on DS86 dosimetry. When individual exposure doses were calculated, the relative
biological effectiveness (RBE) of the neutron beam was defined as 10. Therefore, radiation dose (Sv) was the sum of γ-ray and 10 times the neutron dose. The incidences of meningioma in the groups exposed to 0–0.099 Sv, 0.1–0.99 Sv and more than 1.0 Sv, were 7.7, 9.2 and 18.2 cases per 10^5 persons per year, respectively (Fig. 4). The incidence of meningioma for radiation doses more than 0.1 Sv was significantly higher than that of the non-exposed group (p < 0.005). A less significant difference was observed between the incidences among the group exposed to 0–0.099 Sv and the non-exposed group (p < 0.025).

Histological subtypes of meningioma in relation to radiation doses to brain

Most patients with meningioma were histologically registered as having meningioma, NOS (not otherwise specified) and were not examined further. The remains were histologically subtyped in detail. Among exposed and histologically subtyped patients, 46.9% meningothelial meningioma, 18.9% fibrous meningioma, 12.5% transitional meningioma, 6.2% psammomatosus meningioma, 6.2% angiomatosus meningioma, 3.1% hemangioblastic meningioma, and 6.2% malignant meningioma were observed, which followed the same trend as that among the non-exposed (Fig. 5).
DISCUSSION

Over 50 years have passed since the atomic bombing of Hiroshima and Nagasaki. Because of aging, the number of Hiroshima atomic bomb survivors who had been exposed within 2.0 km decreased from 49,748 to 36,056 during 1975–1992 (Table 1). The incidence of meningioma among Hiroshima atomic bomb survivors had already increased in 1975. The incidence before 1975 is not known because no reliable tumor registration system existed in Hiroshima at that time. The increasing tendency persisted until 1992. In contrast, among Nagasaki atomic bomb survivors, the incidence did not begin to increase until after 1981. The reason why meningioma among Hiroshima atomic bomb survivors began to increase earlier than the Nagasaki survivors is not clear.

A Nagasaki research group reported a correlation between the incidence of meningioma and the distance from the hypocenter. In the present study, we clarified the dose dependency of the meningioma incidence. Our findings showed that the incidences of meningioma for distances of 1.5–2.0 km, 1.0–1.5 km and less than 1.0 km were 6.3, 7.6 and 20.0, corresponding to the trends found in Nagasaki. During 1990–1992, the incidences of meningioma among those within 1.0 km and the non-exposed group were 36.3 and 5.6. Therefore, the relative risk of radiation effect for meningioma was calculated as 6.48. To clarify the effect of radiation on meningioma, we investigated the incidence of meningioma in relation to radiation doses to the brain. The group exposed to more than 0.1 Sv showed a significantly higher incidence than that of the non-exposed group (p < 0.005). However, there was a less significant difference (p < 0.025) between the group exposed to 0–0.099 Sv and the non-exposed group, because of poor reliability of low-dose effect and the small number of patients in the group exposed to 0–0.09 Sv.

In the present study, we also investigated the correlation between histological subtypes of
meningiomas among the exposed and non-exposed groups. Soffer et al. reported that meningiomas arising after therapeutic irradiation with either high doses for brain tumors or low doses for tinea capitis tended to have malignant, biologically aggressive characteristics\cite{19,20}. In our study, there were only 2 patients with malignant meningioma. Therefore, malignant, aggressive meningiomas did not seem to be common among atomic bomb survivor patients in Hiroshima. A Nagasaki research group also could not find the atomic bomb specific histological subtypes of meningioma\cite{16}. The type of exposure to radiation, that is, single exposure vs frequent, long-term exposure, might have influenced the histological subtypes of meningioma.

Recently, Sadamori et al. reported a high incidence of skin cancer among Nagasaki atomic bomb survivors\cite{14}. The incidence of skin cancer began to increase after 1955 with a peak occurrence in 1975–1979. The occurrence of meningioma did not seem to form a peak until now. Therefore, meningioma seems to have a longer latency period than that of skin cancer and other tumors.

Until now, 7 types of tumors have been specifically shown to have been induced by the atomic bomb in Hiroshima, i.e., leukemia, thyroid cancer, breast cancer, lung cancer, gastric cancer, colon cancer and skin cancer. Meningioma can now be considered one of the tumors induced by the atomic bomb.

We conclude that more attention should be paid to meningioma as a late effect of radiation among not only atomic bomb survivors, but also people exposed to other types of radiation.

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