II. BIOLOGICAL EFFECTS

Hyperparathyroidism

SAEKO FUJIWARA

Department of Clinical Studies, Radiation Effects Research Foundation

Hyperparathyroidism/Radiation/Prevalence/A-bomb survivors

An epidemiological survey on hyperparathyroidism (HPT) among A-bomb survivors in Hiroshima has been conducted since August 1986. The results will be summarized below based on proceedings of meetings^{1,2}. The survey demonstrated that the prevalence rate of HPT increased with A-bomb radiation dose. Further analysis is now under way on the relationship between HPT prevalence and radiation dose, sex and age, the results of which will be published in the near future.

INTRODUCTION

It is well known that radiation exposure induces various disorders, HPT for one. In Europe and U.S., X-ray treatment had been performed for benign diseases such as acne, tonsillitis, tuberculous cervical lymphadenitis and tinea capitis until around 1960. In 1950 thyroid cancer was first reported to have developed subsequently to such treatment³, followed by a series of reports on the high risk of thyroid cancer, adenoma and salivary gland tumor following exposure to radiation therapy^{4–7}. However, it was not until 1975 that the first HPT case⁸ associated with prior radiotherapy to the neck and head area was reported.

According to Tisell et al.⁹ the frequency of HPT was 14% among 444 patients who had undergone cervical radiation therapy (exposure dose: 0.6–45.7 Gy). By dose, the frequency was 12.2% among those exposed to 14 Gy or less and as high as 28.9% among those exposed to 14 Gy or more. Of the cases which underwent surgery for HPT, 10%–18% were reported to have had previous radiation therapy^{10,11}. Moreover, animal experiments showed that irradiation affects the occurrence of parathyroid tumor^{12,13}.

There are only two studies on parathyroid disorders among A-bomb survivors; 1) the prevalence of parathyroid tumors in autopsied cases, and 2) the prevalence of hyperparathyroidism among participants of the Adult Health Study (AHS), a program of biennial medical follow-up of the A-bomb survivors.

Parathyroid tumor

The prevalence of parathyroid tumors was studied in autopsied cases among a fixed population of atomic bomb survivors, i.e., in RERF's Life Span Study sample¹⁴. Parathyroid tumors were found in 16 persons among 4,136 autopsied subjects from 1961 to 77. Adenoma of chief cell

type was found in 7 persons, eosinophilic type in 6, and mixed type in 3. The crude prevalence was 1.34% in the ≥ 0.5 Gy (T65D), whereas it was 0.18% in the 0 Gy group and those who were not in Hiroshima at the time of bombing (ATB). Only three cases had parathyroid tumors with clinical symptoms and were diagnosed as having had HPT; and all were atomic bomb survivors exposed, respectively, to 0.28, 0.55, and 0.75 Gy.

Hyperparathyroidism

The prevalence rate of HPT was studied among Hiroshima AHS participants examined between August 1986 and December 1987. In total, approximately 4,000 subjects were screened for serum calcium (Ca) levels. Persons with a serum Ca level exceeding 10.3 mg/100 ml underwent repeated tests of Ca, P, and Al-p as well as serum chloride (Cl) and parathyroid hormone (PTH) measurements, hand X-ray, and history-taking to exclude other diseases that may manifest hypercalcemia. A diagnosis of HPT was determined by an increase of both serum calcium results (≥ 10.3 mg/100 ml) and serum PTH level (PTH[43–63] > 520 pg/ml) with no evidence of other causes of hypercalcemia.

The analysis of a radiation effect was based on 3,259 individuals (males 1,030, females 2,229) after excluding individuals without DS86 dose estimates, or those who were not in the city at the time of the bombing. The estimates of dose were based on the DS86 dosimetry system developed in 1986, which gives estimates of tissue kerma in air at the survivor's location, corrected for shielding by buildings or terrain. The estimated dose to the thyroid is used in our analysis.

Among 3,259 subjects, 15 cases (3 males, 12 females) consistently showed elevation of serum Ca and PTH, and were diagnosed as having HPT. Figure 1 showed the observed prevalence rates by four dose category groups. There appeared to be significant relationship between the prevalence of HPT and A-bomb radiation dose.

Fig. 1. Prevalence of Hyperparathyroidism by Kerma, Hiroshima AHS, August 1986–December 1987.

About 80%–85% of primary HPT cases result from parathyroid adenoma, about 10% from hyperplasia, and a few from cancer. With regard to radiation-induced HPT, it has been reported that the ratios of the pathological findings are the same as above. Among the subjects of this study, of the six cases who underwent surgery, five had parathyroid adenoma and one hyperplasia. There are a few reports^{15–17)} on the occurrence of parathyroid carcinoma after neck irradiation. However, there had been no evidence of an association of radiation exposure with parathyroid cancer in our study to date.

Many papers have reported that between 5 to 11% of patients with HPT had thyroid cancer simultaneously^{18–20)}. The complication rate of HPT and thyroid cancer among those who have undergone radiation therapy is said to be ninefold greater than that among others⁹⁾. In our study, two HPT cases exposed heavily (1 Gy or more) had thyroid cancer also.

From this preliminary analysis, it is concluded that the prevalence of HPT is related to A-bomb radiation exposure. A further analysis is now under way, and trends in prevalence over time remain to be studied.

REFERENCES

1. Fujiwara, S. et al. (1989) Hyperparathyroidism among A-bomb survivors. (Proceedings of the 29th Meeting of Late A-bomb Effects Research) Nagasaki Medical Journal **63**: 582.
2. Fujiwara, S., Ezaki, H., Sposto, R. et al. (1989) High prevalence of hyperparathyroidism among A-bomb survivors. (Abstract of Joint Meeting of ICCRH and ASBMR) J. Bone and Mineral Res. Supplement **4**: S162.
3. Duff, B.J. Jr. and Fitzgerald, P.J. (1950) Thyroid cancer in childhood and adolescence. A report of 28 cases. J. Clin. Endocrinol. Metab. **10**: 1296-1308.
4. Ju, D.M.C. (1966) Salivary gland tumors occurring after radiation of the head and neck area. Am. J. Surg. **116**: 518.
5. Block, M.E., Miller, M.J. and Horn, R.C. (1969) Carcinoma of the thyroid after external radiation to the neck in adults. Am. J. Surg. **118**: 764.
6. Modan, B., Baidatz, D., Mart, H., Steinitz, R. and Levin, S.G. (1974) Radiation-induced head and neck tumors. Lancet **1**: 277.
7. Favus, M.J., Schneider, A.V., Stachura, M.E., Arnold, J.E., Ryo, U.Y., Pinsky, S.M., Colman, M., Arnold, M.J. and Froman, I.A. (1976) Thyroid malignancy occurring as a late consequence of head and neck irradiation; evaluation of 1056 patients. New Engl. J. Med. **294**: 1019-1025.
8. Rosen, I.B., Strawbridge, H.G. and Bain, J. (1975) A case of hyperparathyroidism associated with radiation to the head and neck area. Cancer **36**: 1111-1114.
9. Tisell, I.E., Carlsson, S., Fjalling, M., Hansson, G., Lindberg, S., Lundberg, L.M. and Oden, A. (1985) Hyperparathyroidism subsequent to neck irradiation. Risk factors. Cancer **56**: 1529-1533.
10. Hedman, I., Hansson, G., Lundberg, L.M. and Tisell, I.E. (1984) A clinical evaluation of radiation-induced hyperparathyroidism based on 148 surgically treated patients. World J. Surg. **8**: 96-105.
11. Netelenbos, C., Lips, P. and Meer, C. (1983) Hyperparathyroidism following irradiation of benign diseases of the head and neck. Cancer **52**: 458-461.
12. Berdjis, C.C. (1972) Parathyroid diseases and irradiation. Strahlentherapie **143**: 148-162.
13. Fjalling, M., Hansson, G., Hedman, I., Ragnhalt, I. and Tisell, I.E. (1981) Radiation-induced parathyroid adenoma and thyroid tumors. Acta Path. Microbiol. Scand. **89**: 425-429.
14. Takeichi, N., Fujikura, T., Nishida, T., Wakabayashi, T., Yamamoto, T., Ezaki, H., Nishida, M., Tahara, E., Yotsumoto, I., Matsuura, H. and Ito, T. (1984) Parathyroid gland tumors in A-bomb survivors, Autopsy cases, Hiroshima, Preliminary report. J. Hiroshima Med. Assoc. **37**: 439-441.

15. Christman, T.J., Chapple, C.R., Noble, J.G., Milroy, E.J.G. and Cowie, A.G.A. (1988) Hyperparathyroidism after neck irradiation. *Br. J. Surg.* **75**: 873-874.
16. Tisell, L.E., Hansson, G., Lindberg, S. and Ragbhult, I. (1977) Hyperparathyroidism in persons treated with X-rays for tuberculous cervical adenitis. *Cancer* **40**: 846-854.
17. Ireland, J.P., Fleming, S.J., Levison, D.A., Cattell, W.R. and Baker, L.R.I. (1985) Parathyroid carcinoma associated with chronic renal failure and previous radiotherapy to the neck. *J. Clin. Pathol.* **38**: 1114-1118.
18. Ellenberg, A.H., Goldman, I., Gordon, G.S. and Lindsay, S. (1962) Thyroid carcinoma in patients with hyperparathyroidism. *Surgery* **51**: 708-717.
19. Laing, V.O., Frame, B., Block, M.A. (1969) Associated hyperparathyroidism and thyroid lesions. *Arch. Surg.* **98**: 709-712.
20. LiVolsi, V.A. and Feind, C.R. (1976) Parathyroid adenoma and nonmedullary thyroid carcinoma. *Cancer* **38**: 1391-1393.