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"Long-term effects of radiation exposure and metabolic status on telomere length of peripheral blood T cells in atomic bomb survivors"

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Study Findings

Telomeres, protein-DNA complexes that exist at the ends of chromosomes in cells and consist of TTAGGG sequence repeats, are known to shorten with aging, and when their length falls below a certain level, cells can no longer divide. Research has suggested that telomere length of peripheral blood T cells among atomic bomb survivors is positively associated — in other words, tended to be longer — with radiation doses between 0 to 0.5 Gy but inversely associated — or, shorter — with radiation doses higher than about 0.5 Gy. Telomere length of T cells was inversely associated, or shorter, with plasma level of hemoglobin A1c (HbA1c)* as well as in persons with fatty liver compared to those without fatty liver.

* Hemoglobin A1c (HbA1c): a biomarker that reflects average blood glucose levels over the previous one to two months. HbA1c level is one of the diagnostic criteria for diabetes mellitus.

Explanation

This study examined participants in the Adult Health Study (AHS) of the Radiation Effects Research Foundation to determine the association of telomere length in peripheral blood T-cell populations (naïve and memory CD4 T cells and CD8 T cells) with radiation dose and obesity or metabolic disease-related parameters.

1. Study Purpose

Taking into account that a reduction in number of T cells and impairment in T-cells' capacity to proliferate have been observed among A-bomb survivors exposed to radiation doses higher than about 0.5 Gy, this study tested the hypothesis that radiation exposure accelerates telomere shortening in T cells. Since telomere shortening has been recently demonstrated in obesity and metabolic diseases, this study also tested the hypothesis that long-term effects of radiation on T-cell telomere length may be modified by metabolic status related to obesity and metabolic diseases.

2. Study Methods

Among a group of 620 atomic bomb survivors who participated in AHS health examinations in Hiroshima during the period 2003–2009, we measured telomere length in T-cell subpopulations using fluorescence *in situ* hybridization and flow cytometry. We next conducted analysis of statistical associations of T-cell telomere length with radiation dose and metabolic condition-related parameters (BMI, serum total cholesterol, HDL cholesterol, LDL cholesterol, HbA1c, and CRP levels, and prevalence of diabetes mellitus and fatty liver), using multiple regression and nonparametric smoothing.

3. Study Results

(1) Association between radiation exposure and T-cell telomere length

Analyses conducted with multiple statistical methods, including linear regression and nonparametric smoothing, revealed that T-cell telomere lengths were inversely associated with radiation doses higher than about 0.5 Gy, while a positive association was observed in dose categories lower than that figure.

(2) Association between metabolic parameters and T-cell telomere length

Telomere length in T-cell populations was inversely associated with high HbA1c levels and fatty liver prevalence. In addition, we found effects through the interaction between radiation doses and HDL

cholesterol levels on T-cell telomere length at doses higher than 0.5 Gy: a trend of decreasing telomere length with radiation dose was attenuated among individuals who had higher HDL cholesterol levels.

Study Significance

The study results support the hypothesis that T-cell telomere shortening with aging may be accelerated by radiation exposure, although this result was limited to radiation exposure at doses higher than about 0.5 Gy. The study also suggests that radiation exposure may affect the telomere maintenance system via multiple dose-dependent biological mechanisms, and that the long-term effects of radiation exposure on T-cell telomere length may be modified by metabolic conditions after the exposure. Since this study examined associations among radiation dose, T-cell telomere length, and metabolic parameters in a cross-sectional fashion, it is impossible to determine the presence or absence of causal relationships among these factors based only on this study's results. Further studies, specifically longitudinal studies, will be required to elucidate associations among radiation exposure, telomere maintenance, metabolic conditions, and metabolic diseases.

The Radiation Effects Research Foundation has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for around 70 years. RERF's research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

[§]***Radiation Research***, which is an official monthly journal of the Radiation Research Society, publishes original peer-reviewed papers and review articles on radiation effects and related issues in the fields of physics, chemistry, biology, and medicine. (Impact factor in 2015: 2.67)