Does Low-Dose Radiation Cause Leukemia?

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Data from A-bomb survivors, persons with ankylosing spondylitis and neoplasms treated with radiation therapy, and many other sources show a strong association between exposure to ionizing radiation (particles or electromagnetic waves with sufficient energy to cause an ionization such as photons and gamma rays) and an increase in the risk of developing leukemia.

In A-bomb survivors, the relative risks of developing acute lymphoblastic leukemia (ALL; relative risk [RR] = 2.7), acute myeloid leukemia (AML; RR = 2.1), and chronic myeloid leukemia (CML; RR = 2.8) were markedly increased. [These relative risks are based on assuming exposure to 1 Gy at age 30 and diagnosis at age 70 and averaging risks between males and females. However, it should be noted that younger age at exposure and male gender are associated with the highest relative risks.]

Curiously, past studies reported neither an increased risk of chronic lymphocytic leukemia (CLL) in A-bomb survivors nor in many other radiation-related settings. Based on these data, CLL was assumed to be a nonradiogenic leukemia. However, some recent data have challenged this notion.[1-3]

Increased risks of ALL, AML, and CML in A-bomb survivors were strongly correlated with dose. For example, at estimated doses less than 500 mSv, fewer than 10% of the cases of AML that developed were attributed to radiation exposure. This finding contrasts with data in persons estimated to be exposed to more than 500 mSv, in whom 80% of cases of AML are attributed to radiation. At very low estimated doses (less than 5 mSv), fewer than 0.1% of cases of AML are thought to be caused by radiation exposure.

Relevance to Hematologists and Oncologists

Why is any of this of interest to hematologists and oncologists? These data are important for several reasons. For example, one-half of the current exposure to ionizing radiation of the U.S. population comes from medicine-related radiologic procedures, namely computed tomography (CT), positron-emission tomography (PET), and radionuclide scans. In 2012, there were 80 million CT/PET diagnostic imaging and 20 million nuclear medicine studies. That's nearly one study for every three Americans!

Radiation exposure of A-bomb survivors and most of the situations used to define the association between radiation exposures and leukemia come from unique settings, unlike the types of exposures for which hematologists and oncologists are responsible. For example, the cohort of A-bomb survivors studied for estimation of radiogenic cancer risks received one acute but rather moderate radiation exposure of between < 0.05 and 4 Gy. [In the context of A-bomb survivors, doses in Gy and Sv can be considered equivalent for most purposes.]

By comparison, many persons with cancer receive very high doses of radiation, most of which are high-dose–rate exposures given over several weeks. These data leave us with a dilemma. Does exposure to much lower doses of ionizing radiation, say less than 30 mSv (average dose of a CT/PET scan), received multiple times over several months or even years rather than instantaneously also increase the risk of developing leukemia?

Closing in on an Answer

This question has troubled many scientists, including radiobiologists, health physicists, and epidemiologists, for several decades. Now an answer seems close. Three recent studies have provided data to address this question.

The first is a study by Leuraud and co-workers of about 300,000 nuclear workers exposed to ionizing radiation over many years.[4] Average exposures were very low—a mean of 1.1 mSv per year—with mean cumulative doses of 16 mSv, a dose equivalent to the cumulative background radiation dose of living 4 years in Denver, Colorado. The authors found a significant, dose-dependent increased risk of dying of leukemia, especially CML, at these low doses.

In the second study, Kendall and co-workers reported an association between the background level of terrestrial gamma radiation in the United Kingdom and the risk of developing ALL in children.[5] An increased risk was detected at doses of about 5 mSv.

In the third study, Pearce and co-workers reported a linear correlation between estimated bone marrow dose from a head CT scan in children and the risk of developing ALL.[6]

There are, of course, limitations to each of these studies. A slight increase in leukemia risk imparted by a low dose of ionizing radiation requires data from huge populations to be statistically significant. It is also reasonably certain persons living in high areas of background radiations such as Goa, India (30 mSv/yr); Guarapari, Brazil (175 mSv/yr); and Ramsar, Iran (200 mSv/yr) do not have a detectable increased risk of developing leukemia.

However, the weight of the epidemiologic data and prevailing radiobiologic concepts and data support the notion of a linear no-threshold relationship between radiation dose and leukemia risk. It is also worth recalling that the failure to detect an increased risk at a high level of statistical confidence is not proof that the risk is zero.

Clinical Implications

What are the implications of this conclusion for the readers of *The ASCO Post*? Simple. We should assume every excess radiation exposure—no matter how small—increases the risk of leukemia. In other words, we need to think carefully before ordering diagnostic radiologic procedures such as CT, PET, and radionuclide scans, especially in young persons.

Large numbers of these radiologic procedures are sometimes required by health authorities and drug companies in an effort to determine precisely the time of cancer progression, especially when progression-free survival is used as a surrogate for survival for drug registration. However, considerable data indicate that latency between progression detected by a predefined radiologic assessment and progression triggered by an abnormal clinical or laboratory finding is only about 1 month. More important, there are substantial data indicating earlier detection of cancer progression, and presumably starting anticancer therapy sooner, does not improve survival.

Our conclusions? First, it is more likely than not that low doses of ionizing radiation increase the risk of leukemia. Second, hematologists and oncologists need to ensure the benefit of any radiologic procedure they order—no matter how small the dose—outweighs the associated increased risk of developing leukemia (and other cancers). ■

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References

1. Trabalka JR, Apostoaei AI: Development of a risk model for chronic lymphocytic leukemia for NIOSH-IREP. January 5, 2010. Available at http://www.cdc.gov/niosh/docket/archive/pdfs/NIOSH-209/0209-010510-CLLRiskModelFinal.pdf. Accessed August 28, 2015.

2. Hsu WL, Preston DL, Soda M, et al: The incidence of leukemia, lymphoma, and multiple myeloma among atomic bomb survivors: 1950-2001. Radiat Res 179:361-382, 2013.

3. Zablotska LB, Bazyka D, Lubin JH, et al: Radiation and the risk of chronic lymphocytic and other leukemias among Chornobyl [sic] cleanup workers. Environ Health Perspect 121:59-65, 2013.

4. Leuraud K, Richardson DB, Cardis E, et al: Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): An international cohort study. Lancet Haematol 2:e276-e281, 2015.

5. Kendall GM, Little MP, Wakeford R, et al: A record-based case-control study of natural background radiation and the incidence of childhood leukaemia and other cancers in Great Britain during 1980-2006. Leukemia 27:3-9, 2013.

6. Pearce MS, Salotti JA, Little MP, et al: Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: A retrospective cohort study. Lancet 380:499-505, 2012.

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