Re: Roles of Radiation Dose, Chemotherapy, and Hormonal Factors in Breast Cancer Following Hodgkin’s Disease

The recent study by van Leeuwen et al. (1) quantified the carcinogenic effect of therapeutic radiation on the breast in young women with Hodgkin’s disease. We believe that the results of this important study have implications beyond the treatment of women with Hodgkin’s disease. The study has caused us to rethink the possible hazardous effect of mammography in young women, in particular in those with BRCA1 mutations. The carcinogenic effect of radiation on the breast is highly dependent on the age of exposure, and young women are particularly sensitive. It is striking that early menopause mitigated the effect of the radiation in van Leeuwen’s study, given that surgical menopause is also highly effective in preventing the development of BRCA1 or BRCA2 mutations. N Engl J Med 2002; 346:1616–22.

To date, the established cofactors for BRCA1-associated breast cancers appear to be hormonally based (3).

The parallels between radiation-induced carcinogenesis and BRCA1-associated carcinogenesis are striking. However, this result is not really surprising, given that a primary function of BRCA1 is to help in the repair of double-stranded DNA breaks, and such breaks are the typical consequence of ionizing radiation. It is likely that both radiation-induced and BRCA1-associated breast cancers are initiated by chromosome breakage. Both appear to be promoted by later ovarian hormone exposure. Therefore, we might expect other cofactors to be in common and the tumor types to be similar.

The incidence of breast cancer in BRCA1 carriers is substantial by age 25 and increases until menopause after which it plateaus. An effective surveillance system that begins at age 25 would be of value but, at this age, radiation (even in small doses) is worrisome. Mammography has not been shown to be effective in reducing mortality from high-grade breast cancers in young women (4,5), and the sensitivity of mammography in BRCA1 carriers is poor (6–7). Magnetic resonance imaging is much more effective than mammography in detecting early hereditary breast cancers (7). We feel that it is time to reconsider the justification for presenting mammography as a potential lifesaver to young women with BRCA1 mutations.

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REFERENCES


NOTES

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