

New Primary Neoplasms of the Central Nervous System in Survivors of Childhood Cancer: a Report From the Childhood Cancer Survivor Study

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Abstract

Background: Subsequent primary neoplasms of the central nervous system (CNS) have frequently been described as late events following childhood leukemia and brain tumors. However, the details of the dose–response relationships, the expression of excess risk over time, and the modifying effects of other host and treatment factors have not been well defined.

Methods: Subsequent primary neoplasms of the CNS occurring within a cohort of 14 361 5-year survivors of childhood cancers were ascertained. Each patient was matched with four control subjects by age, sex, and time since original cancer diagnosis. Tumor site–specific radiation dosimetry was performed, and chemotherapy information was abstracted from medical records. Conditional logistic regression was used to estimate odds ratios (ORs), to calculate 95% confidence intervals (CIs), and to model the excess relative risk (ERR) as a function of radiation dose and host factors. For subsequent gliomas, standardized incidence ratios (SIRs) and excess absolute risks (EARs) were calculated based on Surveillance, Epidemiology, and End Results data.

Results: Subsequent CNS primary neoplasms were identified in 116 individuals. Gliomas ($n = 40$) occurred a median of 9 years from original diagnosis; for meningiomas ($n = 66$), it was 17 years. Radiation exposure was associated with increased risk of subsequent glioma (OR = 6.78, 95% CI = 1.54 to 29.7) and meningioma (OR = 9.94, 95% CI = 2.17 to 45.6). The dose response for the excess relative risk was linear (for glioma, slope = 0.33 [95% CI = 0.07 to 1.71] per Gy, and for meningioma, slope = 1.06 [95% CI = 0.21 to 8.15] per Gy). For glioma, the ERR/Gy was highest among children exposed at less than 5 years of age. After adjustment for radiation dose, neither original cancer diagnosis nor chemotherapy was associated with risk. The overall SIR for glioma was 8.7, and the EAR was 19.3 per 10 000 person-years.

Conclusions: Exposure to radiation therapy is the most important risk factor for the development of a new CNS tumor in survivors of childhood cancers. The higher risk of subsequent glioma in children irradiated at a very young age may reflect greater susceptibility of the developing brain to radiation.

Editorial about this Article

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Childhood Cancer—Treatment at a Cost

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