

Neurologic Sequelae in Long-Term Survivors of Childhood Brain Tumors: A Childhood Cancer Survivor Study (CCSS) Update and Expanded Risk Factor Analysis

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PURPOSE: The current study was undertaken to determine incidence of adverse neurologic outcomes and treatment-related risk factors in survivors of childhood brain tumors up to 30 years after diagnosis.

PATIENTS AND METHODS: 1,876 survivors of childhood brain tumors diagnosed between 1970 and 1986 were evaluated for self-reported auditory, visual and focal neurologic deficits, and seizures using the 1994, 2000, and 2007 CCSS questionnaires.

Of survivors, 34% were diagnosed when <5, 30% when 5-9, and 36% when >9 years. Tumors were 66% astroglial, 20% primitive neuroectodermal, 9% ependymoma, and 5% other. Treatments included 23% surgery, 37% surgery + radiation, 25% surgery + radiation + chemotherapy. Median follow-up was 23 years (range 5.1-38.9).

RESULTS: Cumulative incidence continued to increase for all outcomes with 30 year rates of 17% for legal blindness, 23% hearing loss, 41% seizures, 61% coordination or balance problems, and 35% motor problems. In multivariable analyses, relapse increased risk of all neurologic sequelae (RR 2.3-4.8, $p < 0.001$). Hearing loss was increased by radiation to posterior fossa (RR 2.1, $p < 0.01$ for <50Gy; RR 2.9, $p < 0.0001$ for 50+Gy) and temporal lobe (RR 2.8, $p < 0.0001$ 50+Gy) in a dose-dependent fashion. Seizures increased with radiation to temporal (RR 1.8, $p < 0.05$ <50Gy; RR 2.1, $p < 0.005$ 50+Gy), frontal (RR 1.8, $p < 0.05$ 50+Gy) and parietal lobes (RR 1.6, $p < 0.05$) and with secondary malignancies (RR 2.9, $p < 0.05$). Coordination or balance problems increased with brain radiation regardless of location or dose (RR 1.9, $p < 0.005$) and with secondary malignancies (RR 4.4, $p < 0.005$). Motor problems increased with high-dose radiation to temporal (RR 1.6, $p < 0.05$) and parietal (RR 2.0, $p < 0.05$) lobes.

CONCLUSION: Extended cumulative incidence curves demonstrate continuing risk of new onset neurologic deficits in survivors of childhood brain tumors up to 30 years after diagnosis. Cranial radiation and relapse increase risk for late-onset neurologic sequelae.