

ABNORMAL TIMING OF MENARCHE IN SURVIVORS OF CHILDHOOD CENTRAL NERVOUS SYSTEM TUMORS

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ABSTRACT

Purpose

Children with central nervous system tumors who receive radiation therapy (RT) to the hypothalamic-pituitary (H-P) axis are at particular risk for altered timing of puberty or menarche. Early puberty has been well described in childhood acute lymphoblastic leukemia (18-24 Gy). Risk after higher dose RT, as used in the treatment of CNS tumors, has not been well described.

Patients and Methods

We evaluated 235 female survivors of CNS tumors, diagnosed between 1970-1986, and 1,051 sibling controls who are participants in the Childhood Cancer Survivor Study, and provided self-reported data on age at menarche. Logistic regression models were used to estimate various patient and treatment-related risk factors on the risk of early menarche.

Results

Survivors of CNS tumors were more likely to have onset of menarche before age ten compared to their siblings (11.9% vs 1.0%) (odds ratio [OR]=14.1, 95% confidence interval [CI] 7.0-30.89). Twenty of the 138 survivors (14.5%) who received RT to the H-P axis had onset of menarche before age 10, compared to 4.3% of those who did not receive RT (OR=3.8, CI=1.2-16.8). Notably, 17% of participants receiving >50 Gy to the H-P axis experienced menarche before age 10 (OR=4.6, CI=1.2-22.4). Patients diagnosed and treated under four years of age had a four-fold risk of early menarche (p=.002).

To further explore the dose response relationship between CNS RT and timing of menarche, we combined a previously published cohort of 874 patients treated for acute lymphoblastic leukemia with the current CNS cohort. These data suggest an increasing incidence of early menarche with increasing doses of RT (5.4% at 20-30 Gy, 14% at 30-40Gy, and 17% at >50Gy).

Conclusions

Survivors of CNS tumors are at risk of early menarche. Radiotherapy to the H-P axis and young age at the time of treatment are major risk factors.

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