ABSTRACT

Int J Radiat Oncol Biol Phys. 2023 Jan 11:S0360-3016(23)00008-1. doi: 10.1016/j.ijrobp.2023.01.001. Online ahead of print.

Hypogonadism After Treatment for Medulloblastoma: Results from the SJMB03 Trial of Risk-Adapted Radiation Therapy.

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PURPOSE: Estimate the cumulative incidence of hypogonadism in a cohort of pediatric patients treated for medulloblastoma with surgery, risk-adapted craniospinal irradiation, and dose-intensive chemotherapy.
PATIENTS AND METHODS: Children and adolescents (n=156) treated between 2003 and 2013 were evaluated for evidence of hypogonadism and infertility. Clinical information and mean radiation dose to the hypothalamus and gonads and cumulative doses of chemotherapy agents were recorded to estimate cumulative incidence of hypogonadism and infertility with competing risks.
RESULTS: The 5-year cumulative incidence (CI) of hypogonadism was 71.25% (±6.76%) for females and 6.48% (±3.16%) for males (P<0.0001) and 50.00% (±9.70%) for puberty age and 28.99% (±5.05%) for prepuberty age at treatment (P=0.0068). The 5-year CI by gonadal radiation dose exposure (GRDE) was 61.11% (±12.13%) for high (>2Gy), 61.18% (±12.92%) for intermediate (1-2Gy), and 21.97% (±4.76%) for low (<1Gy) (P<0.0001). Sex, puberty status, GRDE, interval from treatment to puberty, and vincristine dose were associated with hypogonadism. Hypogonadism in female sex was highly correlated with GRDE and dose to hypothalamus was significant when included in multivariable models or used in models restricted to patients treated after the age of puberty. Cumulative incidence of infertility at 10 years was 55.36% (±14.07%) for females and 23.53% (±10.64%) for males (P=0.0389) in a sample of 33 patients.
CONCLUSION: In the setting of intensive chemotherapy, low-dose gonadal radiation exposure has a significant effect on gonadal function. Females and those achieving age of puberty at time of radiation therapy (RT) have a higher risk of hypogonadism. GRDE >2Gy was associated with hypogonadism for all groups and >1Gy in prepubertal patients. Hypothalamus dose was significant when included in multivariable models that included postpubertal patients and those with lower GRDE.

DOI: 10.1016/j.ijrobp.2023.01.001
PMID: 36641041