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Risk of Psychosocial, Neurocognitive and Health Impairments in Adult Survivors of Childhood Glioma with Neurofibromatosis Type 1.

Background: Neurofibromatosis type 1 (NF1) is associated with an increased risk of tumors as well as non-malignant health conditions. The effect of NF1 on incidence and severity of late outcomes in adult survivors of childhood glioma is poorly understood.

Methods: 147 >5yr survivors of childhood glioma from the Childhood Cancer Survivor Study (CCSS) were compared to 2,629 non-NF1 glioma survivors and 5,051 siblings for neurocognitive impairment (CCSS neurocognitive questionnaire), emotional (Brief Symptom Inventory-18), socioeconomic outcomes, chronic health conditions (CTCAE v4.0) and late mortality (occurring >5yrs from diagnosis) using logistic and Poisson regression adjusted for age, sex, race, and treatment exposures (central nervous system radiation, surgery and chemotherapy). Specific chronic medical conditions commonly associated with NF1 (including epilepsy, vision loss, hypertension and headache) were also compared between groups.

Results: Compared to siblings, NF1 survivors (age at diagnosis [mean, range]: 6.8yr, 0.3-20.9yr; follow up: 14.4yr, 2.1-24.9yr) were more likely to report anxiety (RR[95%CI]: 2.2[1.1-4.4]), difficulty with task completion (1.5[1.1-2.0]), not being married (1.8[1.1-2.9]), and not having attended college (1.8[1.2-2.2]). NF1 glioma survivors reported more severe/life-threatening chronic health conditions (42.2% vs. 28.1%) than non-NF1 survivors at baseline, but the risk of developing new chronic health conditions or conditions associated with NF1 >5yrs from diagnosis was not different between NF1 and non-NF1 survivors (RR 0.85[0.53-1.38]). However, NF1 survivors had significantly worse late mortality (41.1% 30yrs from diagnosis) compared to non-NF1 survivors (17.5% 30yrs from diagnosis, p<0.001) and siblings (0.9% 30yrs from entry, p<0.001). Among specific causes of late mortality, death due to second neoplasm was more likely in NF1 survivors than in non-NF1 survivors (15.7% vs 4.4% 30 years from diagnosis).

Conclusions: NF1 glioma survivors experience worse psychosocial and neurocognitive outcomes than non-NF1 glioma survivors but were not at increased risk for developing late chronic health conditions. Nevertheless, the risk of late mortality is significantly higher in NF1 survivors compared to non-NF1 survivors. Risk of late mortality due to second malignant neoplasm is an important consideration when choosing upfront treatment options for children with NF1-associated gliomas.