Neurocognitive Outcomes in Survivors of Early Adolescent and Young Adult (eAYA) Hematologic Cancers from the Childhood Cancer Survivor Study (CCSS)

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Background:

Neurocognitive impairment in eAYA hematologic cancer survivors has not been well described, despite intensive neurotoxic therapies. We examined prevalence and risk for such impairment in hematologic cancer survivors diagnosed during eAYA compared to a younger age.

Methods:

We identified 1,213 eAYA (diagnosed at 15-21 years; median [range] follow-up age 40 [30-54]) and 4,538 childhood (diagnosed at <15 years; median age 30 [17-48]) survivors of ALL (n= 301 vs 3274), AML (n= 77 vs 424), and Hodgkin lymphoma (HL; n= 835 vs 840) from the CCSS (diagnosed 1970-1999) who completed the Neurocognitive Questionnaire. Impairment was defined as a score >90% of normative data in task efficiency (TE), organization (Org), memory (Mem), and emotional regulation (ER) domains. 1,014 age-matched siblings were controls. Treatment by diagnosis group, chronic health conditions, health status and health behaviors were examined as risk factors for neurocognitive impairment using multivariable logistic regression. Adjusted odds ratios (ORs) and corresponding 95% CI are reported.

Results:

Prevalence of neurocognitive impairment (≥1 impaired domain) was similar for eAYAs and childhood survivors of HL (31.0% vs 29.6%, p=0.54) and AML (36.4% vs 40.3%, p=0.51), although eAYA AML survivors were more likely to have impaired Mem (OR=2.3, 95% CI 1.0-5.4). eAYA ALL survivors were less likely to have neurocognitive impairment than childhood ALL survivors (28.2% vs 38.5%, p<.001) due to lower risk for impaired TE (OR=0.7, 95% CI 0.4-1.0) and Org (OR=0.5, 95% CI 0.4-0.9). No factors, including cranial radiation (RT), explained these rate differences. Treatment by diagnosis group (including cranial RT in ALL, chest RT in HL, and salvage therapy use) was not consistently associated with neurocognitive impairment in eAYA survivors. However, anthracycline dose ≥120mg/m^2 was a risk factor for impaired ER (OR=6.0, 95% CI 2.0-17.9) only in eAYA ALL survivors. Presence of a neurologic health condition was associated with impairment in all 4 domains in eAYA (ORs ranged 1.7-2.9) and childhood cancer survivors (ORs ranged 1.9-5.3). eAYA survivors with a respiratory condition were more likely to have impaired TE (OR=2.1, 95% CI 1.2-3.8). Being in good general health was associated with less impairment across all 4 domains for eAYA (ORs ranged 0.2-0.4) and childhood survivors (ORs ranged 0.3-0.5). eAYA survivors who never smoked were less likely to have impaired ER (OR=0.4, 95% CI 0.2-0.6) than those who smoke.

Conclusions:

Survivors of hematologic cancers diagnosed during eAYA are susceptible to neurocognitive impairment at rates similar to those diagnosed at younger ages. Having comorbidities and being in fair/poor general health are risk factors for impairment. Higher anthracycline exposure in ALL survivors diagnosed during eAYA was the only therapy associated with impairment rates.

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