Risk of rare Adult-type Carcinomas as a Subsequent Malignant Neoplasm in Survivors of Childhood Cancer: The Childhood Cancer Survivor Study

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Background: Subsequent malignant neoplasms (SMNs) are a leading cause of late mortality in survivors of childhood cancer. Using the Childhood Cancer Survivor Study (CCSS) cohort, we determined the risk of carcinomas occurring as SMNs excepting breast, thyroid and skin cancers.
Methods: A retrospective cohort of 14,352 five-year survivors of childhood cancers treated at 25 US and Canadian institutions was assembled. SMNs were ascertained through self-administered questionnaires and confirmed with pathology reports. Cumulative incidence, age- and gender-matched standardized incidence ratios (SIRs) were calculated.
Results: In 71 individuals, 71 carcinomas of interest were found at a median age of 27 years (range 10-44 years) and a median elapsed time of 15 years (range 6-28 years) from first malignancy. Twenty-five (35%) SMNs occurred in the genitourinary system, 23 (32%) in the head and neck area, 16 (23%) in the digestive tract, 4 (6%) in the thorax and the remainder (4%) in other sites. Fifty-nine subjects (83%) had received radiation therapy, 49 (69%) had a history of alkylator therapy, and 8 (11%) had a history of epipodophyllotoxin therapy. Forty-two carcinomas (59%) arose in a radiation field. An excess of carcinomas was found following all childhood diagnoses, and was highest for neuroblastoma (SIR = 24.2 [95% confidence interval [CI] = 12.6-46.5]), soft tissue sarcomas (SIR = 6.2, [95% CI = 3.5-11]) and Wilms tumor (SIR = 4.8 [95% CI = 1.5-14.8]). There was a significant excess of carcinomas in most of the morphology types examined and was greatest for mucoepidermoid neoplasms (SIR=34.0 [95%CI= 19.3-59.9]) and renal cell carcinomas (SIR = 13.3 [95%CI = 6.7-26.7]). The 20-year cumulative incidence for all SMNs in this report is 0.45%.
Conclusions: Childhood cancer survivors are at increased risk of developing subsequent adult-type carcinomas, but the cumulative incidence is low. Further analyses of the contribution of patient and treatment factors to the increased risk of carcinomas in this population are in progress.