Nonmelanoma Skin Cancer in Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study

Christina Boull, Yan Chen, Cindy Im, Alan Geller, Yadav Sapkota, James Bates, Rebecca Howell, Michael Arnold, Miriam Conces, Louis S. Constine, Leslie Robison, Yutaka Yasui, Gregory Armstrong, Joseph Neglia Lucie Turcotte

Background:
Childhood cancer survivors are at increased risk for nonmelanoma skin cancer (NMSC) associated with radiotherapy exposure. However, prevalence of and risk factors for occurrence of multiple NMSC are not well established.

Methods:
NMSCs were identified via self- or proxy-report and subsequent medical record validation among participants from the Childhood Cancer Survivor Study (CCSS), a cohort of five-year survivors of childhood cancer diagnosed <21 years of age between 1970-1999 in the US and Canada. Cumulative incidence and cumulative burden were estimated and piecewise exponential models were used to assess relative rates (RR) of the first and multiple NMSCs associated with demographic and clinical characteristics.

Results:
Among 25,658 CCSS participants, 1390 developed 5290 NMSCs (95% basal cell carcinoma, 5.0% squamous cell carcinoma) with mean age of onset of first NMSC at 36.9 years (range 7.3-63.8 years) and the overall cumulative burden of NMSCs at 20 years was 3.5 per 100 survivors. Of survivors experiencing NMSC, 90% had received radiation therapy (RT) and there was a mean of 3.8 (range 1-182) NMSCs per individual, with 27% experiencing ≥4 NMSCs. Twenty-year NMSC cumulative incidence was 1.4% (95% CI 1.3-1.5). Radiation exposure rates decreased from 75.9%, to 55.5%, and 35.5% from the 1970s compared to 1980s and 1990s. Cumulative incidence of NMSC at 20 years from diagnosis decreased for those diagnosed in the 1990s (0.9%, 95% CI 0.8-1.1%) compared to the 1970s (1.9%, 95% CI 1.5-2.2) (Figure 1a, p<0.001), but did not show evidence of plateauing for any treatment decade. Cranial radiation therapy (RT) and other site-focused RT were associated with a 5.6-fold (95% CI 4.2-7.3) and a 4.8-fold (95% CI 3.7-6.2) increased NMSC risk, respectively. Survivors treated with total body irradiation (RR 16.6, 95% CI 4.9-56.6) and cranial RT (RR 12.2, 95% CI 6.7-22.5) experienced high relative rates of ≥4 NMSCs compared to non-irradiated survivors. A linear dose-response relationship was seen between maximum RT dose at any site and NMSC logarithm relative rate (Figure 1b). Additional analysis of RR of in-field NMSC is in progress. NMSC risk was not associated with any chemotherapeutic exposure.

Conclusions:
Although the cumulative incidence of NMSCs has decreased for survivors diagnosed and treated in more recent decades, the burden of NMSC remains high with a large subset developing ≥4 NMSC primarily related to RT exposure. In survivors treated with RT, life-long screening beginning in the early adult years is needed.