02-07

CHILDHOOD CANCER SURVIVOR STUDY
Analysis Concept Proposal

Submitted:

1. Title: Occurrence of Secondary Nonmelanoma Skin Cancer (NMSC) in Survivors of Childhood and Adolescent Cancer

2. Working Group and Investigators: This proposed publication will be within the Epidemiology Working Group. Proposed investigators will include (name/email/fax):

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3. Background and Rationale: Ionizing radiation is a well-established carcinogenic agent and a known cause of NMSC. First evidence of this in humans was documented by the occurrence of NMSC on the hands of workers using early radiation devices, such as uranium miners and radiologists. Increased risk of NMSC has also been observed in individuals treated for tinea capitis or thymic enlargement in childhood. Additionally, NMSC is one of the cancers most strongly associated with the atomic bombing of Hiroshima and Nagasaki; a strong positive dose-response association for particularly basal cell carcinomas was observed in this population. In several studies the excess risk has been demonstrated to increase with time since exposure to irradiation. Given radiation-induced NMSC is rarely lethal, these cancers have received little attention in studies evaluating long-term effects of cancer therapy and occurrence of second malignant neoplasms. Furthermore, there is no SEER data available on the incidence of NMSC among children and adolescents in the United States. By evaluating the incidence of NMSC in survivors of childhood and adolescent cancer, we will be able to determine the magnitude of this problem as a late effect for this population. We will investigate the relationship of these second malignancies to the previous history of radiation therapy. We will also be able to evaluate the incidence of NMSC in the sibling cohort in attempt to establish a background baseline for comparison.

4. Specific Aims/Objective/Research Hypotheses: This publication is designed to investigate the long-term effects of cancer therapy and its association with the occurrence of secondary NMSC. Our objectives include: (1) to define the incidence of secondary NMSC in a large cohort of childhood cancer survivors, (2) to evaluate the correlation of the occurrence of secondary NMSC with previous radiation therapy received, and (3) to define the incidence of NMSC in a large cohort of siblings of childhood cancer survivors.

Hypotheses:

1. The occurrence of secondary NMSC is a significant late effect of therapy for childhood cancer.

2. The occurrence and location of secondary NMSC is associated with previous radiation therapy exposure.

3. The incidence of NMSC in survivors of childhood cancer is significantly greater than the incidence in sibling controls.

5. Analysis Framework:

a. Outcome of interest: incidence and location of secondary NMSC in survivors of childhood cancer and their siblings

b. Subject population: all CCSS cases and siblings

c. Explanatory variables: sex, age at diagnosis, age at follow-up, time since diagnosis, diagnosis type, race, previous treatment, radiation therapy location/doses

d. Specific tables:

1) Characteristics of all CCSS cases who have developed a secondary NMSC
-sex
-age at diagnosis
-age at follow-up
-time since diagnosis
-primary malignancy (8 categories)
-race (white, black, Hispanic, Am Indian, Asian, other)
-previous treatment
-chemotherapy only
-radiation therapy only
-surgery only
-chemotherapy+surgery
-chemotherapy+radiation
-chemotherapy+radiation+surgery
-dose and location of radiation therapy (1-999, 1000-2499, 2400-3499, 3500-4499, >4500 cGy)

2) Characteristics of sibling controls
-sex
-age
-race

6. Special Consideration: All reports of secondary NMSC will be confirmed by pathologic/dermatologic reports coordinated through Columbus Children's Hospital Pathology Department. All radiation therapy reports will have specific dosimetry established coordinated through M.D. Anderson Cancer Center.

7. Data Summary: Preliminary analysis of the present cases:
150 patients: 45.3% female (68) and 54.7% male (82)
<u>Primary Diagnosis</u>
48% Hodgkin's disease (72)
23.3% Leukemias (35)
9.3% Brain tumors (14)
8% Sarcomas (12)
6.7% Non-Hodkin's Lymphoma (10)

2% Wilms tumor (3)
1.3% Neuroblastoma (2)
1.3% Osteosarcoma (2)

Breakdown by NMSC Type

85.3% Basal cell carcinoma (128)
6% Squamous cell carcinoma (9)
8.7% unknown (13)

NMSC Location

38% Head & Neck (57)
15.3% Chest/Abdomen (23)
8% Back (12)
4.7% Shoulders (7)
2.7% Extremities (4)
2.0% Genitourinary (3)
29.3% unknown

Multiple Occurences of NMSC

17.3% 3rd malignancy (BCC) (26)
2% 4th malignancy (BCC) (3)
1.3% 5th malignancy (BCC) (2)

Radiation data

received XRT, data at MDA = 129 (86%)
never received XRT = 9 (6%)
received XRT, no data received = 4 (2.7%)
"MRAF Pending" = 4 (2.7%)
refused to sign MR = 4 (2.7%)