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Topic: Non-Neurological Effects in Brain Cancer Survivors

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CCSS Concept Proposal**NON-NEUROLOGICAL MEDICAL LATE EFFECTS AMONG BRAIN CANCER SURVIVORS**

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BACKGROUND

Tumors of the central nervous system, particularly in the developing brain, have the potential to impart permanent damage to many organ systems. Treatment regimens for brain cancer, while often providing cure for an otherwise fatal disease, can result in significant long-term sequelae. Adverse effects have been documented in neurocognitive and neuropsychological function (Packer et al, 1989; Mulhern et al, 1992), quality of life and activities of daily living (Mostow et al, 1991; Lantering et al, 1990), and the neuroendocrine axis. Examples of the latter include growth hormone deficiency, short stature, obesity, and precocious puberty (Sklar, 1997). Most studies on long-term effects, however, have been limited to fairly small case series with limited follow-up periods that were focused on specific histologies or specific treatment regimens. The precise frequencies of many long-term medical outcomes, including adverse reproductive outcomes, are not well described. The Childhood Cancer Survivors Study, because of its retrospective cohort study design and large sample size, provides an unprecedented opportunity to evaluate a broad spectrum of long-term outcomes reported by childhood brain cancer survivors.

The goal of this analysis is to provide a complete description of the types and frequencies of medical late effects in CNS tumor survivors across each of the major non-neurological systems included in the CCSS follow-up questionnaire. We plan to focus on endocrine, urinary, cardiopulmonary, gastrointestinal and surgical outcomes. Frequencies of adverse medical outcomes in brain cancer survivors will be compared to that of sibling controls and, when appropriate, to relevant population data. We believe this paper will provide an important reference source on non-neurologic late effects of brain cancer for pediatric oncologists, radiation oncologists, pediatricians, surgeons, family physicians, and other general practitioners.

Neurological outcomes and psychosocial outcomes of brain cancer survivors will be analyzed in two independent studies that will be coordinated with the present project. Dr. Packer is leading the group for neurologic outcomes (their concept proposal is in development) and Dr. Zeltzer is currently analyzing the psychosocial data. The three groups are working together to assure that the brain cancer data will be presented comprehensively and with minimal overlap.

ANALYSIS APPROACH

We will conduct the analysis at the University of Minnesota Coordinating Center (Jim Gurney will take the lead), although the Statistical Center at Fred Hutchinson will review and approve the analytic approach and subsequent results.

Overall Objective: Provide a comprehensive descriptive analysis of non-neurological medical outcomes among the 1817 brain cancer survivors in CCSS. Variables in sections D – I and M will be evaluated.

Hypothesis 1: Brain cancer survivors will report a greater frequency of endocrine abnormalities, including growth hormone deficiency, hypothyroidism, and sex hormone deficiency compared with sibling controls.

Hypothesis 2: Brain cancer survivors will be shorter, heavier, and have higher body mass index compared with sibling controls and population standards of the same age and sex.

Hypothesis 3: Infertility, precocious puberty, and delayed puberty will occur more frequently in brain cancer survivors than in sibling controls.

Hypothesis 4: There will be few significant differences between brain cancer survivors and controls in outcomes of urinary, gastrointestinal, and cardiopulmonary systems.

Our analysis will include separate stratifications by sex and age at questionnaire completion (<18, 18-24, 25-34, 35-46). For cases, we will also evaluate outcomes by age at diagnosis (<5, 5-9, 10-14, 15-21), initial treatment regimen (surgery only; surgery and radiation; surgery, radiation and chemotherapy), and histologic groups (astrocytoma, PNET, ependymoma, other CNS). Some outcomes will be too infrequent to allow presentation of stratified results. For those that justify more detailed analysis, however, stratified and multivariate regression analysis of outcomes with the factors mentioned above will be conducted.

Age- and sex-specific population standards for height, weight, and BMI will be derived from the 1996 Behavioral Risk Factor Surveillance Study (BRFSS) public use data. The BRFSS data, like the CCSS data, is self-reported. The 1996 BRFSS data tape will be used to correspond with the year that most CCSS respondents completed their questionnaire. BRFSS was a national cross-sectional study that employed a complex, multi-stage sampling design. Accordingly, BRFSS frequencies and means will be appropriately weighted and the variances will be adjusted for intercluster correlations using SUDAAN for SAS/PC.

Other Issues

The Coordinating Center at UMN has the May 2000 data set of brain cancer survivors, because the data were used to generate the CNS “blue book”. Therefore, if this proposal is approved, we will not need the statistical center to generate new data files. We also have acquired the 1996 BRFSS public use CD and the SUDAAN for SAS/PC software.

References:

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