Long-term complications in survivors of neuroblastoma: a report from the Childhood Cancer Survivor Study

Caroline Laverdière1, Qi Liu2, Yutaka Yasui3, Paul C. Nathan1, James G. Gurney4, Marilyn Stovall5, Lisa Diller6, Nai-Kong Cheung7, Suzanne Wolden8, Leslie L. Robison9, Charles A. Sklar10

1Department of Pediatrics, University of Montreal, Montreal, QC, Canada; 2Department of Public Health Sciences, School of Public Health, University of Alberta, Edmonton, AB, Canada; 3Department of Pediatrics, The Hospital for Sick Children, Toronto, ON, Canada; 4Department of Pediatrics, Child Health Evaluation and Research Unit, University of Michigan, Ann Arbor, MI; 5Department of Radiation Physics, University of Texas, MD Anderson Cancer Center, TX; 6Department of Pediatric Oncology, Dana-Farber Cancer Institute/Department of Medecine, Children’s Hospital, Boston, MA; 7Department of Pediatrics, Memorial Sloan-Kettering Cancer Center, New York, NY; 8Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY; 9Department of Epidemiology and Cancer Control, St. Jude’s Children’s Research Hospital, Memphis, TN

ABSTRACT

Background
Neuroblastoma (NB) survivors can develop many complications from their treatment. We evaluated long-term morbidity and mortality in a large cohort of NB survivors.

Methods
Late effects data from 5-year NB survivors diagnosed between 1970-1986 in the Childhood Cancer Survivor Study (CCSS) were collected from self-administered questionnaires. 852 survivors and 3899 siblings were included. Treatment data were abstracted from the medical records of all survivors. Late mortality, second malignant neoplasm (SMN), and chronic health conditions were analyzed in relation to treatment factors.

Results
66 survivors (8%) died more than 5 years after their diagnosis (standardized mortality ratio [SMR] 49.8; 95% CI, 27.9-88.8). Causes of death included: disease recurrence (n=22), SMN (n=12), heart failure (n=5), stroke (n=4), and other (n=13). Exposures to radiation therapy (RT) and to VP-16 (p=0.003) were significant risk factors for SMN. Compared to siblings, survivors were more likely to report any chronic health condition risk factor (RR 1.7; 95% CI, 1.4-2.1). The most prevalent conditions included: musculoskeletal (RR 49.6; 95% CI, 27.9-54.5), endocrine (RR 36.6; 95% CI, 21.5-51.4), and neurological (RR 13.1; 95% CI, 8.6-20.4). Specific risk factors were identified for various health conditions: radiation therapy (RT) and chemotherapy (CT) for musculoskeletal; age < 1 year at diagnosis (RR 10.6; 95% CI, 2.3-46.5) for sensory; and chemotherapy (RR 2.8; 95% CI, 1.3-6.5) for scoliosis; and chest RT (RR 2.8; 95% CI, 1.3-6.5) as risk factors for scoliosis; age < 1 year at diagnosis (RR 1.9; 95% CI, 1.4-2.6) and hypothyroidism.

Conclusions
NB survivors are at risk of developing chronic health conditions. Long-term surveillance is required for early detection of these complications.

INTRODUCTION

OBJECTIVES

• Therapy for low and intermediate risk NB has become less intensive
• High-risk patients continue to fare poorly despite the use of multimodal intensive therapy

RESULTS

• Chronic health conditions attributable to treatment
  – Musculoskeletal (RR 49.8; 95% CI, 27.9-54.5)
  – Endocrine (RR 36.6; 95% CI, 21.5-51.4)
  – Sensory (RR 21.5; 95% CI, 14.6-31.7)
  – Neurological (RR 13.1; 95% CI, 8.6-20.4)
• Secondary malignant neoplasm (n = 33)
  – Types - thyroid (7) - renal (6) - soft tissue sarcoma (3) - breast (2)
  – Risk factors - Exposure to Radiation Therapy (p=0.003)

METHODS

• CCSS cohort of 5-year NB survivors diagnosed between 1970-1986 (n = 832)
• Baseline questionnaire and follow-up surveys
• Medical information abstracted from medical record: chemotherapy agents and cumulative doses, surgical procedures, quantitative radiation therapy data
• Comparison group of siblings of cancer survivors (n=3899)

CONCLUSIONS

• Mortality and risk of chronic health conditions are significantly higher for NB survivors than for siblings
• High risk of musculoskeletal, SMN, hearing loss, endocrine and neurological complications among NB survivors
• Long-term medical follow-up is required for early detection of medical complications in NB survivors