O-15

Neuroendocrine Tumors and Risk of Subsequent Primary Cancers in Early-Onset Disease: A Population-Based Retrospective Cohort Study in the United States

Manas Pustake[1], Charles W. Shi[2], Matthew T. Gao[3], Nicholas J. Hornstein[4], Seth J. Concors[5], Timothy J. Brown[6], Udhayvir S. Grewal[7]

[1]Department of Internal Medicine, Texas Tech University Health Sciences Center, El Paso, TX; [2]Department of Internal Medicine, Emory University School of Medicine, Atlanta, GA; [3]Carver College of Medicine, University of Iowa, Iowa City, IA; [4]Department of Hematology and Oncology, Northwell Health Cancer Institute, New York, NY; [5]Division of Surgical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; [6]Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX; [7]Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA

BACKGROUND

Neuroendocrine tumors (NETs) are increasingly diagnosed and often follow a prolonged clinical course, making survivorship risks clinically important. Although patients with NETs are known to be at risk for subsequent primary cancers (SPCs), the influence of age at NET diagnosis on SPC risk remains unclear. In this study, we aimed to evaluate whether early-onset NETs are associated with distinct patterns of SPC risk in a large nationwide cohort.

METHODS

We conducted a retrospective cohort study using the Surveillance, Epidemiology, and End Results database from 2000 to 2021. Patients with NETs were classified as having early-onset disease if diagnosed before age 50 years and average-onset disease if diagnosed at age 50 years or older. The primary outcome was development of a first SPC after the index NET diagnosis, defined according to SEER multiple-primary rules. Death before SPC was treated as a competing event. Fine-Gray competing-risk regression models were used to estimate adjusted subdistribution hazard ratios (sHRs) and 95% confidence intervals (CIs). Sensitivity analyses were performed by restricting follow-up to 5 years and by separately evaluating patients with very early-onset NETs, defined as diagnosis before age 30 years.

RESULTS

Among 100,717 patients with NETs, 21,146 (20.9%) had early-onset disease. Median follow-up was 47 months. 7,870 patients (7.8%) developed an SPC. SPCs occurred in 5.1% of

patients with early-onset NETs compared with 8.5% of those with average-onset NETs. In adjusted competing-risk analysis, early-onset NET was associated with significantly lower SPC risk compared with average-onset NET (sHR, 0.56; 95% CI, 0.53-0.60; P<.001). Findings remained consistent in sensitivity analyses restricted to 5 years of follow-up (sHR, 0.58; 95% CI, 0.54-0.61) and were more pronounced among patients diagnosed before age 30 years (sHR, 0.23; 95% CI, 0.17-0.31). Higher SPC risk was seen among patients diagnosed at ages 30 to 49 years and among those with gastric, pancreatic, and small intestinal NETs. The most frequent SPC sites overall included lung and bronchus, breast, prostate, colorectal cancer, and melanoma, with a distinct distribution of SPC sites among early-onset patients.

CONCLUSIONS

Early-onset NETs were associated with lower overall SPC risk compared with average-onset NETs. However, clinically meaningful heterogeneity was observed, with selected early-onset subgroups demonstrating elevated risk. These findings suggest that survivorship strategies for patients with NETs may benefit from incorporating age at diagnosis, sex, and primary tumor site to better individualize long-term SPC surveillance.

ABSTRACT ID #36593