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Cervical Neuroendocrine Carcinomas: A Population-Based Analysis of Clinicopathologic Characteristics and Survival Outcomes in Comparison with Conventional Cervical Malignancies

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BACKGROUND

Cervical neuroendocrine carcinomas (CNECs) are a rare and heterogeneous group of cervical neoplasms, with very limited data regarding epidemiology and survival. In this study, we explored clinicopathologic factors and oncologic outcomes of patients with CNECs derived from the Survival, Epidemiology and End Results (SEER) database, in comparison to cervical squamous cell carcinoma (SCC) and adenocarcinoma (AC).

METHODS

The SEER database (18 registries/November 2020) was queried for patients with CNECs, SCC, and AC, with the topography codes C67.0-C67.9 (cervix) and the morphologic codes 8246, 8013, 8042 for NECs (small cell - SCNEC, large cell – LNEC, NEC not-otherwise specified - NEC NOS), 8052, 8070-76 and 8084 for SCC, 8140, 8144, 8145, 8147, 8260, 8310, 8480-82 for AC. Demographic/clinicopathologic/treatment/survival data were extracted. SEER summary staging system (localized, regional, distant) was utilized. Overall survival (OS) from cancer diagnosis to death from any cause was estimated with the Kaplan-Meier method. Chi-squared tests were used for comparative analysis and Cox proportional hazards model for identifying clinical covariates associated with OS.

RESULTS

53,370 patients fulfilling inclusion criteria were identified; 868 patients (2%) with CNECs (547 SCNEC, 80 LCNEC, and 241 NEC NOS), 41,764 (78%) with SCC, 10,738 patients (20%) with AC. SCNEC, LCNEC, and NEC NOS were associated with a significantly higher proportion of distant-stage disease (42%, 48%, and 41% respectively), in comparison to cervical SCC (13%) and AC (12%), all $p<0.001$. Median OS was 18 months (95% CI: 15.4 – 20.6) for SCNEC, and 15 months for LCNEC (95% CI: 12.2 – 17.8) and NEC NOS (95% CI: 12.8 – 17.2) respectively, and was significantly inferior to SCC (194 mos, 95% CI; NR,NR) and AC (NR, 95% CI; NR, NR), all $p<0.001$. The presence of SCNEC, LCNEC, or NEC NOS was independently associated with shorter OS in the multivariate analysis, when adjusted for other significant clinicopathologic factors, including stage, age, ethnicity, and completion of hysterectomy. Hysterectomy (regardless of type), was significantly associated with prolonged OS in the CNECs cohort (HR 0.48, 95%CI; 0.39 – 0.60).

CONCLUSIONS

CNECs were associated with advanced stage of disease and shorter OS compared to SCC and AC, conferring dismal prognosis in patients with cervical neoplasms. Despite their rarity, their aggressive behavior warrants a high index of clinical suspicion, accurate pathologic diagnosis, and early definitive intervention. Further studies are needed to better understand the biological underpinnings behind this aggressive behavior and the role of novel systemic treatments.

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