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Small cell carcinoma of the head and neck: An analysis of the National Cancer Database

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ABSTRACT

Purpose/objective(s): To evaluate treatment trends and overall survival of patients with small cell carcinoma of the head and neck region.
Materials/methods: Patients from 2004 to 2012 were identified from the National Cancer Database. Patient demographics and overall survival were analyzed. Multivariable analysis was used to identify predictors of survival.
Results: Among 347,252 head and neck patients a total of 1042 (0.3%) patients with small cell carcinoma were identified. 17% of patients were diagnosed as stage I/II, 61% as stage III/IVA/IVB and 22% as stage IVC disease. The distribution by anatomic site was 9% oral cavity, 12% oropharynx, 35% larynx, 4% hypopharynx, 10% nasopharynx and 30% nasal cavity and paranasal sinuses. The median overall survival by anatomical site was 20.8 months for oral cavity, 23.7 months for oropharynx, 17.9 months for larynx/hypopharynx, 15.1 months for nasopharynx and 36.4 months for nasal cavity primary tumors. On multivariable analysis across stage, patients with nasal cavity and paranasal sinuses tumors had the best survival and patients with nasopharynx primaries had the worst survival. In stage I/II patients, type of treatment delivered resulted in no overall survival difference ($p = 0.78$). In patients with locally advanced disease, there was no difference in survival between those treated with combined surgery, radiotherapy and chemotherapy compared to those treated only with radiotherapy and chemotherapy ($p = 0.46$). The addition of radiotherapy to chemotherapy in the metastatic setting did not result in improved survival ($p = 0.14$).
Conclusions: Small cell carcinoma of the head and neck is a rare malignancy with a poor prognosis. The addition of surgery to radiotherapy and chemotherapy did not improve survival in patients with locally advanced disease.

Introduction

According to the World Health Organization, small cell carcinoma and poorly differentiated (grade III) neuroendocrine tumors are considered the same entity and are the most aggressive type of neuroendocrine carcinomas [1]. The histological category of neuroendocrine carcinomas includes carcinoid tumors, atypical carcinoid tumors and small cell carcinomas. Other synonyms for small cell carcinoma include small cell neuroendocrine carcinoma, oat cell carcinoma, anaplastic small cell carcinoma and small cell neuroendocrine carcinoma of intermediate type [2]. These tumors are defined microscopically by their small to intermediate sized cells, necrosis, large number of apoptotic cells, high mitotic rate, and lack of neurofibrillary stroma [1]. Electron microscopic examination usually show dense core secretory granules and abortive cell processes.[1] In addition, these tumors often stain positive for at least one neuroendocrine marker such as synaptophysin, CD 56, and chromogranin A [1].

Small cell carcinoma of the head and neck is a rare clinical entity. It's histological appearance is similar to small cell lung carcinoma.[1] Overall, these tumors are highly aggressive, associated with smoking and can occur throughout the head and neck region [3,4]. The larynx, salivary glands and the sinonasal region are the most common sites for small cell carcinoma of the head and neck [2]. Given the rarity of this tumor, there is a paucity of clinical

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outcomes data available to guide treatment recommendations. A previous analysis has reported the outcomes of salivary gland small cell carcinomas [5,6]; however, there is limited data on non-salivary gland head and neck small cell carcinomas. We performed an analysis of the National Cancer Database and report on the largest series of non-salivary gland, non-thyroid head and neck tumors classified as either small cell carcinoma or poorly differentiated neuroendocrine tumors.

Patients and methods

Data source

We conducted a population-based retrospective analysis utilizing the National Cancer Database (NCDB), which is a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The NCDB integrates cancer registry records from more than 1500 accredited hospitals and medical centers and collects data from approximately 70% of all newly diagnosed cancers in the United States [7]. Variables recorded in the database include patient demographics, stage, and interventions received (including surgery, radiotherapy and chemotherapy). The NCDB records overall survival but not local control or toxicity. The American College of Surgeons and the Commission on Cancer have not verified the data and are not responsible for either the analytic or statistical methodology used or the conclusions drawn from these data by investigators.

Study cohort

Data for patients diagnosed with head and neck small cell carcinoma between 2004 and 2012 were obtained from the NCDB participant user files after appropriate approval. The participant user files included: lip, floor of the mouth, gum and other mouth, oropharynx, pharynx, tongue, tonsil, larynx, hypopharynx, nasopharynx, nose, nasal cavity and middle ear. A total of 347,252 patients made up these files and were queried for analysis. Tumors were queried based on their International Classification of Diseases for Oncology 3rd edition (ICD-O-3) code and included small cell carcinoma, NOS (8041), oat cell carcinoma (8042), small cell carcinoma fusiform cell (8043), combined small cell carcinoma (8045) and tumors coded as grade 3 neuroendocrine carcinoma NOS (8246). Patients with missing staging were excluded from this analysis. Fig 1 shows the breakdown of patients that were excluded and included.

Variables

Patient demographic and treatment information were dichotomized for purposes of univariate analysis and multivariable analyses in order to allow for reasonable comparisons. Age was analyzed as a continuous variable and Charlson-Deyo comorbidity score was analyzed as 0, 1, or $\geq$2. Race was dichotomized as white or non-white; insurance type as private or non-private; income as $\geq$\$46,000 or <\$46,000; location as urban ($\geq$250,000 people) or nonurban (<250,000 people); facility-type as academic or non-academic; clinical stage as I, II, III, IVA, IVB or IVC. Tumors were further classified as early stage (stage I/II), locally advanced (stage III/IVA/IVB) or metastatic (stage IVC). Tumors were grouped according to anatomical site, which included oral cavity, oropharynx, larynx, hypopharynx, nasopharynx, nasal cavity/paranasal sinuses. Given the small number of hypopharynx primaries, larynx and hypopharynx were grouped together for survival analysis. Combining these two groups did not significantly change the survival outcomes. Treatments delivered included radiotherapy, chemotherapy and surgery. Details regarding chemotherapy drug names, dose, and treatment duration and details of concurrent or sequential chemotherapy in relation to radiation are not recorded. Patients who only had an excisional biopsy were excluded from the surgery group.

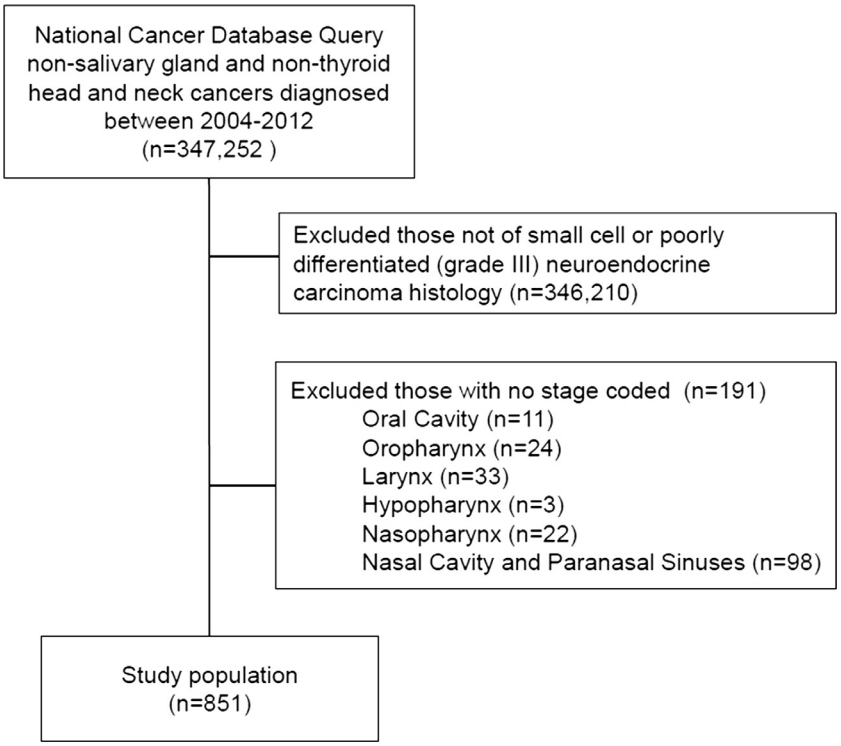

Fig. 1. Inclusion and exclusion flow diagram.