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Original article

Metastatic small cell carcinoma of the prostate: Population-based analysis of patient characteristics and treatment paradigms

Andrew Cohen, M.D., Kyle A. Richards, M.D., Sanjay Patel, M.D., Adam Weiner, B.S., Scott E. Eggener, M.D., Russell Z. Szmulewitz, M.D.*

The University of Chicago Medicine, Chicago, IL

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Abstract

Introduction: Small cell carcinoma of the prostate is a rare malignancy comprising <1% of prostate cancers. Little is known about population-based treatment patterns for metastatic small cell carcinoma of the prostate. We evaluated clinical characteristics, treatment patterns, and survival outcomes.

Methods: Using the National Cancer Database, we identified patients between 1998 and 2011 diagnosed with pure small cell carcinoma of the prostate as their only malignancy who presented with nodal involvement or distant metastasis.

Results: Treatment information was available for 379 patients. Of them, 122 (32.5%) underwent chemotherapy (CT) alone, 25 (6.7%) received hormonal therapy (androgen-deprivation therapy) alone, 10 (2.7%) underwent radiation therapy alone, 3 (1%) underwent radical prostatectomy, and 167 (44.4%) underwent combination therapy. The 1- and 3-year survival rates were 35.3% and 4.4%, respectively. Those receiving any CT as part of their treatment had a median survival of 9.3 vs. 3.2 months for those not receiving it ($P < 0.001$). Those receiving CT, androgen-deprivation therapy, and radiation had a median survival of 15.1 vs. 7 months for those receiving CT alone ($P < 0.001$). On multivariable analysis (controlling for age, Charlson comorbidity index, extent of metastasis, prostate-specific antigen level, and type of treatment), older age (hazard ratio [HR] = 3.87; 95% CI: 1.41–9.34; $P = 0.007$) and distant metastatic disease (HR = 7.17; 95% CI: 1.62–31.8; $P = 0.010$) increased risk of death, whereas receipt of CT (HR = 0.15; 95% CI: 0.05–0.44; $P = 0.001$) decreased risk of death.

Conclusion: Men presenting with metastatic small cell carcinoma of the prostate have poor overall survival. Older patients and those presenting with distant metastases have an increased risk of death. It appears that patients receiving CT experience a modest survival benefit. The role of hormonal therapy in this population remains unclear. © 2014 Elsevier Inc. All rights reserved.

Keywords: Small cell carcinoma; Prostate cancer; Survival; Treatment

1. Introduction

Small cell carcinoma is a rare variant of prostate cancer, and studies have reported metastasis at presentation ranging from 33% to 75% [1–3]. Although several case reports and single series have been published, very little is known about population-based treatment patterns for metastatic small cell carcinoma of the prostate [1,4,5]. There have been several single-arm phase II prospective clinical trials for metastatic small cell prostate cancer; however, the studies are limited by size, lack of randomization against a control arm, and heterogeneity regarding patient inclusion characteristics [6]. Few large multicenter population studies exist, and because of the low prevalence of disease, no guidelines have been proposed regarding treatment. Currently, patients undergo hormone therapy, radiation, systemic chemotherapy (CT), surgery, or multimodal combination therapy [6]. CT regimens are those commonly practiced in the treatment of small cell carcinoma of the lung (SCLC), with the most commonly used first-line regimen in extensive-stage SCLC being cisplatin or carboplatin with etoposide [7]. Small series of men with small cell carcinoma of the prostate have been treated with Adriamycin, vincristine, doxorubicin and cyclophosphamide, or etoposide and cisplatin with or without doxorubicin [8,9].

* Corresponding author. Tel.: +1-773-702-7609.
E-mail address: rszmulew@medicine.bsd.uchicago.edu (R. Szmulewitz).

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As level 1 evidence to guide the management of metastatic small cell prostate cancer is lacking, the preferred therapeutic strategy for those with metastatic disease remains unknown. To our knowledge, no nationwide retrospective study to date has focused solely on men with metastatic small cell prostate cancer. Given the rarity of metastatic small cell prostate carcinoma, we sought to use the National Cancer Database (NCDB), which captures 70% of all newly diagnosed cancers in the United States each year, to better describe the patient characteristics, treatment modalities, and survival rates for patients with the disease [10]. The goal of this study was to capitalize on the size and clinical annotation of the NCDB to investigate any associations between clinical characteristics and treatment strategies and effect on overall survival.

2. Methods

2.1. Data source

Institutional review board exemption was acquired as no patient, physician, or hospital identifiers were examined. The NCDB is a hospital-based cancer registry that captures approximately 70% of all cancer diagnoses in the United States yearly from more than 1,400 hospitals. The NCDB includes data on patient demographics, socioeconomic status, clinical and pathologic staging, treatment course, comorbidities, vital status based on patient records and death registry updates, and hospital level data. The disease course and therapy of each patient diagnosed and treated at a participating NCDB institution are coded and reported based on the American College of Surgeons' Facility Oncology Registry Data Standards (http://www.facs.org/cancer/coc/fordsmanual.html).

2.2. Inclusion criteria

We identified all patients diagnosed with prostate cancer between 1998 and 2011. Of these men, we included those who were diagnosed with pure small cell carcinoma of the prostate (International Classification of Diseases (ICD)-O-3 morphologic codes 8002 and 8041–8044). We limited our study to men with prostate cancer as their first and only malignancy and those who presented with metastatic disease either via regional (American Joint Committee on Cancer [AJCC] category cN1) or distant metastasis (AJCC category cM1).

2.3. Study variables

Patient demographic and clinical characteristics included age, race, cancer facility (type and location), metropolitan/urban/rural, home county, cancer characteristics (prostate-specific antigen [PSA] level and AJCC clinical stage), and Deyo-Charlson comorbidity index (CCI) [11]. Race was categorized as non-Hispanic white, black, or other/unknown. The CCI was calculated based on the reporting of up to 6 preexisting comorbidities. Clinical stage was coded according to the AJCC Cancer Staging Manual edition in use during the year in which the case was diagnosed. Patients were initially categorized by treatment type, including radical prostatectomy (RP), CT, hormonal therapy (androgen-deprivation therapy [ADT]), radiation therapy (RT), or multimodality therapy. The NCDB recorded PSA levels starting in 2004, as per collaborative staging stipulations, as the highest values before the diagnostic procedure or, if that value is unavailable, the earliest pretreatment but postdiagnostic value [12]. Gleason scores were not analyzed because a 2005 modification of the Gleason grading system determined that small cell carcinoma of the prostate should not be assigned a Gleason score [13].

The NCDB defines the patient's setting as their hometown population. These are categorized as metropolitan—more than 250,000 residents, urban—more than 2,500, and rural—fewer than 2,500. Hospital variables include geographic location and program type. Community programs were defined as those where more than 100 but fewer than 500 patients with cancer were treated per year. Comprehensive programs were defined as those where more than 500 cancer cases per year were treated. Academic programs were defined as those where more than 500 cancer cases per year were treated and graduate medical education was provided in at least 4 areas. Facility geographic location was categorized into 4 categories, including the Northeast, Southeast, Midwest, and West.

2.4. Statistical analysis

Analysis was performed with Stata version 12 (Stata, College Station, TX). The Fisher exact, chi-square, and Mann-Whitney U tests were used for comparison of categorical variables. Kaplan-Meier survival analysis and the stratified log-rank test were used to compare overall survival stratified by extent of metastases (regional vs. distant) and various treatment modalities. Overall survival was estimated as time from diagnosis to death. Patients known to be alive were censored at the last follow-up evaluation or the last contact by correspondence. A multivariable Cox proportional hazards model was performed to identify independent predictors of overall survival. A 2-sided $P < 0.05$ was considered statistically significant.

3. Results

3.1. Patient and disease variables

Of the 1,774,062 cases of prostate cancers noted between 1998 and 2011, 896 (0.05%) were diagnosed with pure small cell carcinoma. Of those, 684 (76.3%) were diagnosed as only/first malignancy and 387 (43.2%) were diagnosed as metastatic upon presentation. Of the 387 patients in the cohort, the median age at diagnosis was 70 years, and 88.9% of the patients were white (Table 1). PSA data were

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