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An Unusual Etiology of Urinary Retention – Small Cell Prostate Carcinoma

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ABSTRACT

We report the case of a 63-year-old male who presented with painless gross hematuria and urinary retention. Pathology obtained from transurethral resection of the prostate revealed pure small cell carcinoma of the prostate. Metastatic evaluation confirmed stage IV disease with lymphatic and hepatic metastasis. Despite aggressive systemic chemotherapy, the patient succumbed to his disease eleven months after initial diagnosis. Small cell carcinoma is an aggressive variant of prostate cancer that often presents late in the clinical course. We review the literature and discuss the clinical features associated with this rare subset of prostate cancer.

Introduction

Small cell carcinoma of the prostate (SCP) is an aggressive, rare tumor compromising less than 1% of all prostate cancer, although autopsy studies have suggested it may be present in up to 20% of castrate resistant disease.[1] This subset of prostate tumors carries a poor prognosis given their rapid progression with extensive local and visceral involvements. SCP often presents late in the clinical course with marked prostate enlargement and low PSA levels despite metastatic disease.[2] Given the lack of routine prostate cancer detection, prostate cancer variants should be kept in mind when evaluating urinary retention and hematuria.

Case report

A previously healthy 63-year-old male presented with worsening lower urinary tract symptoms over a three months span and new onset painless gross hematuria. Digital rectal examination revealed a diffusely nodular prostate with obliteration of the median sulcus. Serum PSA was 1.4 ng/mL. Urine cytology revealed hematuria without malignant cells. Trans-rectal ultrasound revealed a volume of 61 cc with an enlarged median lobe and hypoechoic focus in the left lateral lobe. The patient elected for prostate resection (TURP) to relieve his bladder outlet obstruction.

TURP specimen revealed small cell carcinoma of the prostate with round small cells, scant cytoplasm, and hyper-cellularity (Fig. 1). This was confirmed with immunohistochemistry showing positive staining for Synaptophysin, while PSA, P504S, CK20, CK7 and CD45 were all negative. Ki67 exceeded 80%, consistent with the small cell diagnosis. Serum carcinoembryonic antigen (CEA) was 9.6 ng/mL (normal, 0–3 ng/mL). CT imaging of the chest, abdomen and pelvic revealed multiple liver and lymphatic metastases (Figs. 2 and 3).

Given his stage IV small cell prostate cancer, he was offered palliative chemotherapy. Four cycles of systemic etoposide and cisplatin were administered. Radiotherapy was also offered to the patient but was refused. The patients clinical condition continued to deteriorate and he passed away from disease progression eleven months after the initial diagnosis.

Discussion

Similar to adenocarcinoma of the prostate, SCP typically arises from the peripheral zone of the prostate, often with a dominant nodule or grossly abnormal digital rectal examination. The PSA can be elevated but often is not therefore, it cannot be used as a reliable marker for the disease.[2] SCP can present with a variety symptoms including lower urinary tract symptoms, neurologic findings, constitutional symptoms, hematuria, hematospermia or paraneoplastic syndromes. Literature review of SCP presenting symptoms revealed that majority of patients presented with urinary retention, followed by neurologic symptoms.[2] It often involves early and frequent metastatic disease, most commonly involving liver, bone, lung, and the central nervous

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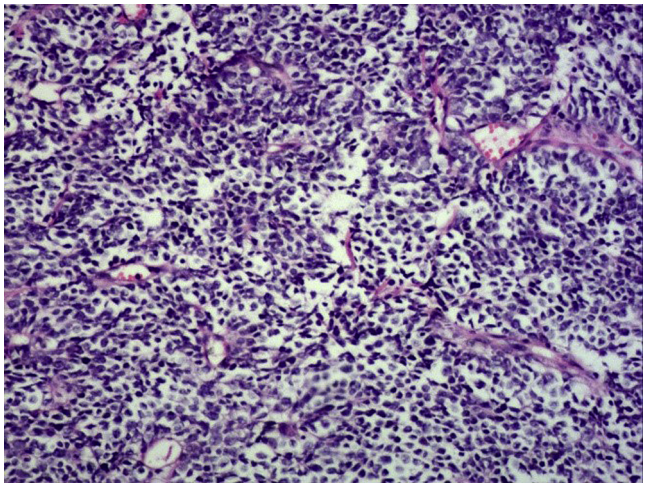

Figure 1. Histological findings of the prostatic tumor. H&E (×20) staining shows small cell morphology consistent with SCP, including round or spindle-shaped small cell, nuclear molding, hyper-cellularity, and scant cytoplasm.

system. In contrast to adenocarcinoma, bone lesions tend to be lytic with associated bone pain and pathologic fractures.

Given its rare presentation, there are no guidelines for specific therapy of SCP. For localized disease, radical prostatectomy is suggested although multimodal treatment is often recommended.[2,3] One retrospective series of localized SCP treated by radical prostatectomy involved 16 patients showing over 90% biochemical free survival at 5 years. Radiotherapy also been used in this setting with good results.[3] Despite these encouraging results, Spiess et al suggested local therapy should be multimodal with surgery, possible post-operative radiotherapy and systemic chemotherapy to maximize the potential survival benefit.[4]

Unfortunately, like our patient, many patients present with metastatic disease given its aggressive course and lack of biomarkers. Extrapolating from lung small cell tumors, it has mainly been treated with platinum-based chemotherapy with short-lived results. Given the propensity of SCP to present late with other sites of disease, local control with surgery is rarely employed and surgical intervention is mainly palliative in the form of relief of bladder outlet obstruction and performed transurethrally. Although no guidelines exist and studies sizes have been small, locally

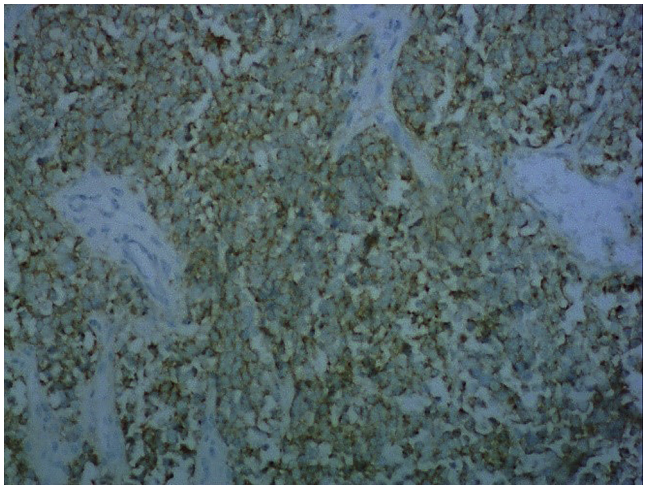

Figure 2. Immunohistochemical findings of the prostatic tumor. A: The tumor cells stain positive for synaptophysin (×20).

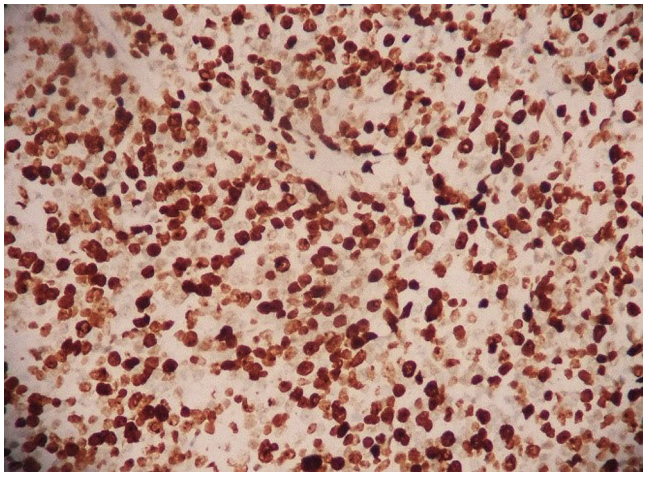

Figure 3. Ki67 staining (×20). Tumor cells show >80% Ki67 proliferative index, suggesting a high cellular proliferation, leaning the diagnosis toward SCP.

invasive disease without metastatic disease has responded to radiation and systemic chemotherapy.[3] Radiotherapy can be used for palliation in the metastatic setting.

SCP has a very poor prognosis despite aggressive therapy. In an analysis of the SEER database, Deorah analyzed 191 patients collected from 1973–2003. Metastatic disease was the presentation reported for 60% with a 2-year survival rate of 27%. By 60 months, only 14% had survived.[5] Median survivals reported in systemic chemotherapy series ranged 8–19 months. Overall, given the late presentation and with aggressive therapy, median survival is often reported under 2-years.

Intriguingly, although *de novo* SCP only accounts for <1% of all prostate carcinoma,[1] focal neuroendocrine differentiation in adenocarcinoma is a common finding that has been reported in 10% to 100%.[1] It remains controversial if focal neuroendocrine differentiation contributes to the prognosis of adenocarcinoma of the prostate. It is often reported with a poor prognosis although it is confounded by other poor prognostic indicators (prior treatment failure, higher Gleason grade disease). Currently there isn't data to conclude that focal neuroendocrine involvement is by itself a predictor of poor outcome and it is not recommended to be routinely examined for during pathological analysis.

Conclusion

SCP is a rare but highly aggressive entity with a poor prognosis. The presentation is often urinary retention or neurologic based which makes the diagnosis difficult. The standard of care is platinum based chemotherapy which has a short response with poor overall survival.

Disclosure

The authors declare that there are no conflicts of interest.

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