# Prostate Cancer with a Normal PSA: Small Cell Carcinoma of the Prostate – A Rare Entity

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Pure small cell carcinoma of the prostate is extremely rare. When it does occur, it is usually in concordance with prostatic adenocarcinoma. Early diagnosis is difficult as the carcinoma tends to spread early to visceral organs without concordant elevation of prostate-specific antigen (PSA). Because this condition is rare, no standard treatment regimen has been established, and the overall prognosis remains poor.

This case report describes clinical characteristics of a 67-year-old man with pure small cell carcinoma of the prostate. The unique clinical and biological features of this histologic type of prostate cancer are discussed.

## Case Report

A 67-year-old man came to the emergency department complaining of a 2-week history of progressively worsening, right, upper quadrant abdominal pain associated with night sweats and a recent 15-pound weight loss. He denied any obstructive or irritative urinary symptoms, change in bowel habits, jaundice, or overseas travel.

He was under the care of a urologist for benign prostatic hypertrophy and 4 years earlier had had benign findings on a prostate biopsy. His last PSA test 4 months before his current illness was normal. Other than benign prostatic hypertrophy, his medical history was notable only for mild hypertension, which was well controlled with metoprolol. He was a social drinker, nonsmoker, and had no family history of malignancies.

When examined, he was a well-nourished older adult man who was anicteric, afebrile, and had no adenopathy. Important findings were confined to his abdomen, where he had mild right upper quadrant fullness and tenderness, but no guarding or rebound tenderness. A firm, nontender prostate with an enlarged left lobe was found during a digital rectal examination. His stool was positive for occult blood.

Laboratory investigations included normal complete blood count, electrolyte levels, serum urea nitrogen level, creatinine level, and coagulation studies. Findings of liver function tests were normal except for an elevated alkaline phosphatase of 239 U/L (normal, 38–126 U/L). His PSA was 1.3 ng/mL (normal, 0–4 ng/mL); carcinoembryonic antigen, α-fetoprotein, and CA 19–9 were also within normal limits.

Computerized tomography (CT) of his abdomen and pelvis showed an abnormal density in the left lobe of the prostate and multiple hypoechogenic lesions in the liver consistent with extensive metastatic disease.

After evaluation in the emergency department, he was subsequently admitted to the hospital for pain control and further evaluation of what appeared to be metastatic tumor. A CT scan of the chest showed right hilar adenopathy and a small peripheral nodule of the right lung. His head CT scan was negative for metastatic disease. Upper gastrointestinal endoscopy and colonoscopy findings were benign. Immunohistochemical findings from a CT-guided liver biopsy were consistent with a diagnosis of small cell (neuroendocrine) carcinoma. The malignant cells were positive for neuron-specific enolase and chromogranin. Subsequently, a transrectal sonograph-guided prostate biopsy found extensive small cell carcinoma, suggesting a final diagnosis of small cell carcinoma of the prostate with extensive hepatic metastases.

He was started on a course of palliative chemotherapy with cisplatin and irinotecan (Camptosar).

## Discussion

Primary small cell carcinoma of the prostate is uncommon and is usually discovered incidentally in

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concordance with histologic samples of adenocarcinomas. Pure small cell carcinoma of the prostate is an extremely rare occurrence with clinical features unlike those of prostatic adenocarcinoma. In a review of the literature,[1] 33 reported cases of small cell carcinoma of the prostate were noted, of which 13 were in patients with previously diagnosed prostatic adenocarcinoma, 7 had mixed adenocarcinoma with small cell carcinoma, and 13 had pure small cell carcinoma. To date, no etiologic factors unique to small cell carcinoma of the prostate have been proposed.

Histologically, small cell carcinoma of the prostate is characterized by a pattern similar to small cell carcinoma of the lung.[2] Three theories of histogenesis have been proposed. One theory suggests that small cell carcinomas of the prostate arise from amine precursor uptake decarboxylation cells of local endodermal origin. Another theory proposes that small cell prostatic carcinomas arise from dedifferentiation of prostatic adenocarcinomas, suggesting that small cell carcinomas are part of a spectrum of prostatic adenocarcinomas rather than a separate disease entity. Because of the histologic similarities between prostate and lung small cell carcinomas and the occurrence of similar neuroendocrine paraneoplastic syndromes, the most widely accepted view is that prostatic small cell carcinomas arise from totipotential stem cells of the prostate, which have the ability to differentiate into either epithelial or neuroendocrine type carcinomas.[1,3]

Whereas mixed small cell carcinomas and adenocarcinomas usually are aggressive recurrences of a primary adenocarcinoma, pure small cell carcinoma of the prostate often is associated with early metastatic disease because of its aggressive nature. Like adenocarcinomas, small cell prostate cancers arise in the periphery of the prostate gland and hence can occur without urinary symptoms. The disease has a propensity to metastasize to visceral organs, including the liver, bone, lungs, central nervous system, and pericardium, and regionally to the pelvic lymph nodes, rectum, and bladder.[3] In addition, small cell prostate cancers have been reported to produce paraneoplastic syndromes associated with the production of adrenocorticotrophic hormone.[4]

In contrast to prostatic adenocarcinoma, PSA is an unreliable tumor marker for small cell prostate carcinoma and is usually normal, even when there is metastatic disease. One study suggested that carcinoembryonic antigen is a more reliable marker, because increases and decreases in antigen levels are found with disease progression and regression, respectively.[3] More recently, the tumor marker neuron-specific enolase has been proposed as a prognostic indicator; high levels suggest a poor prognosis.

Despite treatment with chemotherapy, the prognosis of small cell prostate cancer is extremely poor, and the median survival is 7 months.[5] Because of the rarity of the condition, no standard therapeutic regime has been developed. Reported cases have generally been managed by chemotherapeutic regimens similar to those recommended for small cell lung cancer. The results, however, have not been as favorable. In addition, small cell prostate cancer, in contradistinction to adenocarcinoma, has been found to be unresponsive to hormone therapy.

One recent study reported a clinical response and normalization of the tumor markers neuron-specific enolase and lactate dehydrogenase after treatment with a combination of cyclophosphamide, etoposide, and doxorubicin.

## Conclusion

Primary small cell carcinoma of the prostate can occur in isolation or in concordance with a previously or newly diagnosed prostatic adenocarcinoma. As this case typifies, early diagnosis is difficult because of a tendency for early spread to visceral organs and lack of concordant elevation of PSA. Because this condition is rare, no standard treatment regimen has been established, and the overall prognosis remains poor.

## References


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