



Oncology

Gross Findings of Widespread Visceral Metastasis of Prostatic Adenocarcinoma With Neuroendocrine Features: A Case Report



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ABSTRACT

Although prostate cancer is common in the western world and is associated with favorable overall survival, neuroendocrine prostate cancer is difficult to detect and is known to aggressively metastasize throughout the body. This subset of disease thus has a poor prognosis, and early detection and treatment of neuroendocrine prostate cancer may increase overall survival. We present a case of a now deceased 63 year old male with extensive epicardial, respiratory, hepato-biliary, adrenal, genitourinary, and osseous tissue metastasis.

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Introduction

The overwhelming majority of prostate cancers (PCa) are adenocarcinomas, most of which are low-risk cases with excellent long-term survival rates. In contrast, neuroendocrine differentiated (NED) prostate adenocarcinoma is rare and has poor overall survival.¹ Here, we report a case of a man presenting with advanced NED with diffuse metastasis to the viscera, including the heart, lung, liver, adrenal gland, and thoracic-lumbar spine.

Case presentation

In October 2014, a 63-year old Caucasian male with a past medical history notable for benign prostatic hypertrophy status post transurethral resection of the prostate presented to our outpatient clinic complaining of acute urinary retention. A Foley catheter was placed to relieve his obstruction and bladder distention. The digital rectal exam (DRE) was deferred to a later time.

Abbreviations: PCa, prostate cancer; NE, neuroendocrine; NED, neuroendocrine differentiated; DRE, digital rectal exam; NE, neuroendocrine; ADT, androgen deprivation therapy.

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The patient returned to office a month later with lab results that showed an elevated PSA of 5.5 ng/mL and a sonogram report that was notable for an enlarged prostate as well as multiple hepatic masses suggestive of hepatocellular carcinoma or metastatic disease. On DRE, the prostate was non-tender, enlarged, firm, and irregular. A prostate biopsy and MRI were obtained a week later and the patient was instructed to follow-up for results. However, 2 days prior to follow-up the patient presented to the Emergency Department complaining of progressively worsening back pain over the past 3 weeks. Review of symptoms showed a 10 lb weight loss over the past 6 weeks, anorexia, fever, constipation, and dyspnea. Lab results showed WBC 15 K/ μ L, hemoglobin 9 g/dL, hematocrit 27.1%, creatinine 1.7 mg/dL, alkaline phosphatase 833 U/L, calcium 12.6 mg/dL, and PSA 6.5 ng/mL. The patient was admitted and treated for lower back pain, incontinence, and metastatic disease. MRI studies demonstrated diffuse hepatic metastasis and distal obstruction of the left ureterovesical junction, with further widespread bony metastasis to the thoracic and lumbar spine, as well as a recent T-12 fracture (Fig. 1). Radiation oncology was consulted at this time to provide palliative radiotherapy to metastatic sites in his spine.

Later that same day, the patient was reported to have hematuria and urology was consulted to perform continuous bladder irrigation. Around the time of urinary catheter insertion on the third day of hospitalization, the patient went into asystole and subsequently expired. The patient's family requested an autopsy.

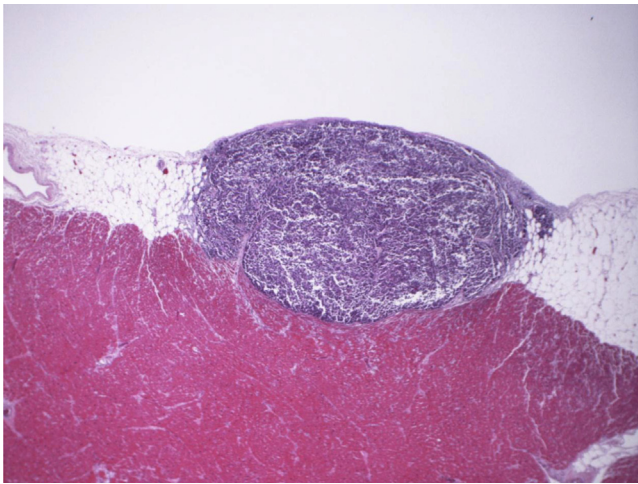


Figure 1. Microscopic examination of a single epicardial metastasis invading into myocardium.

Pathological findings

Upon microscopic examination of the prostate, the cancer was rated a Gleason score of 10 (5 + 5) in 11 of 12 cores with mixed conventional acinar adenocarcinoma and small cell NE carcinoma. Local invasion of the seminal vesicle and periprostatic fat was observed with extension into the serosal and subserosal surfaces of the bladder. Metastatic prostatic adenocarcinoma was identified on the epicardial surface of the heart invading into the myocardium (Fig. 1). Immunohistochemical studies of the cancer cells were diffusely positive for synaptophysin and chromogranin. Immunostains were also positive for PAP, but negative for PSA, CK7, CK20, p63, and TTF1.

Gross findings on the autopsy were widespread, involving cardiac, respiratory, hepato-biliary, adrenal, genitourinary and osseous tissue. Cardiac findings included a singular firm, tan nodule on the posterior epicardial surface. Respiratory findings included multiple subpleural nodules seen in bilateral, upper and lower lobes. Liver parenchyma and external surface had areas of pallor and multiple well circumscribed, metastatic nodules resulting in hepatomegaly (Fig. 2). The bladder was thin and distended with multiple solid irregular nodules distributed diffusely on the serosal surface. A 160 g blood clot was noted internally on section. The bladder mucosa was hemorrhagic with a polypoid mass that extended up from the prostate into the bladder. There were multiple metastatic nodules that invaded into the perineum between the rectum and the bladder. The thoracic-lumbar spine was found to have multiple areas metastasis with cortical destruction and evidence of a mild T12 fracture (Fig. 3).

Discussion

Neuroendocrine (NE) prostate carcinomas aggressively metastasize to the lymphatics, bone, bladder, vocal chords, and drastically reduce cancer specific survival.^{1,2} The epicardial metastasis of PCA as described herein is a rare occurrence that has scarcely been cataloged in clinical practice.

NE tumorigenesis does not result from the proliferation of prostate NE cells. Rather, this carcinoma arises from the differentiation of prostate adenocarcinoma into “NE-like” cells.¹ These cells do not express androgen receptors or PSA, elucidating why NE PCA is not responsive to aggressive androgen deprivation therapy (ADT) and is not associated with an elevated PSA.¹ In addition, several

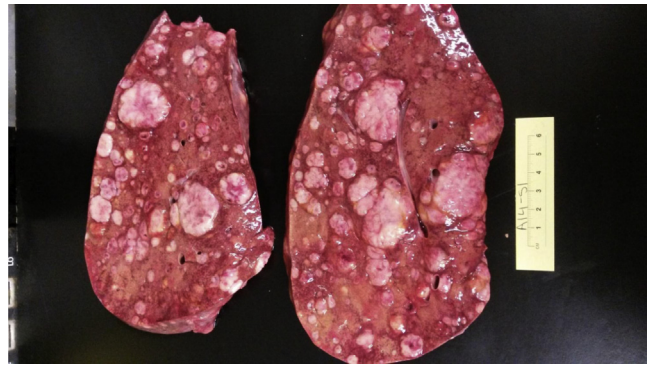


Figure 2. Coronal section of the liver showing diffuse metastasis and hepatomegaly.

series have suggested that ADT, the standard treatment in men with advanced PCa, may induce neuroendocrine differentiation.³ The vast majority of prostate cancers are adenocarcinomas, which rely on androgens to grow and proliferate. Nevertheless, nearly all tumors treated with hormones eventually develop resistance to androgen deprivation and can grow even in the absence of these hormones. Given that our patient had not received any hormonal treatment prior to diagnosis, his NE tumorigenesis likely developed spontaneously.

Since men rarely undergo prostate biopsy following metastasis, NE prostate cancers may be misclassified as simply metastatic-castration-resistant cancer, and so its detection rate is likely substantially lower than its incidence rate. This confusion is only further exacerbated by the similar aggressive nature of both of these subsets of disease. Since PCA with neuroendocrine differentiation does not present with high serum PSA, a high degree of clinical suspicion must be utilized to detect and eradicate this disease in its early stages. Metastasis-induced pericardial effusion is one of the first clinical signs of a cardiac malignant tumor and can be assessed for in patient with no history of neoplasms. Cross-sectional imaging such as CT or MRI may be utilized in place of serum biomarkers.⁴ Proper immunostaining is always recommended for young patients with high grade tumors in order to investigate the possibility of NED. In regards to our patient, a physical examination must include a DRE to rule out suspicion of PCA.



Figure 3. Metastatic lesions of the thoracolumbar vertebra and disc space on gross examination. There was evidence of a mild T12 fracture.

Currently, no consensus has been reached regarding the optimal management of NED PCa. However, physicians often adopt a multimodal approach, utilizing chemotherapy systemically and radiation for local control or palliation.

Conflicts of interest

The authors have no conflicts of interest to disclose.

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