





# Primary Large Cell Neuroendocrine Carcinoma of the Prostate Gland: An Uncommon Case

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## Abstract

Primary large cell neuroendocrine prostate cancer is a rare and aggressive cancer commonly observed as a transformation of an already known prostate adenocarcinoma and on long-term androgen deprivation, although it can arise de novo. It has high potential for distant metastatic spread and is generally associated with poor survival compared to the classical adenocarcinoma type of prostate cancer. We present a case of an 83-year-old who had orchidectomy for treatment of metastatic prostate adenocarcinoma with normalization of prostate-specific antigen levels and subsequently developed recurrence with large cell neuroendocrine transformation.

## Keywords

- ▶ large cell
- ▶ neuroendocrine
- ▶ primary
- ▶ prostate
- ▶ carcinoma

## Introduction

Neuroendocrine prostate cancer is rare; large cell neuroendocrine prostate cancer is even rarer.<sup>1</sup> Neuroendocrine prostate cancer accounts for approximately 0.5 to 2% of all prostate cancers and typically has a high metastatic potential with a preponderance of visceral metastases.<sup>1,2</sup> Large cell neuroendocrine prostate cancers are commonly observed as a transformation of an already known classical prostate adenocarcinoma and on long-term androgen deprivation, although they can arise de novo.<sup>3,4</sup> Neuroendocrine tumors differ from classical adenocarcinoma by the absence of prostate-specific antigen (PSA) secretion, resistance to hormone therapy, early metastasis, and rapid progression. They are also associated with poor survival compared to the adenocarcinomas. We present a case of metastatic large cell neuroendocrine prostate cancer transformation following orchidectomy for classical prostate adenocarcinoma.

## Case Description

The patient was an 83-year-old male under follow-up after orchidectomy treatment for metastatic classical prostate

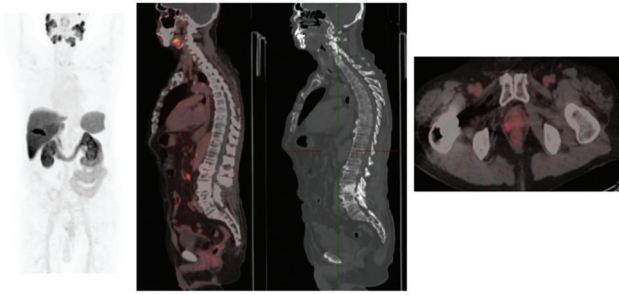
adenocarcinoma with initial PSA levels of 99 ng/mL. Follow-up PSA levels were normal, with the nadir recorded as 0.01 ng/mL, and an <sup>18</sup>F-PSMA positron emission tomography (PET)/computed tomography (CT) scan was unremarkable (▶ **Fig. 1**). He subsequently developed lower urinary tract symptoms of frequency, nocturia, and incomplete voiding, 2 years later. The PSA levels remained within normal range with the readings of 0.03, 0.02, and 0.02 ng/mL. A CT scan chest and abdomen done revealed an irregular, large prostate gland with liver and lung nodules suspicious for metastases. A repeat biopsy of the prostate and the liver lesions was performed, revealing a large cell neuroendocrine tumor of the prostate with metastases. He afterwards had an <sup>18</sup>F-PSMA PET/CT scan (▶ **Fig. 2**), which showed a large prostate gland mass with heterogeneous low-level PSMA ligand uptake, involving the seminal vesicles, urinary bladder, and the rectum, along with pelvic nodes, skeletal, lung, and nonavid liver metastases. A supplementary <sup>18</sup>F-FDG (<sup>18</sup>F-fluorodeoxyglucose) PET/CT scan (▶ **Fig. 3**) revealed intensely FDG-avid locally aggressive prostate gland disease extending to involve the rectum and urinary bladder with moderate right hydro-ureteronephrosis and intensely avid nodal, liver, lung, and skeletal metastases.

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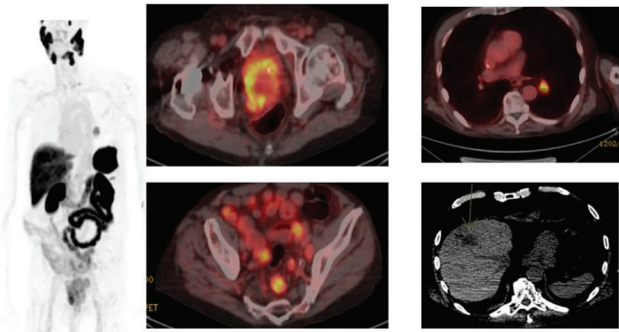
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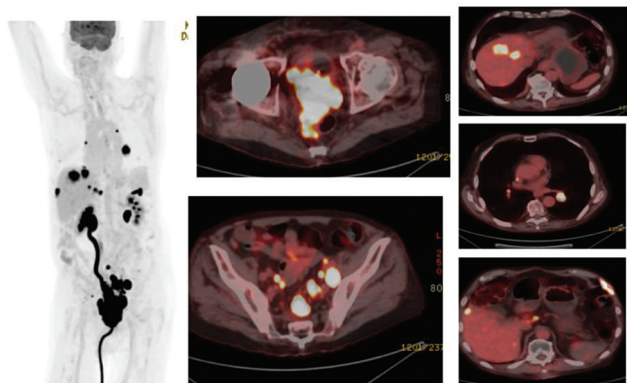
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**Fig. 1** Initial follow-up 18F-PSMA PET/CT scan, which was considered negative for disease recurrence. CT, computed tomography; PET, positron emission tomography.



**Fig. 2** 18F-PSMA PET/CT done 2 years later showing a large prostate gland mass with heterogeneous low-level PSMA ligand uptake, pelvic nodes, skeletal, lung, and non-avid liver metastases. CT, computed tomography; PET, positron emission tomography.



**Fig. 3** Supplementary 18F-FDG PET/CT revealing intensely FDG-avid locally aggressive prostate gland disease extending to involve the rectum and urinary bladder with moderate right hydronephrosis and intensely avid nodal, liver, lung, and skeletal metastases. CT, computed tomography; PET, positron emission tomography.

## Discussion

Large cell neuroendocrine carcinoma is an exceedingly rare subtype of neuroendocrine prostate cancer.<sup>5</sup> Other subtypes of neuroendocrine prostate cancer include usual adenocarcinoma with neuroendocrine differentiation, adenocarcinoma with Paneth-like cell neurodifferentiation, well-differentiated neuroendocrine tumor (carcinoid tumor), and small cell neuroendocrine carcinoma.<sup>1,6</sup> Histologically, large cell neuroendocrine prostate cancers show neuroendocrine differentiation

with large polygonal cells, abundant cytoplasm, and nuclei that contain coarse chromatin and a prominent nucleolus.<sup>1</sup>

Although they can arise de novo, large cell neuroendocrine prostate cancers are commonly observed as a transformation of an already known classical prostate adenocarcinoma and on long-term androgen deprivation.<sup>3,4,7,8</sup> Neuroendocrine manifestations of prostate cancer are increasing because of the prolongation of survival and the use of new hormone therapies.

Clinically, neuroendocrine prostate cancer is suspected when a prostate cancer is seen with absent or a low/moderate rise in PSA, presents at an advanced stage, or has a preponderance of visceral metastasis.<sup>1</sup>

There are only a few reports on neuroendocrine differentiation of the prostate gland on PET/CT imaging. Dual imaging with FDG PET/CT and PSMA PET/CT or SSRT PET (somatostatin receptor-targeted PET) is of significant value because it allows whole-body tumor grading, prognostication, and assessment of tumor heterogeneity. Neuroendocrine prostate cancer tends to have low avidity in PSMA PET imaging.<sup>9</sup> Some low-grade neuroendocrine tumors may not be intensely FDG-avid and rather may be more intensely avid on SSRT PET. This is useful in determining the mode of treatment, just like in other neuroendocrine tumors where <sup>177</sup>Lu-dotatate therapy can be utilized. It also remains a promising area given the poor prognosis of these tumors and the potential efficacy of <sup>177</sup>Lu-dotatate therapy. In our case, the patient had an FDG PET/CT scan that showed intense FDG uptake with mild avidity on PSMA PET, suggesting poor differentiation of the disease.

## Conclusion

Primary neuroendocrine prostate cancer is a rare entity; specifically, large cell neuroendocrine prostate cancer is extremely rare and quite aggressive, with a poor prognosis and very few reported cases. These types of cancers should be suspected in individuals presenting with prostate gland cancer, insignificant elevations of serum PSA even with high tumor volume, low avidity on PSMA PET/CT, and a preponderance for visceral metastases.

### Authors' Contributions

All authors contributed to the content, design, literature search, article preparation and writing, article editing, and article review. The article has been approved by all the authors. Each author believes that the article represents honest work.

### Conflict of Interest

None declared.

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