IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 9 Ser. 1 (September. 2025), PP 22-25
www.iosrjournals.org

A Rare Case Of Large Cell Prostate Neuroendocrine Carcinoma: Case Report And Review Of Literature.

Aymane Bijbij[1], Monsif Salek[2], Habib Belamlih[3], Soufiane Belabbes[4], Taoufik Africha[5]

Department Of Diagnostic And Interventional Radiology, Military Hospital Of Meknès, Hassan II University Hospital, Fez, Morocco
Faculty Of Medicine And Pharmacy, Sidi Mohamed Ben Abdellah University, Fez, Morocco

Abstract:
Large cell prostate neuroendocrine carcinoma (LCNEC) stands as a rare and exceptionally aggressive malignancy. This case report details a 68 year old morrocan male who presented with intermittent gross hematuria and perineal pain persisting for six months. PSA level was 90 ng/ml, a digital rectal examination revealed a substantial and indurated prostate mass. Cystoscopy revealed a large and irregular prostate that invaded the bladder trigone. The patient underwent transurethral resection of the prostate and histological analysis of the shavings revealed a high-grade large cell neuroendocrine carcinoma through histopathological analysis. Immunohistochemical markers demonstrated positivity for synaptophysin. Notably, Uroplakine GATA3 and chromogranin A markers were negative.
Contrast-enhanced computed tomography of the thorax, abdomen, and pelvis (CT TAP) demonstrated locally advanced prostate tumor process with hepatic, pulmonary, bone and lymph node metastases, responsible for moderate left uretero-hydronephrosis, classified T4N1M1. A collaborative decision, following a multidisciplinary team discussion, prescribed concluded to postpone chemotherapy in view of the alteration in the patient's general condition and to start hormonal treatment, symptomatic treatment and care with active monitoring pending improvement in his condition. During the two months following his admission and diagnosis, the patient died following a rapid worsening of his clinical condition.
The management of LCNEC lacks consensus, particularly in advanced (stage IV) cases, where chemotherapy becomes a primary approach. This malignancy, characterized by its high aggressiveness, presents a grim prognosis and remains unresponsive to hormonal therapy.

Keywords: *Prostate neuroendocrine tumor, Large cell carcinoma, immunohistochemical markers, synaptophysin, chromogranin A*

Date of Submission: 25-08-2025 Date of Acceptance: 05-09-2025

I. Introduction:

Prostate carcinoma stands out as the prevailing non-cutaneous malignancy and ranks as the second leading cause of cancer-related mortality among men in Western countries (1, 2). Recent data from the Malaysia National Cancer Registry spanning 2012 to 2016 revealed its prominence as the seventh most prevalent cancer across all populations (3.6%) and the third among men (7.7%) (3–6). The predominant subtype is adenocarcinoma, commonly originating in the glandular region (7). Normal prostatic tissue incorporates neuroendocrine cells, typically situated in periurethral and ductal regions (8, 9).

The spectrum of neuroendocrine prostate carcinoma encompasses a transition from prostate adenocarcinoma to large cell carcinoma, occurring either in pure or mixed forms. Notably, primary Large cell prostate neuroendocrine carcinoma is an exceedingly rare entity, with occurrences either de novo or emerging in later stages (9–12). In this report, we present a distinctive case of locally advanced (cT4) large cell prostate neuroendocrine carcinoma prostate cancer—an unusual finding given the typical aggressiveness of the disease and its tendency to manifest with distant metastasis.

II. Case Report:

A 68-year-old Moroccan male, previously unafflicted by medical conditions or familial malignancies, presented with a six-month history of recurring gross hematuria and perineal pain. Absent constitutional or additional complaints, a digital rectal examination disclosed a sizable and indurated prostate mass. The prostate-specific antigen (PSA) level measured 90 ng/ml. Subsequent to this, a cystoscopy revealed a large and irregular prostate that invaded the bladder trigone. The patient underwent transurethral resection of the prostate and

histological analysis of the shavings revealed a high-grade large cell neuroendocrine carcinoma. Immunohistochemical markers demonstrated positivity for synaptophysin. Notably, Uroplakine GATA3 and chromogranin A markers were negative.

Thoraco-abdomino-pelvis contrast-enhanced computed tomography (CT) scan illustrated demonstrated locally advanced prostate tumor process with hepatic, pulmonary, bone and lymph node metastases, responsible for moderate left UHN, classified T4N1M1 (Figure 1-2).

In a multidisciplinary consultation, A collaborative decision, following a multidisciplinary team discussion, prescribed concluded to postpone chemotherapy in view of the alteration in the patient's general condition and to start hormonal treatment, symptomatic treatment and care with active monitoring pending improvement in his condition.

During the two months following his admission and diagnosis, the patient died following a rapid worsening of his clinical condition.

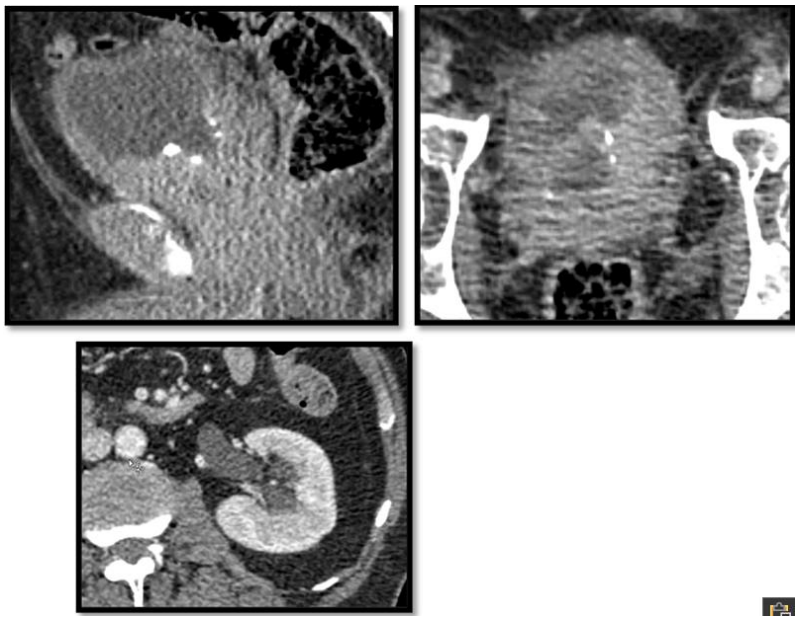

FIGURE 2 : CT of pelvis with sagittal and axial reconstruction. Locally advanced prostatic cancer with bladder trigone and lateral wall invasion, responsible for moderate homolateral uretero-hydronephrosis.

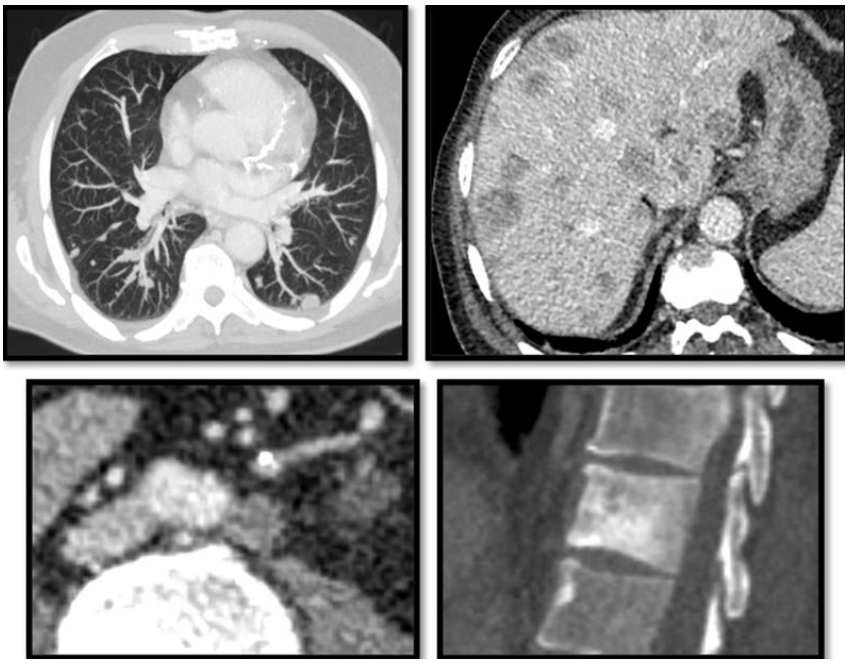

FIGURE 3: Thoracic-abdominal-pelvic enhanced CT scan showing lung, liver, bone and para-aortic lymph node metastases

III. Discussion:

LCNEC is an exceedingly rare entity, especially when arising de novo. This entity is so rare that there are just a few case reports in the literature. The largest series of LCNEC described only seven cases. These case were identified using the histologic criteria of LCNEC of the lung described by Travis et al: large polygonal cells with low nuclear to cytoplasmic ratio, nuclei with prominent nucleoli and coarse chromatin, mitotic count greater than 10 mitosis per 10 high power fields, and evidence of neuroendocrine differentiation by immunohistochemistry or ultrastructurally.

Patients with primary LCNEC commonly present with symptoms related to an enlarged prostate, manifesting as lower urinary tract symptoms (LUTS), with changes in the stream of urination being the most prevalent (1,2). The gold standard for diagnosis remains biopsy, revealing distinctive histological features such as a high nuclear/cytoplasmic ratio, nuclear molding, increased mitotic figures, and necrosis. Immunohistochemical markers, including chromogranin A, synaptophysin, and neuron-specific enolase, play a pivotal role in confirming the diagnosis, with synaptophysin being the most sensitive and chromogranin A being the most specific. Notably, neuroendocrine tumors lack androgen receptors and do not secrete PSA. Serum PSA levels do not correlate with disease burden (3, 4, 5, 6).

Ongoing studies explore non-invasive diagnostic tools for prostatic neuroendocrine tumors, employing serum biomarkers like chromogranin A, synaptophysin, neuron-specific enolase, and CD56 for prognostic screening (6). Chromogranin A, in particular, has emerged as the most reliable serum marker (3).

In the diagnostic landscape, imaging techniques such as PET/CT and metabolic MRI are being investigated as alternatives to prostatic biopsy for neuroendocrine tumors. While CT has a limited role in LCNEC detection, it is important for detection of distant metastasis and staging and not recommended for diagnosis (7). PET/CT and PET/MRI, especially for distant extraprostatic staging, have demonstrated significant value. mpMRI, now considered the technique of choice for initial and local tumor staging, differentiates prostatic carcinoid from adenocarcinoma based on size and hyperintensity on T2W images. Biopsy guided by MRI-TRUS fusion has gained prominence for increased accuracy and precision. (7)

The advent of somatostatin receptor analogs labeled with gallium-68 for PET imaging, such as DOTATE, has enhanced sensitivity in neuroendocrine tumor diagnosis as compared to planar and single-photon emission computed tomography (SPECT) imaging. ^{177}Lu-DOTATE is also being used as a therapeutic agent in neuroendocrine tumors. However, their widespread availability remains a challenge. (8,9)

Therapeutically, the management of neuroendocrine tumors lacks consensus compared to adenocarcinoma. For localized disease, prostatectomy post-neoadjuvant chemotherapy is a consideration (10). However, in advanced stages, chemotherapy, primarily platinum-based regimens like cisplatin (11), takes precedence. The National Comprehensive Cancer Network (NCCN) recommends combinations like cisplatin and etoposide or docetaxel (11,12,13). Carboplatin is an alternative, often combined with concurrent radiation. Despite these efforts, overall survival remains modest, ranging from 9 to 13 months. Half of the patients with prostatic neuroendocrine tumors exhibit mixed types, incorporating adenocarcinoma, and hormonal therapy is employed in these cases. A notable challenge is the lack of a standardized study differentiating metastasis from distant sites and primary neuroendocrine carcinoma.

Recent studies propose a "tumor cell autonomous" phase in the development of prostate neuroendocrine tumors, marked by an enrichment of androgen-negative cells and mutations in tumor-suppressor genes like *RB* and *p53*. Resulting in genetic instability and influencing genes involved in the cell cycle, particularly during the transition to the M-phase, such as aurora kinase A (AURKA) and proline kinase 1 (PLK1). As reported by Beltran et al., the amplification of MYCN in cancer cells induces a neuroendocrine characteristic, thereby enhancing our comprehension of the molecular underpinnings of neuroendocrine tumors. This insight paves the way for targeted therapies and a deeper exploration of tumor behavior. For example, using *AURKA* inhibitors such as danusertib, has been proposed in clinical trials (14). The current hurdle involves discerning the distinction between metastasis from distant sites and primary neuroendocrine carcinoma, necessitating further research.

IV. Conclusion:

In summary, this case report highlights the rarity of a locally advanced lage cell prostate neuroendocrine carcinoma with bladder invasion, with distant metastasis. The atypicality of diagnosing a locally advanced case unaccompanied by distant spread underscores the aggressive nature of this disease. Low PSA levels coupled with a prostate mass on examination should prompt suspicion of neuroendocrine prostate cancer, but high PSA levels like in our case should not exclude it. The diagnostic process involves a combination of clinical and radiological assessments, with definitive confirmation through histopathological examination. Techniques such as TRUS biopsy, multiparametric MRI, and MRI-TRUS fusion biopsy are increasingly pivotal in both imaging evaluation and disease management.

Multidisciplinary collaboration is imperative in managing this complex disease. However, due to its rarity, a consensus on management strategies remains elusive. In advanced stages (stage IV), chemotherapy, mirroring approaches used in small cell lung carcinoma, emerges as the primary modality. The disease's highly aggressive nature, coupled with a poor prognosis and resistance to hormonal therapy, accentuates the need for novel therapeutic approaches. Ongoing clinical trials exploring targeted therapies, such as AURKA inhibitors like danusertib, underscore the evolving landscape of potential treatment options. As we navigate the challenges posed by this infrequent malignancy, ongoing research efforts are crucial for refining management strategies and improving outcomes for individuals facing this formidable disease.

References :

[1]. Singam P, Hong GE, Ho C, Hee TG, Jasman H, Inn FX, Et Al.. Nocturia In Patients With Benign Prostatic Hyperplasia: Evaluating The Significance Of Ageing, Co-Morbid Illnesses, Lifestyle And Medical Therapy In Treatment Outcome In Real Life Practice. Aging Male (2015) 18(2):112–7. Doi: 10.3109/13685538.2015.1011614 [Pubmed] [Crossref] [Google Scholar]

[2]. Ho LY, Chu PSK, Consigliere DT, Zainuddin ZM, Bolong D, Chan CK, Et Al.. Symptom Prevalence, Bother, And Treatment Satisfaction In Men With Lower Urinary Tract Symptoms In Southeast Asia: A Multinational, Cross-Sectional Survey. World J Urol (2018) 36(1):79–86. Doi: 10.1007/S00345-017-2097-2 [Pubmed] [Crossref] [Google Scholar]

[3]. Grigore AD, Ben-Jacob E, Farach-Carson MC. Prostate Cancer And Neuroendocrine Differentiation: More Neuronal, Less Endocrine? Front Oncol (2015) 5(FEB). Doi: 10.3389/Fonc.2015.00037 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[4]. Kránitz N, Szepesváry Z, Kocsis K, Kullmann T. Neuroendocrine Cancer Of The Prostate. Pathol Oncol Res (2020) 26(3):1447–50. Doi: 10.1007/S12253-019-00712-2 [Pubmed] [Crossref] [Google Scholar]

[5]. Berruti A, Vignani F, Russo L, Bertaglia V, Tullio M, Tucci M, Et Al.. Prognostic Role Of Neuroendocrine Differentiation In Prostate Cancer, Putting Together The Pieces Of The Puzzle. Open Access J Urol (2010) 109–24. Doi: 10.2147/OAJU.S6573 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[6]. Li Q, Zhang CS, Zhang Y. Molecular Aspects Of Prostate Cancer With Neuroendocrine Differentiation. Chin J Cancer Res (2016) 28:122–9. AME Publishing Company. Doi: 10.3978/J.Issn.1000-9604.2016.01.02 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[7]. Taher A, Jensen CT, Yedururi S, Surasi DS, Faria SC, Bathala TK, Et Al.. Imaging Of Neuroendocrine Prostatic Carcinoma. Cancers (2021) 13(22):5765. Doi: 10.3390/Cancers13225765 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[8]. Ballinger JR. Theranostic Radiopharmaceuticals: Established Agents In Current Use. Br J Radiol (2018) 91(1019):20170969. Doi: 10.1259/Bjr.20170969 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[9]. Desai H, Borges-Neto S, Wong TZ. Molecular Imaging And Therapy For Neuroendocrine Tumors. Curr Treat Options Oncol (2019) 20(10). Doi: 10.1007/S11864-019-0678-6 [Pubmed] [Crossref] [Google Scholar]

[10]. Kránitz N, Szepesváry Z, Kocsis K, Kullmann T. Neuroendocrine Cancer Of The Prostate. Pathol Oncol Res (2020) 26(3):1447–50. Doi: 10.1007/S12253-019-00712-2 [Pubmed] [Crossref] [Google Scholar]

[11]. Spetsieris N, Boukovala M, Patsakis G, Alafis I, Efstathiou E. Neuroendocrine And Aggressive-Variant Prostate Cancer. Cancers (2020) 12:1–20. MDPI AG. Doi: 10.3390/Cancers12123792 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[12]. Patel GK, Chugh N, Tripathi M. Neuroendocrine Differentiation Of Prostate Cancer— An Intriguing Example Of Tumor Evolution At Play. Cancers (2019) 11(10):1405. MDPI AG. Doi: 10.3390/Cancers11101405 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[13]. Conteduca V, Oromendia C, Eng KW, Bareja R, Sigouros M, Molina A, Et Al.. Clinical Features Of Neuroendocrine Prostate Cancer. Eur J Cancer (2019) 121:7–18. Doi: 10.1016/J.Ejca.2019.08.011 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]

[14]. Logothetis CJ, Gallick GE, Maity SN, Kim J, Aparicio A, Efstathiou E, Et Al.. Molecular Classifi Cation Of Prostate Cancer Progression: Foundation For Marker-Driven Treatment Of Prostate Cancer. Cancer Discov (2013) 3:849–61. Doi: 10.1158/2159-8290.CD-12-0460 [PMC Free Article] [Pubmed] [Crossref] [Google Scholar]