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NEUROENDOCRINE CARCINOMA OF THE PROSTATE: A RARE AGGRESSIVE VARIANT WITH DIAGNOSTIC INSIGHTS

Pathology

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ABSTRACT

Neuroendocrine prostate cancer is a rare and highly aggressive malignancy with poor prognosis. It comprises less than 1% of all prostate cancer and the mean age of presentation is 68.3 years. We report a case of a 68-year-old male, known case of advanced carcinoma prostate who presented with lower urinary tract obstruction and normal prostate specific antigen (PSA) levels. On digital rectal examination a tender, hard prostate mass was found, prompting further imaging studies and subsequent transuretheral resection of prostate. Histopathological evaluation, supported by immunohistochemical analysis, confirmed the diagnosis of small cell neuroendocrine carcinoma of the prostate. Management involved a multidisciplinary approach, with chemotherapy serving as the primary treatment modality. This case underscores the importance of considering neuroendocrine differentiation in the differential diagnosis of prostatic masses, particularly in patients presenting with advanced disease and disproportionately low PSA levels.

KEYWORDS

Prostate, neuroendocrine tumor, NEPC, small cell carcinoma, PSA, IHC.

INTRODUCTION:

Prostate cancer is the leading cause of malignancy in males, with vast majority of cases comprising of the androgen sensitive adenocarcinoma subtype.[1] Neuroendocrine prostate cancer (NEPC) is a rare and highly malignant tumor representing less than 1% of all prostate cancers with an annual incidence of 35 per 10,000.[2] Neuroendocrine tumors originating from various anatomical regions including larynx, esophagus, urinary bladder and urogenital system have been extensively documented in the literature.[3] The average age at which individuals present with symptoms is approximately 68 years (range: 59-79 years).[4] Diagnosis of small cell neuroendocrine prostate carcinoma is mainly based on histopathology and ancillary techniques like immunohistochemistry (IHC). NEPC exhibits a remarkably aggressive behavior and is associated with poor prognosis. Following diagnosis, average survival duration is merely 1 to 2 years.[2]

CASE REPORT:

A 68-year-old male, presented with chief complaint of lower urinary tract obstruction. Both general physical and systemic examinations were within normal limits. Laboratory investigations, including complete blood count, renal function tests and liver function tests, all showed values within the normal range including PSA which was 0.98 ng/ml. A digital rectal examination (DRE) was performed, revealing a large, tender and hard prostate mass.

Magnetic resonance imaging (MRI) of the prostate showed a prostate mass with invasion to the rectum, while contrast-enhanced computed tomography of the thorax, abdomen, and pelvis ruled out any distant metastasis.

Transuretheral resection of prostate (TURP) was performed and chips were sent for histopathological examination. Microscopic examination revealed sheets and nests of small round cells with intervening stroma. These tumor cells had high N:C ratio, scant cytoplasm, pleomorphic nuclei, nuclear moulding and granular chromatin (Fig.1 A&B). Immunohistochemical markers were positive for CD56, synaptophysin, chromogranin. However, AMACR, NKX3.1, GATA3, PSA were negative on IHC. Based on histomorphological features and IHC findings, a final diagnosis of small cell neuroendocrine carcinoma of prostate was made.

Patient subsequently underwent a regimen of chemotherapy, followed by radiotherapy. However, following discharge, the patient died within six months.

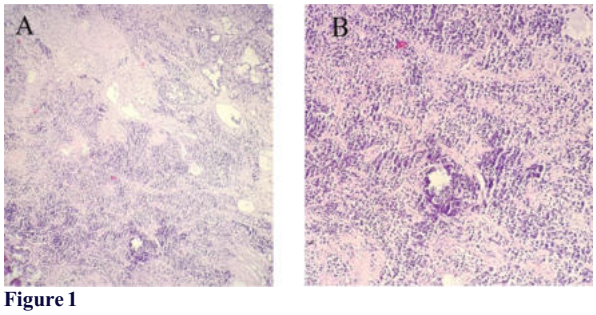

Figure 1

A) Sections show sheets and nests of small, round to oval cells with intervening stroma. (H&E, 200X)

B) Uniform tumor cells having high N:C ratio, nuclear molding, hyperchromatic nuclei with stippled chromatin and scant amount of cytoplasm. (H&E, 400X)

DISCUSSION:

Prostate cancer is the most common extracutaneous malignancy in males. Majority of prostate malignancy are of adenocarcinoma subtype, which are androgen driven tumors.[1] Small cell neuroendocrine prostate cancer is an uncommon, highly aggressive variant comprising of less than 1% of prostatic malignancies.[2] It was first described by Wenk et al in 1977.[5]

The pathogenesis underlying the development of neuroendocrine prostate cancer remains unclear.[4] Various hypotheses have been proposed regarding the origin of neuroendocrine subtype. One hypothesis suggests that NEPC typically emerges from adenocarcinoma following androgen deprivation therapy, characterized by the loss of tumor suppressor genes such as TP53 and RB.[6] This genetic alteration leads to instability and impacts cell cycle regulation.[5] Notably, the classical association of prostate cancer with prostate-specific antigen (PSA) is frequently diminished during the progression of NEPC.[1] According to Balteran et al, MYCN amplification in tumor cells leads to the emergence of neuroendocrine characteristics, thereby contributing to the molecular basis of

neuroendocrine prostate cancer and its targeted therapies.[5] NEPC may infrequently arise from de novo mutations.[1] It presents diagnostic challenge due to normative prostate-specific antigen (PSA) levels and nonspecific clinical manifestations.[2]

The 2016 histological classification of urinary and genital tract includes well differentiated neuroendocrine tumors, small cell neuroendocrine carcinoma or large cell neuroendocrine carcinoma and adenocarcinoma with neuroendocrine differentiation which can be focal or show Paneth like cell features. Primary neuroendocrine tumors of the prostate can be pure or mixed (both neuroendocrine and glandular features in mixed pattern).[6]

The clinical presentation is non-specific and show similarity with other prostate tumours. Patient usually present with complaints related to enlarged prostate mass such as lower urinary tract symptoms, change in stream of urination, burning micturition, nocturia. Most patients are diagnosed in advanced stages and usually are unresectable.[5]

Radio imaging (USG, MRI, CT scan or PET-CT) plays crucial role in detecting, localizing and staging of NEPC.[5] However, imaging is not helpful for the diagnosis of NEPC because there are no distinctive radiological features for NEPC and other prostate tumours like adenocarcinoma, metastases.[1]

The diagnosis of NEPC mainly rely on histomorphology and IHC findings. Microscopically, sections examined show small, uniform, round to oval tumour cells arranged in sheets and nests with high N:C ratio, nuclear molding, inconspicuous nucleoli, scant cytoplasm and granular chromatin.[5]

NEPC diagnosis is established through a comprehensive evaluation of clinical and radiological findings, with final confirmation by histopathological analysis in conjunction with immunohistochemistry. Considering the overlapping clinical, radiological and morphological features, the differentials includes prostatic adenocarcinoma, mixed NEPC and metastatic NET.[1] Therefore, careful selection and use of panel of IHC markers are crucial for differentiating PNEC from its differential diagnosis. In our case positive expression of CD56, synaptophysin and chromogranin were noted. However, AMACR, NKX3.1, GATA3 and PSA were negative.

Neuroendocrine tumors are distinguished from adenocarcinomas by their absence of prostate-specific antigen (PSA) secretion, resistance to hormonal therapies, propensity for early metastasis, and rapid disease progression.[6]

Mixed NEPC exhibits elevated levels of prostate-specific antigen and prostatic acid phosphatase both of which are utilized for assessing therapeutic responses. Nevertheless, the treatment response and prognosis for mixed NEPC and small cell neuroendocrine prostate cancer are similar.[3]

The distinction of metastatic neuroendocrine tumor from primary NEPC relies on multimodal approach incorporating the patient's clinical history, prior treatments, biopsy, lineage specific immunomarkers and radio imaging tests.

Treatment of NEPC employs chemotherapy regimens similar to those employed for small cell lung cancer, given the notable similarities in their morphology and pathology. Immune checkpoint inhibitors and innovative biomarker targets are currently under investigation for prospective management strategies of NEPC. However, prognoses remain dismal, with a response rate of less than 50% observed in conventional platinum-based chemotherapy.[1]

CONCLUSION:

Small cell neuroendocrine carcinoma of the prostate is an exceedingly aggressive neoplasm associated with a dismal prognosis. Early detection remains challenging, as serum prostate-specific antigen levels are typically low or within the normal range. Therefore, digital rectal examination, advanced imaging modalities, and histopathological evaluation supported by an immunohistochemical panel constitute the gold standard for diagnosis. A multidisciplinary team discussion is essential to determine the optimal treatment strategy, which often involves concurrent chemotherapy and radiotherapy. This case underscores the importance of a comprehensive diagnostic approach for the accurate identification and management of neuroendocrine carcinoma of the prostate.

REFERENCES:

1. Nixon B, Aher A. Neuroendocrine prostate cancer: Report of a prostate cancer subtype with atypical metastatic imaging and clinical findings. Radiol Case. 2024;18(5):17-23.
2. Rahmani Y, Hafez YA, Agha A, Jarari MZ, Millan Basiliu NM, Azad EM et al. Denovo small cell prostate cancer: An atypical case presentation. Urol Case Rep. 2025; 59:102970. doi: 10.1016/j.eucr.2025.102970.
3. Demirtas A, Sahin A, Ozturk F, Akinsal EC, Demirtas T, Ekmekcioglu O et al. Small cell prostate carcinoma: A case report and review of literature. Case Rep Urol. 2013; 2013:387931. doi: 10.1155/2013/387931.
4. Kranitz N, Szepesvary Z, Kocsos K, Kullman T. Neuroendocrine cancer of prostate. Pathol Oncol Res. 2020; 26:1447-50.
5. Teh S, Inn FX, Rizuana IH, Muhaizan WM. A rare case of prostate neuroendocrine tumor: A case report. Front Oncol. 2022; 12:1009146. doi:10.3389/fonc.2022.1009146.
6. Jijhane C, Hajar M, Imane O, Oumaima S, Samia E, Samia M et al. Neuroendocrine prostate tumor: A case report and literature review. Afr J Med Pharma Rep. 2024;2(1)5-8.