Case Report

A rare presentation of neuroendocrine prostate carcinoma in young adult: A case report

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ABSTRACT

Neuroendocrine prostate carcinoma (NEPC) is an aggressive malignancy characterized by a poor prognosis and distinct clinical and histopathological features compared with the more common prostatic adenocarcinoma. We report a case of a 37-year-old male who presented with lower urinary tract symptoms and was initially managed as having high-grade invasive urothelial carcinoma of the bladder, but was ultimately diagnosed with high-grade neuroendocrine carcinoma of the prostate. This case highlights the diagnostic complexity arising from overlapping clinical and imaging findings with bladder carcinoma and underscores the importance of histopathological and immunohistochemical evaluation for accurate diagnosis. Despite aggressive therapy, the disease followed a rapid course, emphasizing the need for further research into more effective treatment strategies.

Key words: Immunohistochemistry, Neuroendocrine prostate carcinoma, Rare prostate malignancy

Neuroendocrine prostate carcinoma (NEPC) is a rare histology which may arise de novo (approximately 1%of all prostatic malignancies) or develop from pre-existing adenocarcinoma, often following androgen deprivation therapy (ADT), called as treatment-emergent (t-NEPC, accounting for 20% of all prostatic malignancy [1,2]. These tumors encompass a spectrum ranging from well-differentiated carcinoid tumors to highly aggressive small-cell carcinomas [3]. Typically, NEPCs are androgen receptor (AR)-negative and may present with atypical symptoms and low serum prostate-specific antigen (PSA) levels, creating diagnostic challenges. Early identification is crucial, as these tumors respond poorly to conventional hormonal therapies and are associated with a poor prognosis. Here, we present a rare and diagnostically challenging case of *de novo* NEPC in a young adult.

CASE REPORT

A 37-year-old male presented to a private clinic with symptoms of acute urinary retention, including suprapubic pain, increased urinary frequency, urgency, and intermittent hematuria. Ultrasonography revealed an enlarged prostate measuring approximately 53.1 cc in volume, with ill-defined hypoechoic right-sided lesions consistent with prostatic abscesses measuring about 33 × 37 mm. The patient's baseline PSA level was 0.52 ng/mL. He had no family history of malignancy and a Karnofsky Performance Status of 90.

He underwent a meatotomy followed by optical internal urethrotomy with drainage of the prostatic abscess and a transurethral resection of the prostate.

Histopathological examination initially suggested a diagnosis of high-grade invasive urothelial (transitional cell) carcinoma of the bladder.

The patient was subsequently evaluated at a tertiary care center for adjuvant therapy. Computed tomography (CT) of the abdomen and pelvis revealed a heterogeneously enhancing infiltrative mass lesion centered in the prostate, measuring 5.8 × 6.5 × 7 cm, with infiltration into the posterior-inferior wall and neck of the urinary bladder, posterior urethra, lateral pelvic wall, seminal vesicles, and transmural extension into the lower third of the anterior rectal wall (Fig. 1). Multiple variable-sized regional pelvic lymph nodes were also noted. Digital rectal examination revealed a hard, irregular prostate, while serial urine cytology was negative for malignant cells.

Whole-body positron emission tomography (PET) - CT scan demonstrated a hypermetabolic prostate mass (5.8 × 6.5 × 7 cm), pelvic lymphadenopathy involving bilateral external and internal iliac, obturator, peri-rectal, and pre-sacral lymph nodes, as well as multiple liver and lung lesions suggestive of metastatic disease.

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The patient was referred to the oncology department for further management. A second review of the histopathology slides (Fig. 2) showed fibromuscular stroma infiltrated by tumor nests composed of poorly differentiated atypical cells with mild anisonucleosis, round to oval nuclei, stippled chromatin, inconspicuous nucleoli, and granular cytoplasm, along with increased mitotic figures. The Ki-67 proliferation index was 36%. On immunohistochemistry (IHC), the tumor cells were diffusely positive for chromogranin, synaptophysin, and alpha-methylacyl-coenzyme A racemase, and negative for CK7, GATA3, and PSA, findings consistent with a diagnosis of NEPC.

The patient was initiated on platinum-based chemotherapy consisting of cisplatin (25 mg/m² IV, days 1–3) and etoposide (100 mg/m² IV, days 1–3) every 21 days. He has completed six cycles of chemotherapy, which he has tolerated well, and is currently awaiting response assessment imaging. Notably, his initial urinary symptoms improved following completion of the chemotherapy cycles.

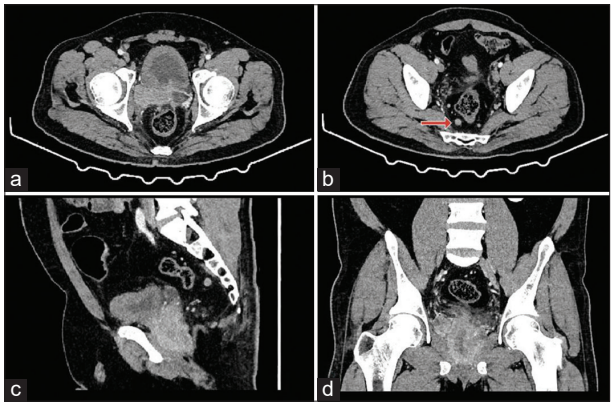

Figure 1: (a, b, c and d) Contrast-enhanced computed tomography of the abdomen and pelvis showed an enlarged prostate gland with a multilobulated appearance involving all zones, predominantly the peripheral zone, measuring 7.3 × 7.4 × 9.1 cm (volume: 255 cm³), with invasion of seminal vesicles, urinary bladder, posterior urethra, anterior rectal wall, and right lateral pelvic wall. (b) Multiple variable sized lymph nodes noted in peri-rectal, pre-sacral, obturator, and external iliac regions (Denoted by arrow)

DISCUSSION

NEPC is an uncommon but clinically significant subset of prostate cancers [2]. These tumors often present with non-specific urinary symptoms and demonstrate a poor correlation with PSA levels, which can delay diagnosis. Histologically, NEPCs are classified into well-differentiated (carcinoid) and poorly differentiated (small- or large-cell) neuroendocrine carcinomas, the later being associated with more aggressive behavior and a poorer prognosis [3]. According to the classification proposed by the Prostate Cancer Foundation, prostate carcinomas exhibiting neuroendocrine differentiation can present in several forms, including conventional adenocarcinoma with neuroendocrine features, Paneth cell–like variants, carcinoid tumors, small- and large-cell neuroendocrine carcinomas, and mixed histologies [4,5].

NEPC may arise *de novo*, without prior prostate adenocarcinoma or ADT, likely originating directly from neuroendocrine cells within the prostate, or as t-NEPC, which develops from pre-existing prostate adenocarcinoma as an adaptive response

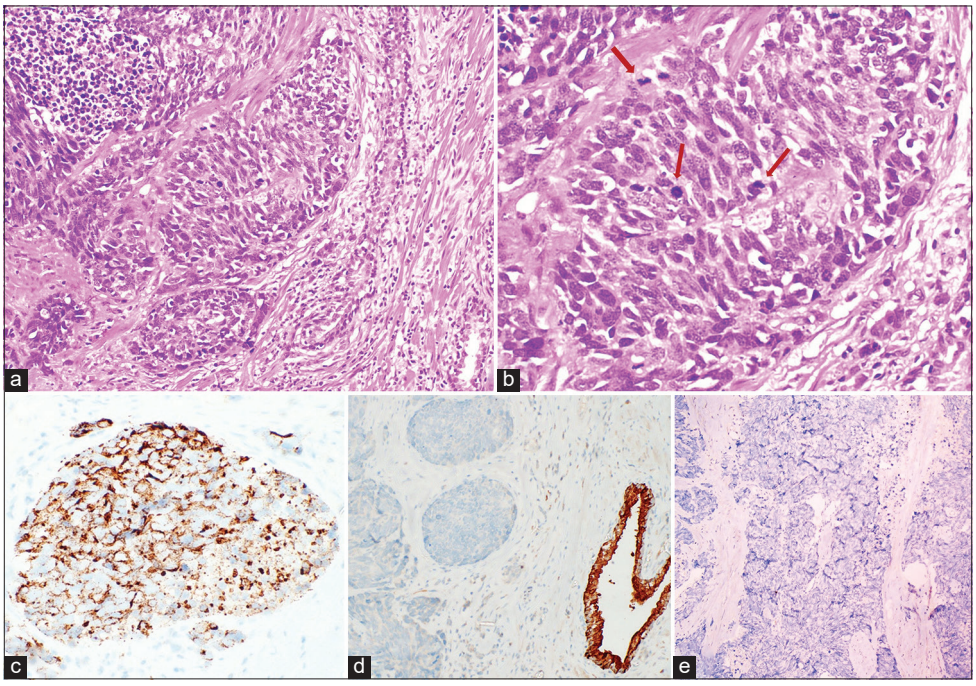

Figure 2: Histomorphology shows fibromuscular stroma and infiltrating tumor in nests (a; H&E stain; ×200). The tumor comprises atypical cells with mild anisonucleosis, round to oval nuclei, stippled chromatin, inconspicuous nucleoli, and granular cytoplasm (b; H&E stain; ×400). Increased mitotic figures were noted (marked with an arrow). On immunohistochemistry, the tumor cells are diffusely positive for chromogranin (c: CG; immunohistochemistry [IHC]; ×200) and negative for CK 7 (d: CK7; IHC; ×100) and prostate-specific antigen (e: PSA; IHC; ×100)

to prolonged ADT [3,6]. The incidence of *de novo* NEPC is approximately 1%, while that of t-NEPC is 15%–20% [5,7]. The pathophysiological mechanisms underlying t-NEPC include loss of AR signaling, *TP53* and *RB1* gene alterations, and amplification of MYCN and AURKA, which collectively drive tumor aggressiveness [8].

Initially, the tumor in this case was diagnosed as a transitional (urothelial-like) carcinoma, likely based on morphological features such as nested or solid growth patterns, prominent nucleoli, and scant cytoplasm, which can mimic urothelial differentiation, especially in poorly differentiated prostate malignancies. However, on second review, IHC revealed expression of neuroendocrine markers, supporting reclassification as NEPC. The second opinion was not have been performed in the same laboratory but incorporated additional ancillary testing, highlighting the diagnostic dilemma among poorly differentiated adenocarcinoma, urothelial carcinoma, and NEPC. This underscores the critical role of IHC in resolving morphological ambiguity and guiding appropriate management.

In this case, the patient's young age, low PSA level, positive immunohistochemical staining for synaptophysin and AMACR, and extensive local invasion in the absence of prior hormonal therapy support a diagnosis of *de novo* NEPC. Diagnostic confusion with urothelial carcinoma was compounded by overlapping radiological findings and the presence of urinary tract inflammation. The lack of PSA and GATA3 expression effectively ruled out typical prostatic adenocarcinoma and urothelial carcinoma, respectively.

At present, there is no standardized treatment for NEPC. These tumors typically do not respond to ADT due to the absence of AR expression. Chemotherapy with platinum-based regimens, most commonly cisplatin combined with etoposide or docetaxel, remains the mainstay of treatment, although outcomes are often unsatisfactory given the aggressive nature of the disease [9-11]. Prognosis remains poor, with median survival typically <1 year in metastatic cases [12-14]. This case emphasizes the need for further molecular studies to identify potential therapeutic targets and improve clinical outcomes.

CONCLUSION

NEPC, though rare, represents a distinct and aggressive form of prostate cancer with unique diagnostic and therapeutic challenges. Early recognition and tailored treatment are essential for optimal management; however, clinical outcomes remain poor. Greater awareness and continued research are crucial to improving prognosis and developing effective targeted therapies.

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