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Oncology

A rare case of de novo large cell neuroendocrine carcinoma of the prostate with long-term survival after cystoprostatectomy and androgen deprivation

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Introduction

More than 95% of prostate cancers are adenocarcinoma, and neuroendocrine carcinomas (NECs) are very rare, representing less than 1% of prostate cancers. Among NECs of the prostate including small cell carcinoma (SmCC), carcinoids, and large cell neuroendocrine carcinoma (LCNEC), LCNEC is extremely rare. Only 15 cases have been reported to date and their prognoses were very poor. Here, we report a patient with de novo LCNEC of the prostate that was successfully treated with radical surgery and adjuvant androgen deprivation therapy (ADT).

Case report

An 87-year-old man visited our outpatient clinic with chief complaints of voiding difficulty and gross hematuria in August 2014. He previously underwent left nephroureterectomy for a renal pelvic tumor in July 2010 and transurethral resection of the bladder tumor (TURBT) for a urinary bladder tumor in June 2014. The pathological findings were low-grade pTa urothelial carcinoma (UC) of the left renal pelvis and high-grade pTa UC of the urinary bladder, respectively.

The cystoscopy showed a sessile tumor on the neck of the urinary bladder, which we suspected as a muscle-invasive bladder cancer. The computed tomography and magnetic resonance imaging scans showed no evidence of metastases. The preoperative serum prostate-specific antigen (PSA) level was 3.3 ng/mL; however, the patient's prostate was found to be stony hard on a digital rectal examination. In October 2014, he underwent TURBT and the pathological findings indicated high-grade pT2 UC of the urinary bladder.

In November 2014, we performed radical cystoprostatectomy with urethrectomy, regional lymphadenectomy and right ureterocutaneostomy. The tumor was located mainly in the prostate and partially in the urinary bladder. The left side of the prostate firmly adhered to the pelvic wall, and it was difficult to peel off the site. Pathological findings were LCNEC with microscopic focus of acinar adenocarcinoma, Gleason score of 2 + 3, of the prostate. The LCNEC consisted of large tumor cells with high nucleus-to-cytoplasm (N/C) ratios, coarse nuclear chromatin, high mitotic rates, rosette structures, and fine granular cytoplasm (Fig. 1). The tumor replaced most of the prostate organ, confirming the origin as prostatic, invading into the urinary bladder. Immunohistochemical staining (IHS) of LCNEC and adenocarcinoma showed positivity for both PSA and androgen receptor (AR). Only the LCNEC showed positivity for CD56, chromogranin A, and synaptophysin. Two pathologists (KT and SM) independently diagnosed the patient with pT4 LCNEC and adenocarcinoma of the prostate with bladder invasion. A retrospective evaluation revealed that the muscle-invasive part in the previous TURBT specimen was LCNEC. Although there was no lymph node metastasis, the tumor had a positive surgical margin, perineural invasion, and extracapsular invasion; therefore, we started adjuvant ADT. Forty months after the surgery, the patient has survived with no evidence of tumor recurrence.

Discussion

NECs are rare histological types of prostate cancer with poor prognosis, and amongst them LCNEC is extremely rare. Fifteen cases have been reported to date. Ten cases occurred after long-term ADT, and five cases are de novo LCNEC.[1–4]

The clinical features of 6 case of de novo LCNEC including the present case are shown in Table 1. Azad et al. reported that ADT is likely effective for de novo LCNEC because such tumors remain androgen-dependency.[1] Of five patients with de novo LCNEC whose

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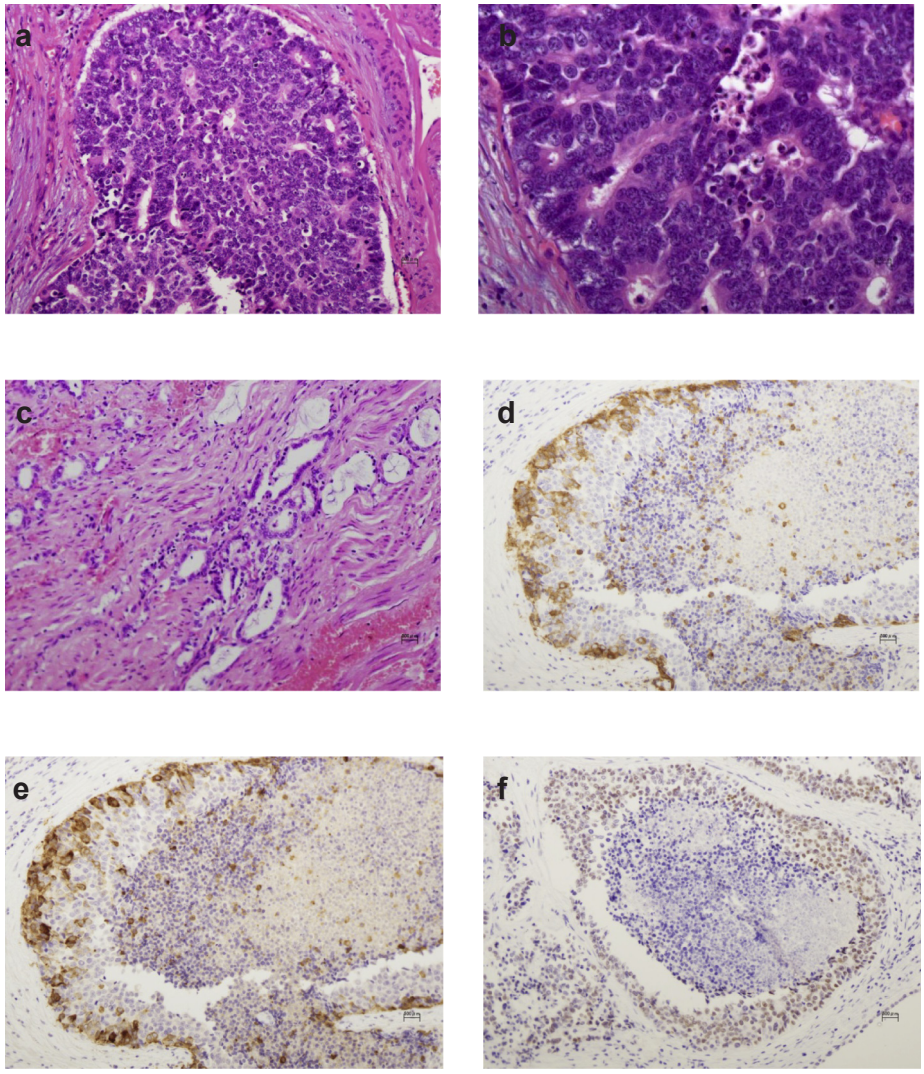

Fig. 1. Hematoxylin-Eosin staining of cystoprostatectomy specimen exhibits infiltration of tumor cells in solid nests showing rosette structures (magnitude, 100×) (a). High power view of the cancer shows large tumor cells with high mitotic rate and fine granular cytoplasm (magnitude, 200×) (b). Microscopic focus of acinar adenocarcinoma (magnitude, 200×) (c). Immunohistochemical staining shows positivity for synaptophysinin (d), chromogranin A (e), and AR in the LCNEC (magnitude, 200×) (f).

Table 1
Clinical Parameters and IHS features of LCNEC patients.

Case	Age (years)	PSA (ng/mL)	Treatment after diagnosis	Outcome	Observation period	IHC of AR
No.1	69	4.3	RP→Craboplatin + Etoposide	DOD	Average 7 months after chemotherapy[a]	N/A
No.2	70	9.6	ADT	Alive	15 months	N/A
No.3	71	170	ADT	Alive	30 months	N/A
No.4	66	97	N/A	N/A[b]	N/A	+
No.5	48	N/A	Cisplatin + Etoposide + Paclitaxel + ADT→RP	DOD	13 months	N/A
Present case	87	3.3	Cystoprostatectomy→ADT	Alive	45 months	+

AbbreviationsIHC, immunohistochemical staining; LCNEC, large cell neuroendocrine carcinoma; PSA, prostate specific antigen; AR, androgen receptor;RP, radical prostatectomy; DOD, died of disease; N/A, not applicable; ADT, androgen deprivation therapy.

[a] The observation period of cases is described collectively with other 6 cases, not respectively.

[b] There is no description of outcome after diagnosis.

prognoses were available in detail, three are alive without progression for more than 1 year. Although LCNEC generated after long-term ADT has a miserable prognosis,[4] it is considered that de novo LCNEC has a relatively good prognosis.

IHS of AR was performed for two patients and both of them were positive for AR. Neuroendocrine cells, which commonly exist in prostate tissue including prostate cancer, and NEC cells are generally negative for AR and are considered androgegn-independent.[5] The expression of ARs on IHS indicates androgen-dependency in hormone naïve prostate cancer. AR-positivity of NEC also suggegsts androgen-dependency and efficacy of ADT. The long survival of the present AR-positive and surgical margin-positive LCNEC of the prostate after adjuvant ADT supports the hypothesis.

Conclusion

LCNEC of the prostate is extremely rare. Most of cases present secondary to long-term ADT and the prognoses are generally very poor. This case suggests effectiveness of ADT for androgen-dependent LCNEC of the prostate. Androgen receptor-staining may be useful to predict efficacy of ADT on LCNEC of the prostate.

Conflicts of interest

None declared.

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