Case Report

A case of neuroendocrine tumor at the external urethral meatus after total cystectomy

Koji Miki,[1] Kazutoshi Fujita,[1] Ken Kuwahara,[1] Shogo Adomi,[1] Takafumi Minami,[1] Masahiro Nozawa,[1] Kazuhiro Yoshimura,[1] Misa Kojima,[2] Osamu Maenishi[2] and Hirotsugu Uemura[1]

Departments of [1]Urology and [2]Pathology, Kindai University Faculty of Medicine, Osakasayama, Japan

Abbreviation & Acronyms
CIS = carcinoma in situ
MRI = magnetic resonance imaging
CD56 = cluster of differentiation 56

Correspondence: Kazutoshi Fujita M.D., Ph.D., Department of Urology, Kindai University Faculty of Medicine, 377-2 Ohno-higashi, Osaka-Sayama 589-8511, Osaka, Japan. Email: kazu.fujita2@gmail.com

How to cite this article: Miki K, Fujita K, Kuwahara K *et al*. A case of neuroendocrine tumor at the external urethral meatus after total cystectomy. *IJU Case Rep*. 2023; 6: 424–427.

Received 7 July 2023; accepted 25 August 2023.
Online publication 9 September 2023

Introduction: The histological types of urethral cancer are mainly squamous cell or transitional cell carcinoma. Neuroendocrine tumor is extremely a rare type of urethral cancer.

Case presentation: A 72-year-old man visited with an erythema at the external urethral meatus. After 3 months, a 1-cm reddish solid tumor was found on the external urethral meatus. He had a history of bladder cancer (pTa with carcinoma in situ), including the prostatic urethra, and underwent radical cystectomy with urethrectomy and ileal conduit construction 11 years ago. After 3 months, a 1-cm reddish solid tumor was found on the external urethral meatus. The pathological diagnosis was a neuroendocrine tumor. Partial penectomy was performed.

Conclusion: Small cell neuroendocrine tumor could occur on urethral remnant after radical cystectomy with urethrectomy for urothelial cancer. Inspection of the penis and urethral meatus is important during regular follow-up of patients after radical cystectomy.

Key words: N: neuroendocrine tumor, R: radical cystectomy, T: total cystectomy, U: urethral cancer, U: urethrectomy.

Keynote message

Neuroendocrine tumors arising in the urethra are rare, with only nine reported cases documented to date. Among these cases, two individuals had a previous history of bladder cancer. Hence, we aimed to explore the potential relationship between neuroendocrine tumors of the urethra and bladder cancer development.

Introduction

The histological types of urethral cancer are mainly squamous cell carcinoma, transitional cell carcinoma, and adenocarcinoma.[1] Neuroendocrine tumor is extremely a rare type of urethral cancer. Herein, we reported a case of small cell neuroendocrine tumor found in the external urethral orifice after 11 years radical cystectomy and ileal conduit construction.

Case presentation

A 72-year-old male patient visited with an erythema at the external urethral meatus. He had the history of bladder cancer with CIS (pTa with CIS) involving the bladder trigone, left wall, neck, and prostatic urethra and had undergone radical cystectomy with urethrectomy, and ileal conduit construction 11 years ago. After 3 months, a 1-cm reddish, solid tumor was found on the external urethral meatus. (Fig. 1). Pelvic MRI showed that the tumor was limited to the glans penis on T2-weighted imaging, with no corpus cavernosum invasion, and showed a high signal intensity only in the tumor on diffusion-weighted imaging (Fig. 2). A biopsy of the tumor was performed, and tumor cells were mainly small cells and immunohistochemical analysis showed that tumor cells were positive for CD56, synaptophysin, and chromogranin A. The pathological diagnosis was a neuroendocrine tumor (Fig. 3).

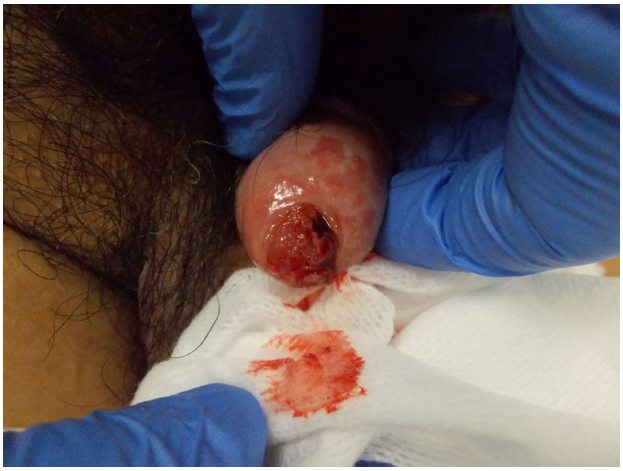

Fig. 1 Firm, reddish, protruding mass measuring 1 cm is observed at the external urethral orifice.

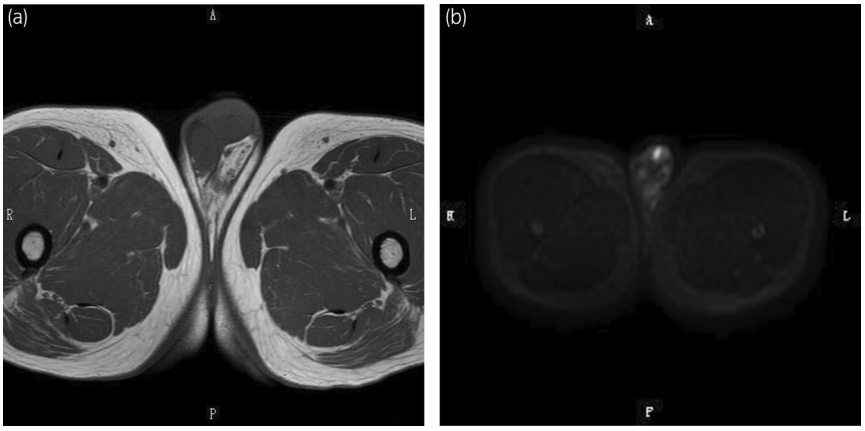

Fig. 2 Pelvic MRI T2-weighted (a panel) and diffusion-weighted (b panel) images. The mass is localized to the glans. There is no evidence of cavernous body invasion. Diffusion-weighted image shows high signal intensity only in the mass.

Partial penectomy was performed. The pathological examination showed that the tumor was originated from the vicinity of the multi-row columnar epithelium, which is the histology of urethra. He was diagnosed as a neuroendocrine tumor originating from the columnar epithelium of the urethra. The tumor cells were mainly small cells. (Small cell neuroendocrine tumor of the urethra, pT1N0M0 Stage I). The patient has no recurrence 10 months after the surgery.

Discussion

Neuroendocrine tumors are rare cancers with an incidence of 0.5–5 per 100 000 population.

It occurs most frequently in the gastrointestinal tract and respiratory tract, which have many neuroendocrine cells, but it is also found in the nervous system and urinary tract which have many neuroendocrine cells.[2] The reported incidence of neuroendocrine tumors in the urinary tract is <0.7% of all bladder tumors.[3] There have been only nine reported cases of urethral neuroendocrine tumors, which are extremely rare.[4–12] The origin of neuroendocrine tumors arising in the urinary tract is not clear.[13]

Urothelial carcinoma may differentiate as a neuroendocrine tumor because it has been reported that cancerous transformation of multipotent epithelial cells in transitional epithelial cells may become a neuroendocrine tumor and that transitional epithelial cells themselves may have neuroendocrine differentiation potential.[13,14] In addition, this case was diagnosed as a neuroendocrine tumor of urethral columnar epithelial origin. This is because the tumor, which is not stained by uroplakin3 (not of transitional epithelial origin), arises from the vicinity of the multi-row columnar epithelium, the urethral epithelium near the fossa navicularis (Fig. 4). Among previously reported nine cases of urethral neuroendocrine tumors, these cases had the history of bladder cancer.[4–12] Thus, the pathogenesis of neuroendocrine urethral tumor might be associated with the history of bladder cancer. It is possible that the urethral epithelium exposed to carcinogens

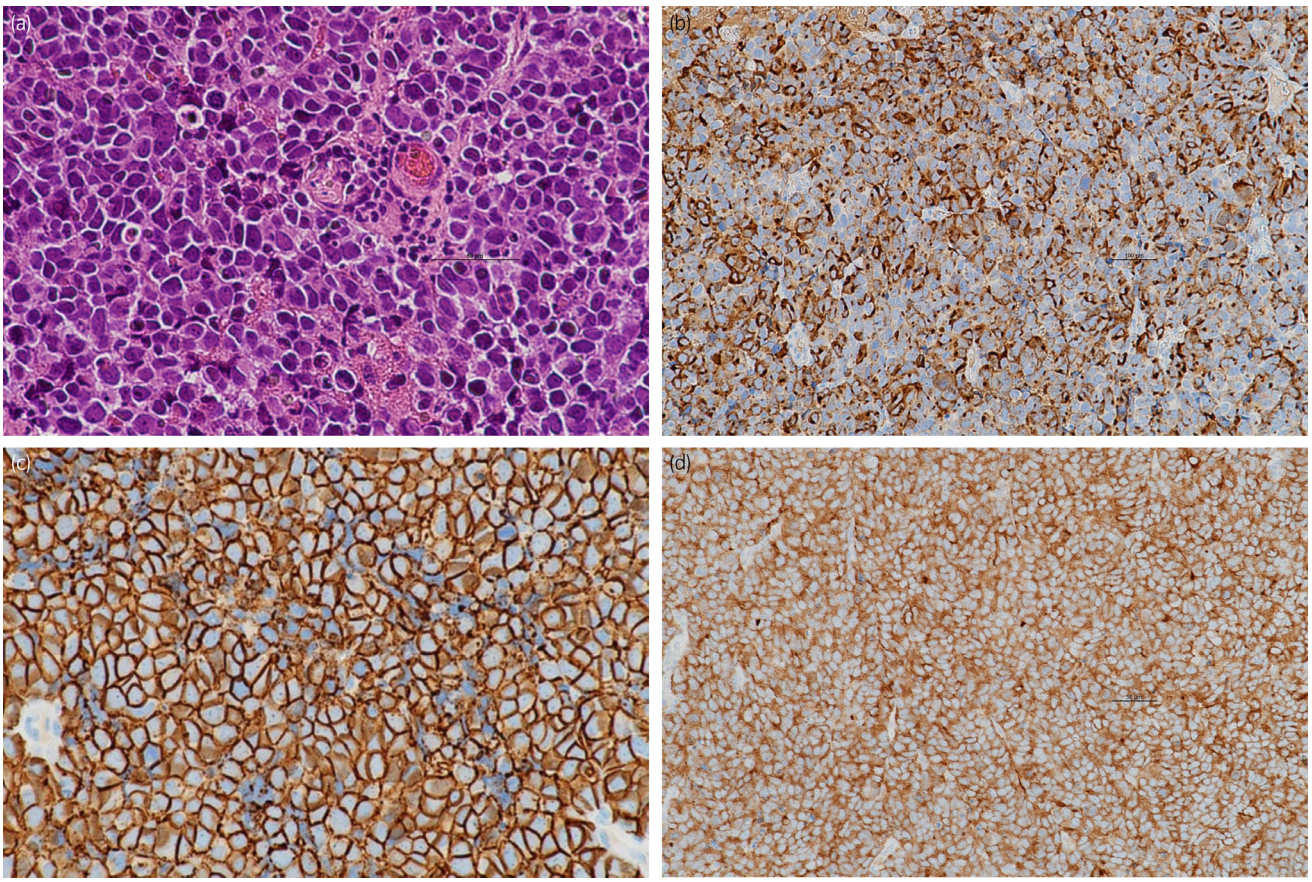

Fig. 3 Microscopic findings. The proliferating cells (a: HE×400) are composed of atypical cells with a high N/C ratio and darkly stained nuclei of unequal size. The tumor cells (b: chromogranin A, c: CD56, d: synaptophysin) are positive for CD56, chromogranin A, and synaptophysin, with scanty cytoplasm and round to oval nuclei rich in chromatin, indicating a neuroendocrine tumor.

such as smoking may have developed a precancerous lesion, resulting in some genetic mutation that caused a new neuroendocrine tumor to develop from the urethra left behind at the time of urethrectomy.

Neuroendocrine tumors in the urinary tract are generally treated with surgical resection and adjuvant chemotherapy (etoposide and cisplatin) as the first choice,[8] and are often detected after progressive and invasive disease and have a poor prognosis.[4–12] However, primary neuroendocrine tumors of the urethra are often detected early and may have a better prognosis than primary neuroendocrine tumors of other urinary tracts.[4–12]

Conclusion

Small cell neuroendocrine tumor could occur on urethral remnant after radical cystectomy with urethrectomy for urothelial cancer. Inspection of the penis and urethral meatus is important during regular follow-up of patients after radical cystectomy.

Author contributions

Koji Miki: Writing – original draft. Kazutoshi Fujita: Conceptualization; writing – review and editing. Ken Kuwahara: Writing – review and editing. Shogo Adomi: Writing – review and editing. Takafumi Minami: Writing – review and editing. Masahiro Nozawa: Supervision. Kazuhiro Yoshimura: Supervision. Hirotsugu Uemura: Supervision. Osamu Maenishi: Data curation. Misa Kojima: Data curation.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Written informed consent was obtained.

Registry and the Registration No. of the study/trial

Not applicable.

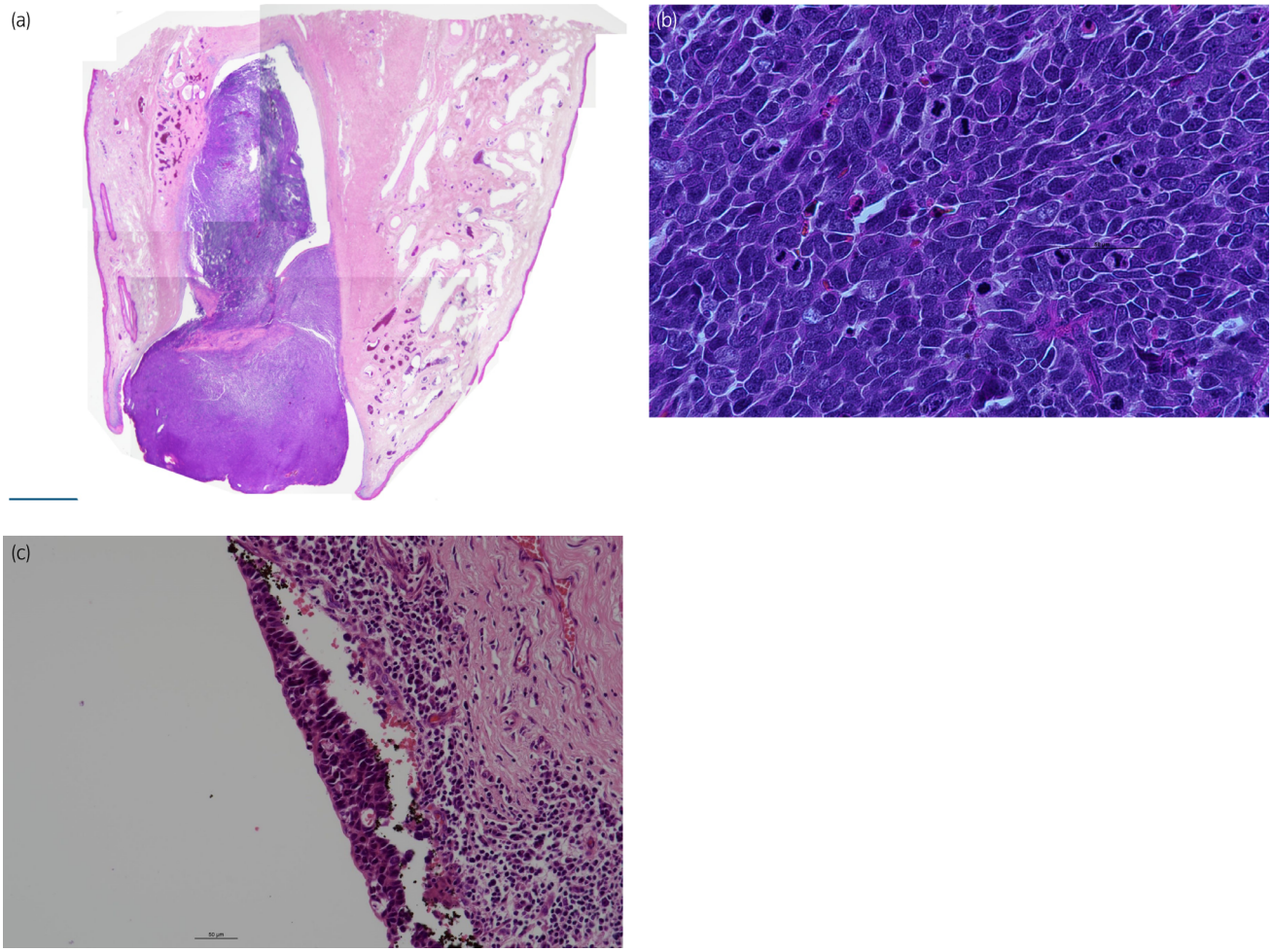

Fig. 4 Microscopic findings. Diffusely proliferating atypical cells (a: HE×50, b: HE×400) with small naked nuclei and coarse chromatin are observed. The atypical cells lack sporulation, are relatively small, and show numerous fission images. The atypical cells are positive for synaptophysin and chromogranin A, and have a Ki67 labeling index of around 90%, suggesting a small-cell carcinoma. Considering the location of the tumor (c: HE×400), which arises near the multi-layered columnar epithelium of the urethra, the diagnosis of urethral neuroendocrine carcinoma of columnar cell origin is considered.

References

1 Wenzel M, Collà Ruvolo C, Würnschimmel C *et al*. Epidemiology of unconventional histological subtypes of urethral cancer. *Urol. Int.* 2023; **107**: 15–22.
2 Riihimäki M, Hemminki A, Sundquist K, Sundquist J, Hemminki K. The epidemiology of metastases in neuroendocrine tumors. *Int. J. Cancer* 2016; **139**: 2679–86.
3 Qayoom S, Chakrabarti D, Khan F, Goel MM. Primary small cell carcinoma of the urinary bladder. *BMJ Case Rep.* 2019; **12**: e230185.
4 Fukuda T, Kamishima T, Saito T, Itoh S, Suzuki T. Small cell carcinoma arising from the outer urethral orifice: a case report examined by histologic, ultrastructural and immunohistochemical methods. *Pathol. Int.* 1997; **47**: 497–501.
5 Parekh DJ, Jung C, Roberts R, Shappell S, Smith JA Jr. Primary neuroendocrine carcinoma of the urethra. *Urology* 2002; **60**: 1111.
6 Rudloff U, Amukele SA, Moldwin R, Qiao X, Morgenstern N. Small cell carcinoma arising from the proximal urethra. *Int. J. Urol.* 2004; **11**: 674–7.
7 Altintas S, Blockx N, Huizing MT *et al*. Small-cell carcinoma of the penile urethra: a case report and a short review of the literature. *Ann. Oncol.* 2007; **18**: 801–4.
8 Yoo KH, Kim GY, Kim TG, Min GE, Lee HL. Primary small cell neuroendocrine carcinoma of the female urethra. *Pathol. Int.* 2009; **59**: 601–3.
9 Kanagarajah P, Ayyathurai R, Saleem U, Manoharan M. Small cell carcinoma arising from the bulbar urethra: a case report and literature review. *Urol. Int.* 2012; **88**: 477–9.
10 Facio FN, Spessoto LC, Ferraz de Arruda GJ, Arruda JF, Ferraz de Arruda JG, Facio MF. Primary mixed glandular-endocrine tumor of the male proximal urethra: a case report. *Urol. Case Rep.* 2016; **6**: 1–3.
11 Sisler K, Knutson A, McLennan M. Primary small cell neuroendocrine tumor within a urethral diverticulum. *Obstet. Gynecol.* 2019; **133**: 308–11.
12 Murata Y, Shinojima T, Nakahira Y, Hamada M, Sasaki A, Asakura H. Recurrent urethral tumor with neuroendocrine differentiation in a female patient after radical cystectomy for bladder cancer. *IJU Case Rep.* 2023; **6**: 199–202.
13 Pósfai B, Kuthi L, Varga L *et al*. The colorful palette of neuroendocrine neoplasms in the genitourinary tract. *Anticancer Res.* 2018; **38**: 3243–54.
14 Bertaccini A, Marchiori D, Cricca A *et al*. Neuroendocrine carcinoma of the urinary bladder: case report and review of the literature. *Anticancer Res.* 2008; **28**: 1369–72.