International Journal of Clinical Urology
2024, Vol. 8, No. 2, pp. 35-38
https://doi.org/10.11648/j.ijcu.20240802.14

Research Article

Late Local Recurrence of Carcinoma *in situ* - Only Bladder Cancer

Masanori Nishimura*, Syun Ueno, Takeshi Nomura

Department of Urology, Misugikai Sato Hospital, Osaka, Japan

Abstract

Late recurrence (LR) of bladder cancer after radical cystectomy (RC) is rare, and few studies have been conducted. We report a case of local LR of bladder cancer 10.3 years after RC. The pathology at RC was almost carcinoma *in situ* (CIS) only. The patient underwent metastasectomy, and treatment with an immune checkpoint inhibitor (ICI) achieved a complete response (CR). A 61-year-old woman was referred to our hospital for macrohematuria and bladder irritability in June 2012. She underwent RC along with pelvic lymph node dissection and ileal conduit creation. The pathologic findings were CIS, G2>G3, pT1, pN0. She visited our hospital with complaints of lower abdominal discomfort in November 2022, and recurrence was found on the pelvic floor by abdominal computed tomography. Metastasectomy confirmed metastasis of urothelial carcinoma. As salvage therapy, systemic chemotherapy with a platinum agent and an ICI were administered, leading to CR. Long-term follow-up should be considered for patients with bladder cancer, even for early-stage CIS-only tumors. Metastasectomy could be the primary option for LR of bladder cancer after RC.

Keywords

Late Local Recurrence, Bladder Cancer, Carcinoma in Situ, Metastatectomy

1. Introduction

Recurrence of bladder cancer after radical cystectomy (RC) generally occurs within 2 years and carries a poor prognosis. However, late recurrence (LR) is rare, and few investigations has been performed. We report a case of local LR of bladder cancer 10.3 years after RC. Recurrence occurred at the soft tissue of the pelvic floor opposed to the remaining urothelium. The patient underwent metastasectomy, which confirmed recurrence of invasive bladder cancer. Treatment including an immune checkpoint inhibitor (ICI) achieved a complete response (CR).

2. Case Report

A 61-year-old woman was referred to our hospital in June 2012 because of macrohematuria and bladder irritability [1]. Cystoscopy revealed a low-grade papillary tumor scattered across a large part of the bladder mucosa. Transurethral resection biopsy revealed pT1, G1–G2 urothelial cancer with flat lesions. No metastatic lesions were detected on abdominal and chest computed tomography (CT). Tumor staging was assessed according to the 2002 American Joint Committee on Cancer tumor–node–metastasis staging system. Tumor grading was based on the 1973 World Health Organization system.

In July 2012, the patient underwent RC, pelvic lymph node

*Corresponding author: mnishimu@fa2.so-net.ne.jp (Masanori Nishimura)

Received: 13 September 2024; **Accepted:** 14 October 2024; **Published:** 12 November 2024

dissection, and ileal conduit creation because of the wide spread of the tumor. The pathologic findings were almost carcinoma *in situ* (CIS) only involving more than half of the area of the bladder mucosa with tiny stromal invasion (pT1), G2>G3, pN0 [2, 3]. The postoperative course was uneventful. Adjuvant chemotherapies were not administered. The patient was followed-up postoperatively at 3-month intervals the first 2 years and 6-month intervals thereafter. Follow-up consisted of physical examination, blood tests, and ultrasonography. Chest and abdominal CT was performed annually and when clinically indicated. The patient exhibited no evidence of recurrence for 10.3 years.

The patient returned to our hospital in November 2022 with complaints of lower abdominal discomfort. A mass with cystic elements was found on the pelvic floor by abdominal CT (Figure 1). In December 2022, metastasectomy was performed along with resection of the uterus and ovaries to confirm the precise pathological diagnosis. Complete resection was impossible. The pathology was invasive carcinoma, compatible with GATA3+ urothelial carcinoma (Figure 2), and gynecological malignancy was not detected.

As salvage therapy, systemic chemotherapy consisting of carboplatin and gemcitabine was administered, following by pembrolizumab. This regimen achieved CR (Figure 1). Immunotherapy with pembrolizumab has been subsequently provided as maintenance therapy. The patient has remained healthy with no signs of recurrence.

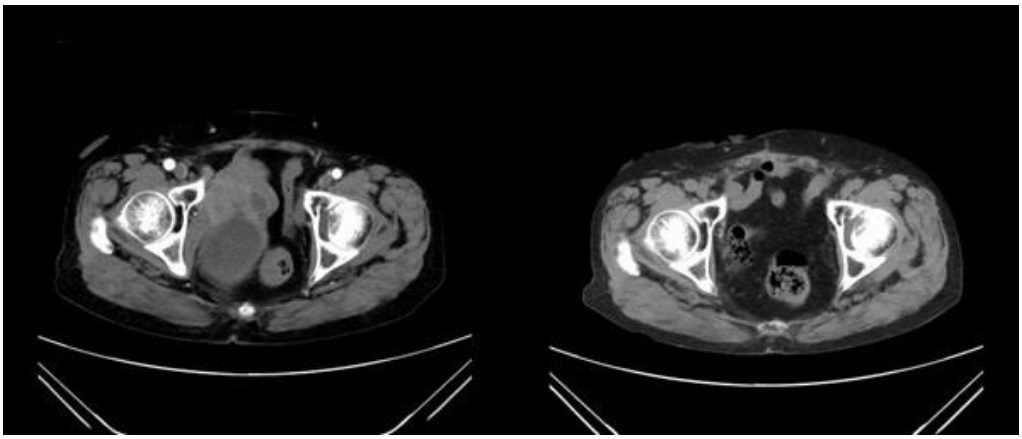

Figure 1. *Abdominal CT revealed a recurrent tumor with cystic elements (left). Metastasectomy along with adjuvant treatments using platinum-based chemotherapy and ICI therapy achieved CR (right).*

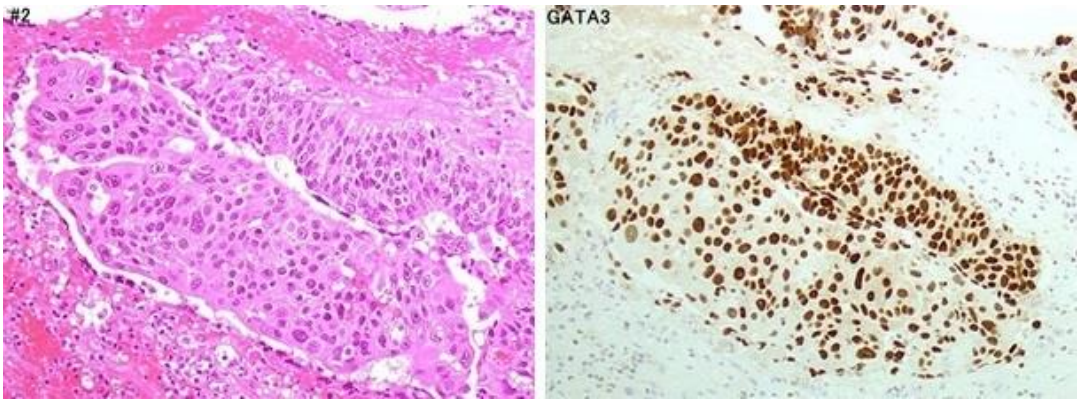

Figure 2. *Histology revealed invasive carcinoma compatible with urothelial carcinoma (left). Immunostaining for GATA3 was positive (right).*

3. Discussion

Bladder cancer recurrence after RC usually occurs within 2 years, and its prognosis is poor [4, 5]. LR after RC is a relatively uncommon but non-negligible event with unique characteristics and prognoses [6, 7]. The most common site of LR is the remnant urothelium. It was reported that nonurothelial LR carried a worse prognosis than urothelial LR [8]. Dawson et al. reported in their series that soft tissue recurrence occurred within 3 years in most cases [9]. Contrarily, excellent outcomes have been reported for CIS-only disease after RC [10]. Zehnder et al. found that only 1 of 52 patients with CIS-only disease developed local LR in the vaginal vault 3.8 years after RC [11]. In our case, LR

occurred 10.3 years after RC in the soft tissue of the pelvic floor, which was considered an exceptionally long interval. Therefore, our case supports the need for lifelong follow-up in patients with bladder cancer, even if the tumor is CIS-only [12, 13, 14]. Younger age, non-muscle invasive disease, and a lower frequency of nodal involvement were reported as predictors of LR [8, 9, 15].

Moreover, LR is associated with better overall survival than early recurrence. Dawson et al. reported that local consolidative therapy (metastasectomy or radiation) was more common in patients with LR [9]. Our patient underwent metastasectomy following ICI therapy [16], leading to CR and a good posttreatment course. Metastasectomy is rarely selected for early recurrence of bladder cancer because of its poor prognosis. However, it might be considered in the treatment of LR. In our case, disease-free survival of 20 months was observed.

4. Conclusions

Lifelong follow-up should be considered for patients with bladder cancer, even if the tumor is early-stage and CIS-only. Metastasectomy might represent a treatment option for LR of bladder cancer after RC.

Abbreviations

LR	Late Recurrence
RC	Radical Cystectomy
CIS	Carcinoma in Situ
ICI	Immune Checkpoint Inhibitor
CR	Complete Response
CT	Computed Tomography

Informed Consent

Written informed consent was obtained from the patient for publication of the details of her medical case and any accompanying images.

Ethical Approval

Our institution does not require ethics approval for reporting individual cases or case series. Ethical approval was not required for this study in accordance with local or national guidelines. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Author Contributions

MN and SU were involved in the patient's treatment and in image acquisition. MN, SU, and TN searched the literature and contributed to writing the case discussion. All authors of this paper have read and approved the final version submitted.

Funding

This work was not supported by any extra-institutional funding.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Tachibana M, Tsubouchi K, Fukuhara Y et al.: Factors Related to Overactive Bladder-like Symptoms in Bladder Cancer. Anticancer Res. 2023 43(8): 3607-3613.

[2] Samantha Conroy, Ibrahim Jubber, Aidan P Noon et al.: Real-word outcomes for high-risk non-muscle-invasive bladder cancer: screened patients for the BRAVO trial. BJU international. 2024 Sep 26.

[3] Vincenzo Serretta: BCG and bladder cancer. Forty-eight years after Morales report. Urologia. 2024 91(3): 459-467.

[4] Stein JP, Lieskovsky G, Cote R et al.: Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. J Clin Oncol 2001 19: 666-675.

[5] Bochner B, Kattan MW and Vora KC: Post-operative nomogram predicting risk of recurrence after radical cystectomy for bladder cancer. J Clin Oncol; 2006 24: 3967-3972.

[6] Yoo SH, Kim H, Kwak C et al.: Late Recurrence of Bladder Cancer following Radical Cystectomy: Characteristics and Outcomes. Urol Int. 2019 103(3): 291-296.

[7] Hirata Y, Higuchi M, Osawa T et al.: Late recurrence in patients with non-muscle-invasive bladder cancer after 5-year cancer-free periods. J Urol. 2022 29(10): 1140-1146.

[8] Linder BJ, Boorjian SA, Hudolin T et al.: Late recurrence after radical cystectomy: patterns, risk factors and outcomes. J Urol 2014 191: 1256-1261.

[9] Dawson S, Cha EK, Falavolti C et al.: Late recurrences following radical cystectomy have distinct prognostic and management considerations. J Urol; 2020 204: 460-465.

[10] Hassan JM, Cookson MS, Smith, Jr JA et al.: Outcomes in patients with pathological carcinoma in situ only disease at radical cystectomy. J Urol; 2004 172: 882-884.

[11] Zehnder P, Moltzahn F, Daneshmand S et al.: Outcome in patients with exclusive carcinoma in situ (CIS) after radical cystectomy. BJUI; 2014 113: 65-69.

[12] Villegas E, Lajkosz K, Din S et al.: Long-term recurrence risk, metastatic potential and length of cystoscopic surveillance of low-grade non-muscle invasive bladder cancer. J Urol. 2024 29: 101097.

[13] Naspro R, La Croce G, Finati M et al.: Oncological outcomes of concomitant carcinoma in situ at radical cystectomy in pure urothelial bladder cancer and in histological variants. Urol Oncol. 2022 40(2): 61. e9-61. e19.

[14] Beijert IJ, Hentschel AE, Bründl J et al.: Prognosis of Primary Papillary Ta Grade 3 Bladder Cancer in the Non-muscle-invasive Spectrum. Eur Urol Oncol. 2023 6(2): 214-221.

[15] Niyati Lobo, Zhigang Duan, Akshay Sood et al.: Association of Age with Non-muscle-invasive Bladder Cancer: Unearthing a Biological Basis for Epidemiological Disparities? European urology oncology. 2024 7(5): 1069-1079.

[16] Witjes JA, Bruins HM, Cathomas R et al.: European Association of Urology Guidelines on Muscle-invasive and Metastatic Bladder Cancer: Summary of the 2020 Guidelines. Eur Urol. 2021 79(1): 82-104.