



# Recurrence of Subepithelial Non-Muscle Invasive Bladder Cancer Following Transurethral Resection: A Case Report

비근침윤성 방광암의 경요도절제술 후 방광 내 상피하종양 형태의 재발: 증례 보고

Nokjung Kim, MD , Sung Kyoung Moon, MD\* ,  
Myung-won You, MD , Joo Won Lim, MD

Department of Radiology, Kyung Hee University Hospital, Seoul, Korea

Transurethral resection (TUR) is the gold standard treatment of non-muscle invasive bladder cancers. Recurrence occurs in approximately half of the patients with bladder cancer after initial TUR. Most recurrent bladder cancers present as polypoid masses with intraluminal growth originating from the mucosa. To the best of our knowledge, there has been no report on imaging findings of recurrent bladder cancers located within the subepithelial and intramural layers. Recurrent cancers within the intramural layer are difficult to detect with cystoscopy; they are also difficult to remove surgically. Imaging studies reveal the most important indicators for diagnosing subepithelial recurrent cancers. Here, we present a rare case of a recurrent bladder cancer within the subepithelial layer detected on imaging.

**Index terms** Bladder Cancer; Recurrence; Metastasis; Treatment

## INTRODUCTION

Recurrence after transurethral resection of bladder tumor (TUR-BT) occurs in approximately half the patients with bladder cancer after initial TUR-BT. Repeat TUR-BT is recommended for recurrent non-muscle invasive bladder cancers (1).

Peritoneal or perivesical metastasis due to bladder perforation is very rare (2). To the best of our knowledge, there have been no reports on imaging findings of recurrent bladder cancers located in subepithelial layer, particularly in intramural layer. Here, we

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\*Corresponding author  
Sung Kyoung Moon, MD  
Department of Radiology,  
Kyung Hee University Hospital,  
23 Kyungheedaero,  
Dongdaemun-gu,  
Seoul 02447, Korea.

Tel 82-2-958-9502  
Fax 82-2-968-0787  
E-mail skmoonrad@gmail.com

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### ORCID iDs

Nokjung Kim   
<https://orcid.org/0000-0003-2213-0247>  
Sung Kyoung Moon   
<https://orcid.org/0000-0003-4831-3439>  
Myung-won You   
<https://orcid.org/0000-0001-6262-5784>  
Joo Won Lim   
<https://orcid.org/0000-0002-7989-3408>

present a case of recurrent bladder cancer in subepithelial layer detected on imaging.

## CASE REPORT

A 55-year-old male visited the urology department and underwent follow-up imaging studies. He had a history of bladder cancer treated by TUR-BT 22 years ago and recurrence treated by 3 additional TUR-BT since the first surgery. Histopathologic examinations of all four resected specimens from four TUR-BT revealed low-grade papillary urothelial cell carcinoma [World Health Organization (WHO) grade 2] without subepithelial connective tissue invasion.

Last TUR-BT was undergone for removal of intraluminal protruding masses at the dome and left posterior wall of the urinary bladder (UB). The masses were confirmed to be eliminated without recurrence in the postoperative CT scan after 1 month.

however, new small enhancing masses were found in the muscle layer and adjacent perivesical fat of UB dome and posterior wall on follow-up CT 7 months after last TUR-BT. MRI of UB was performed for further evaluation of these nodules.

Initial MRI revealed 5 masses located in the muscle layer with protrusion toward perivesical fat. On T2-weighted image (T2WI), the lesions showed intermediate signal intensity. Contrast-enhanced T1-weighted image (T1WI) with intravenous gadolinium administration demonstrated homogeneous enhancement of the masses. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) map with a b-value of 1000 showed diffusion restriction of the masses (Fig. 1A).

Leiomyomas and neurogenic tumors are the usual differential diagnoses for bladder tumors located in the subepithelial layer. Leiomyomas typically exhibit low signal intensity on T2WI, while neurogenic tumors, such as neurofibroma and paraganglioma, usually exhibit high signal intensity on T2WI. These tumors usually do not show diffusion restriction (3). These MR features appear dissimilar from the findings of our patient. Therefore we concluded that it is unlikely to be identified as leiomyoma or neurogenic tumor. Urothelial carcinoma typically exhibits intermediate signal intensity on T2WI and avid enhancement on contrast-enhanced T1WI images. It also shows restrictive diffusion on DWI and ADC map with high b-values (4). In this case, subepithelial recurrent bladder cancer was initially suspected based on the history of bladder cancer with repeat TUR-BT and similar MR features of bladder cancer despite its unusual location. Hematogenous metastasis and bladder wall invasion of peritoneal seeding should also be considered as differential diagnoses.

Cystoscopy was performed to confirm intramuscular lesions, and it revealed 5 submucosal mass-like lesions with normal epithelium (Fig. 1B). Partial cystectomy was attempted for them. However, they were so unclear in surgical field that the resected specimens revealed negative results. As he had refused radical cystectomy, neoadjuvant chemotherapy with gemcitabine was performed. Follow-up MRI was performed to evaluate treatment response 6 months later, and showed interval growth of all masses with intermediate signal intensity on T2WI, peripheral enhancement with central necrosis or cystic change on contrast-enhanced T1WI, and peripheral diffusion restriction on DWI and ADC map with a b-value 1000 (Fig. 1C).

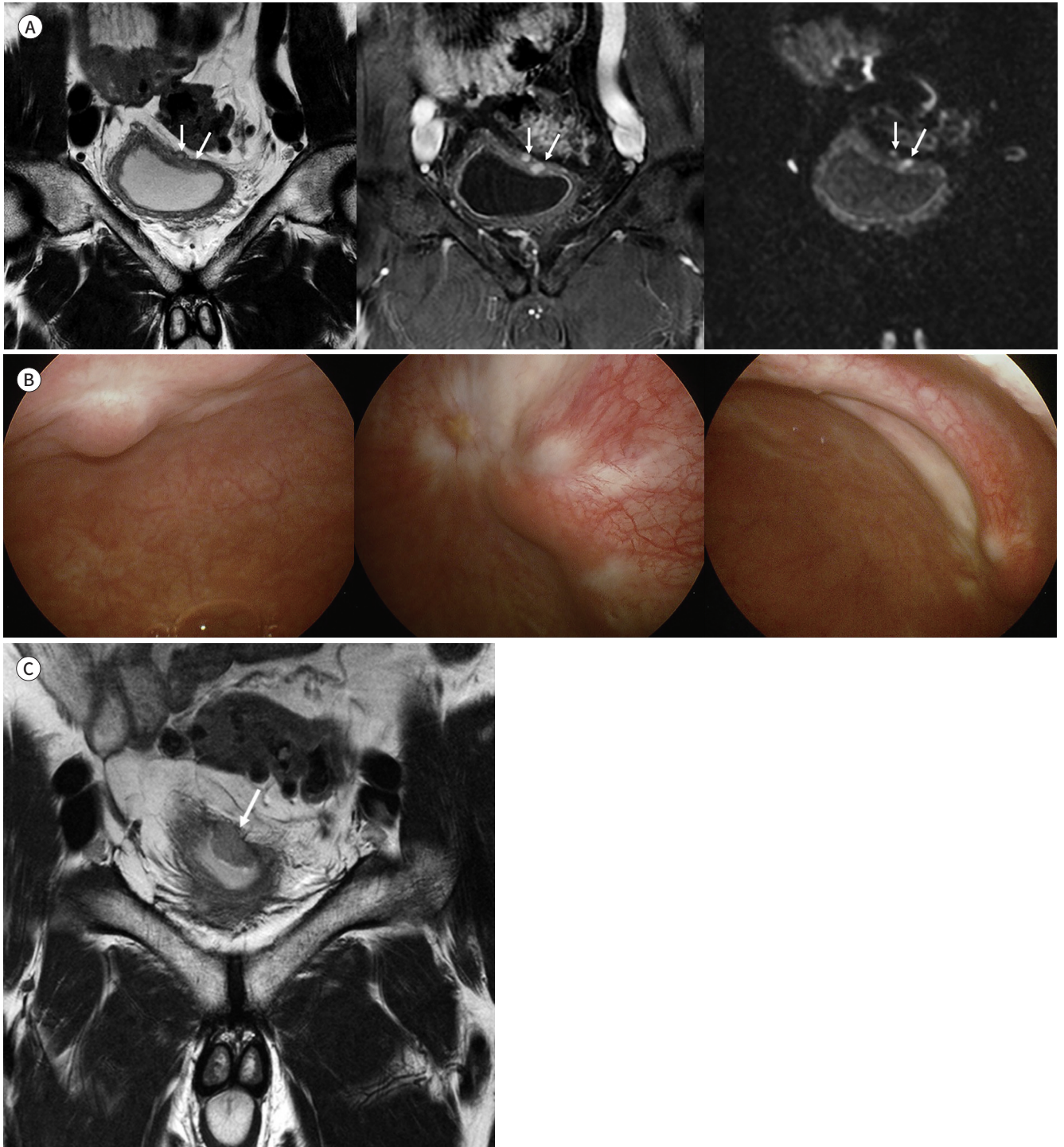
Partial cystectomy confirmed high-grade infiltrating urothelial carcinoma (WHO grade 2) with perivesical soft tissue invasion (T3a). Furthermore, the patient received concurrent

**Fig. 1.** Subepithelial recurrence of bladder cancer following transurethral resection of bladder tumor.

**A.** Initial coronal T2-weighted image (left image) shows intramural masses with intermediate signals located within the dome of the urinary bladder (arrows). The inner layer of the mucosa is intact without disruption by the masses. A contrast-enhanced T1-weighted image (middle image) shows homogeneous enhancement of the small masses (arrows). A diffusion-weighted image (b = 1000, right image) shows a strong diffusion restriction of the masses (arrows).

**B.** Cystoscopy performed after the initial MRI. Five submucosal mass-like lesions with normal epithelium are shown.

**C.** Follow up coronal T2-weighted image shows intermediate to high signal intensity of the two previous adjacent small masses that increased in size and conglomerated as one mass (arrow).



chemoradiotherapy.

## DISCUSSION

TUR-BT eradicates all visible tumors and provides tissue for histological type, grade, and depth of invasion. Complete resection of the tumor, including areas of suspected carcinoma in situ, abnormal areas in the prostatic urethra and bladder neck, and the detrusor muscle, should be performed to rule out T2 disease and reduce the rate of understaging. Resection of high-grade tumors without including the detrusor muscle in the specimen are associated with residual tumor or progression to muscle invasive disease in up to 50% of the cases.

Recurrence rate following initial TUR-BT of urothelial carcinomas is 15–61% after 1 year and 31–78% after 5 years. Up to 17% cases of non-muscle-invasive bladder cancer progress to a muscle-invasive tumor after 1 year, and up to 45% cases of them progress to a muscle-invasive tumor after 5 years (5).

Most recurrent bladder cancers present as polypoid masses with intraluminal growth originating from mucosa and may invade muscle layer. However, the present case showed the recurrent cancers as the subepithelial masses mimicking other bladder subepithelial tumors. We presumed incomplete microperforation or increased internal pressure by repeat TUR-BT might cause tumor spillage and implantation beneath mucosa and deeper layers in this case. There have been a few reports on perivesical or intraperitoneal metastasis due to UB perforation following TUR-BT (6-8). There are 2 mechanisms about microperforation of UB due to TUR-BT. First, TUR-BT technique usually requires deep and extensive resection, which increases the risk of bladder microperforation (6). Factors that increase the risk of perforation include heavily pretreated thin bladder wall, repeat TUR-BT, large tumor size, and tumor located posteriorly or in bladder dome (7). There have been reports of extravesical metastasis, which is a rare complication due to microperforation of bladder following TUR-BT (8, 9). Second, increased internal pressure of UB during TUR-BT is a contributing factor for bladder perforation. As the internal pressure of UB exceeds the surrounding venous pressure because of fluid infusion during TUR-BT, it may lead to infusion of cancer cells in the surrounding venous system and result in seeding in the adjacent structures (10). Although bladder microperforation or tumor cell spillage is an uncommon complication, it is important to suspect the feasibility of peritoneal metastasis or subepithelial recurrence because of its poor prognosis.

MR characteristics of subepithelial recurrence were the same as those of usual bladder cancers arising from mucosa, although the location was atypical. Therefore, a mass showing the same imaging characteristics at the bladder surface or bladder wall beneath the mucosa should be diagnosed as bladder cancer metastasis or subepithelial recurrence, if the patient has a history of repeat TUR-BT. Radiologists should be well aware of the unusual location of recurrent cancer after TUR-BT, and carefully interpret the follow-up imaging not only just inside it but also around it.

### Author Contributions

Conceptualization, M.S.K., L.J.W., Y.M.; data curation, M.S.K.; formal analysis, M.S.K., L.J.W., K.N.;

funding acquisition, M.S.K.; investigation, K.N.; methodology, M.S.K., L.J.W., K.N.; project administration, M.S.K.; resources, M.S.K.; software, M.S.K., K.N.; supervision, M.S.K.; validation, M.S.K., K.N.; visualization, M.S.K., K.N.; writing—original draft, K.N.; and writing—review & editing, M.S.K.

### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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## 비근침윤성 방광암의 경요도절제술 후 방광 내 상피하종양 형태의 재발: 증례 보고

김녹정 · 문성경\* · 유명원 · 임주원

방광암의 경요도절제술은 비근침윤성 방광암의 1차 치료 방법이다. 첫 번째 경요도절제술 이후 약 절반가량의 방광암 환자에서 재발을 보인다. 대부분의 방광암 재발은 방광점막에서 방광내막 쪽으로 자라는 용종 모양의 종괴로 나타난다. 지금까지 알려진 바에 의하면, 재발한 방광암이 상피하종양의 형태로 보고된 증례는 없다. 근육내층에 국한된 재발암은 방광경에서 발견하기가 쉽지 않고, 또한 수술적으로 완전히 제거하는 것 역시 쉽지 않다. 근육내층에 재발한 방광암을 진단하는 데에 있어서 영상 검사가 가장 중요한 정보를 제공할 수 있다. 이 증례에서는 영상 검사에서 진단할 수 있는 아주 드문 상피하 재발 방광암에 대해 보고하고자 한다.

경희대학교병원 영상의학과