

# Submucosal urothelial bladder cancer: A case report

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**Abstract.** Bladder tumors can be broadly divided into those of epithelial or mesodermal origin. Furthermore, 90% of bladder tumors arise from the epithelium of the bladder, and most cases of bladder cancer are histologically urothelial carcinomas. Mesodermal tumors are exceptionally rare and often benign. Of the mesenchymal tumors of the bladder, leiomyomas are the most common, and their prognosis depends on their histology. The present report describes a case of submucosal urothelial cancer in a patient with no past history of bladder cancer. To the best of our knowledge, there are no previous reports of urothelial cancer occurring in the submucosa. The present report was the first to document a case of submucosal urothelial cancer, whose diagnosis was made possible only by transurethral resection of bladder tumor. Although the precise pathomechanism of the present case was unclear, two hypotheses were considered. First, the urothelial cancer developed within a diverticulum, then the entrance of the diverticulum closed, sealing in the cancer. Second, the bladder cancer stemmed from aberrant urothelium in the submucosal tissue. If submucosal urothelial bladder carcinoma develops within the diverticular environment, its prognosis can be as poor as that of invasive bladder cancer due to the features of the diverticular environment. Even in a patient with a submucosal bladder tumor but no previous history of bladder cancer, bladder cancer should be considered in the differential diagnosis.

## Introduction

Bladder tumors can be broadly divided into those of epithelial or mesodermal origin. Ninety-percent of bladder tumors arise from the epithelium of the bladder, and most cases of bladder cancer are histologically urothelial carcinomas. Bladder cancer can be broken down further into non-muscle invasive bladder

cancer (NMIBC) and muscle invasive bladder cancer (MIBC). Most cases of bladder cancer (70-80%) are NMIBC and have a good prognosis; the remaining cases are MIBC and have a poor prognosis (1). However, mesodermal tumors are exceptionally rare and often benign. Of the mesenchymal tumors of the bladder, leiomyomas are the most common, and their prognosis depends on their histology (2).

The present report described a case of primary submucosal urothelial cancer which was difficult to diagnose preoperatively. To the best of our knowledge, there are no previous reports of primary urothelial cancer occurring in the submucosa. In addition to the case description, two hypotheses were advanced to account for the oncogenesis of the present case. First, the urothelial cancer developed within a diverticulum, then the entrance of the diverticulum closed, sealing in the cancer. Second, the bladder cancer stemmed from aberrant urothelium in the submucosal tissue. If submucosal urothelial bladder carcinoma develops within the diverticular environment, its prognosis can be as poor as that of invasive bladder cancer due to the features of the diverticular environment. Even in a patient with a submucosal bladder tumor but no previous history of bladder cancer, bladder cancer should be considered in the differential diagnosis.

## Case report

An 87-year-old, male patient was referred to our hospital for a bladder tumor which was found incidentally on follow-up CT for hepatic cancer (Fig. 1). He had a past history of aortic valve stenosis, hepatocellular carcinoma (HCC), and liver cirrhosis due to chronic hepatitis C. He was a not a smoker and had no hypertension. He had a partial hepatectomy for HCC, followed by radiofrequency ablation and transarterial chemo-embolization for a recurrence. He had no previous history of bladder cancer. Contrast-enhanced CT revealed a 30x20 mm, homogeneously enhancing, multilobulated mass invading the perivesical fat in the left wall but no metastasis (Fig. 1). He had no symptoms, such as gross hematuria. Blood analysis revealed slight renal insufficiency and anemia, but urine analysis denied microscopic hematuria and pyuria. Cystoscopy revealed a sessile, non-papillary tumor covered with normal bladder mucosa on the left bladder wall showing the typical cystoscopic features of a submucosal bladder tumor (Fig. 2A). The preoperative diagnosis was submucosal bladder tumor originating in the mesoderm.

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Figure 1. CT findings. Abdominal CT revealed a bladder tumor on the left bladder wall infiltrating the perivesical fat. CT, computed tomography.

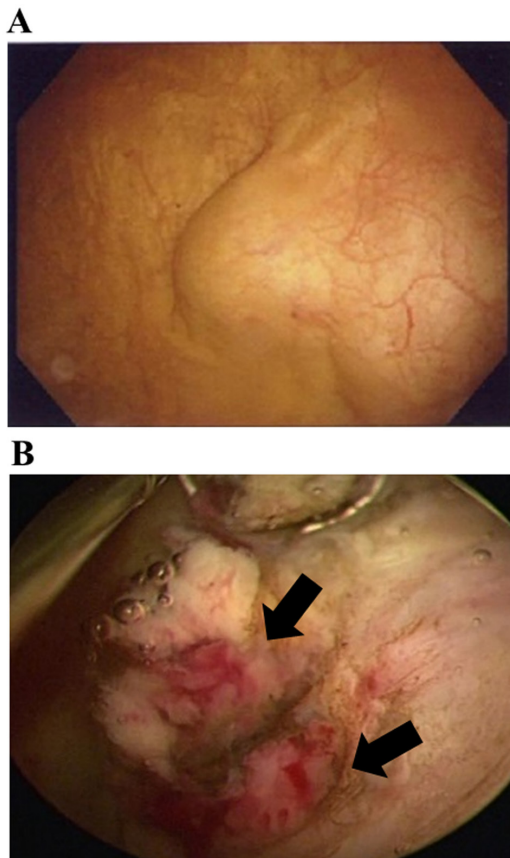


Figure 2. Cystoscopy findings. (A) Cystoscopy revealed a sessile, non-papillary tumor on the left bladder wall covered with normal bladder mucosa. (B) Resection of the normal bladder mucosa by transurethral resection of the bladder tumor revealed typical bladder cancer with papillary morphology (arrows).

Because of the patient's old age and medical history, transurethral resection of bladder tumor (TURBT) was performed for histological evaluation. The normal bladder mucosa covering the tumor was resected to reveal typical urothelial bladder cancer with a papillary morphology (Fig. 2B). The bladder tumor showed minimal invasion of the muscle layer and was resected to the greatest extent possible. Pathological analysis

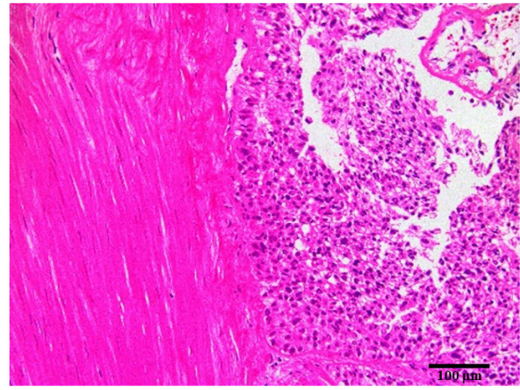


Figure 3. Pathological findings. Hematoxylin and eosin staining of the bladder tumor. Magnification, x400. Scale bar, 100  $\mu$ m.

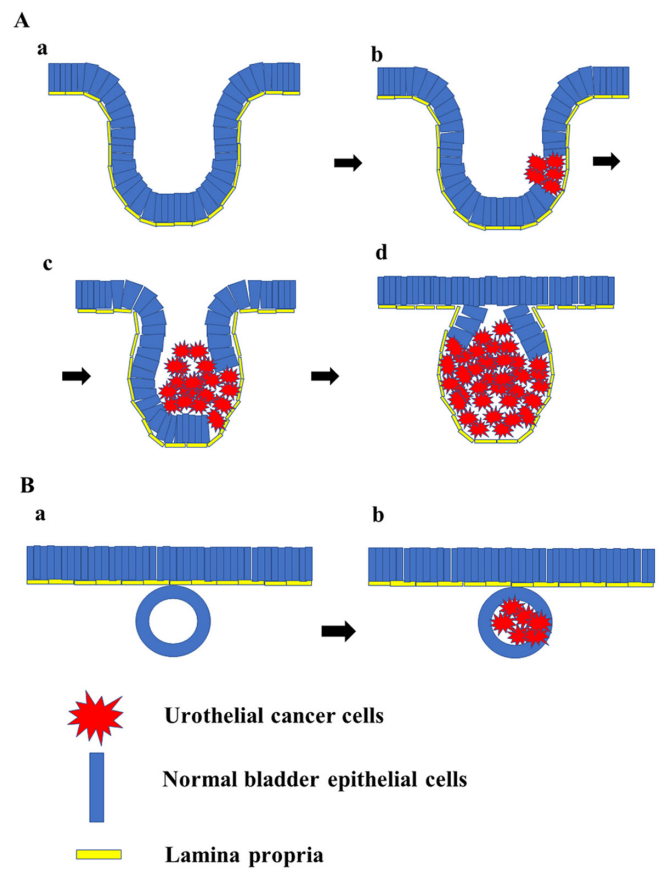


Figure 4. Two hypotheses on the development of the present submucosal urothelial bladder cancer. (A) Bladder cancer developed within a diverticulum, then the entrance of the diverticulum closed, enveloping the cancer. (a) There was a diverticulum. (b) Urothelial cancer developed within the diverticulum. (c) Urothelial cancer grew. (d) Entrance of the diverticulum closed, sealing in the cancer. (B) Bladder cancer stemmed from aberrant urothelium in the submucosal tissue. (a) There was aberrant urothelium in the submucosal tissue. (b) Bladder cancer stemmed from the aberrant urothelium.

revealed that the urothelial carcinoma, which was characterized by largely delicate and separate papillae as well as uniformly enlarged nuclei (low grade), had invaded the submucosa (Fig. 3). No infiltration of the cancer cells into the muscle layer was observed. Two months later, CT showed a local recurrence. The patient then underwent systemic chemotherapy.

## Discussion

Preoperatively identifying the histological subtype of a submucosal bladder tumor can be difficult because this type of tumor comprises diverse histological types, including both benign and malignant varieties. Most cases of submucosal bladder tumor present similar clinical symptoms, such as a pelvic mass, hematuria, and dysuria. Imaging methods also have limitations (3-5). MRI is slightly better than CT and ultrasound sonography because it has better resolution and contrast (6,7). Cystoscopy is only useful in discriminating mesenchymal tumors from epithelial carcinomas. The definitive diagnosis is made by histopathological and immunohistological analysis of TURBT specimens. In the present case, the asymptomatic tumor was incidentally detected on CT, and cystoscopy revealed a sessile, non-papillary tumor covered by normal urothelium. The preoperative diagnosis was submucosal bladder tumor, but its histological subtype was unknown. Because the patient had no previous history of bladder cancer, urothelial bladder cancer was not considered in the preoperative diagnosis.

To the best of our knowledge, the present study is the first to report a case of submucosal urothelial bladder cancer. TURBT of the normal bladder mucosa revealed a tumor with a papillary morphology typical of urothelial bladder cancer. While it remains unclear why the carcinoma was covered by normal uroepithelium, two explanations are possible. First, the urothelial cancer developed within a diverticulum, then the entrance of the diverticulum closed, sealing in the cancer (Fig. 4A). Second, the bladder cancer stemmed from aberrant urothelium in the submucosal tissue (Fig. 4B). However, other pathomechanisms may also be possible. One of the limitations of this study was its inability to clarify the pathomechanism in the present case.

The bladder diverticulum is a special environment from which cancer can easily invade the perivesical fat surrounding the bladder. Bladder cancer arising from a diverticulum is not considered to be as aggressive as a common invasive cancer, which frequently invades the normal bladder wall. However, Tamas *et al* (8) reported that invasive bladder cancer in a diverticulum can sometimes be aggressive in terms of local recurrence or metastasis. In the present case, the extravescical occurrence was detected on a postoperative follow-up CT.

The present report is the first to document a case of submucosal urothelial cancer, whose diagnosis was made possible only by TURBT. Even in a patient with submucosal bladder tumor but no previous history of bladder cancer, bladder cancer should be considered in the differential diagnosis. Although the precise pathomechanism of the present case was unclear, two hypotheses were advanced. The prognosis of submucosal urothelial bladder carcinoma is as poor as that of invasive bladder cancer within a diverticulum due to the diverticular environment.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

TA, FN and SH made substantial contributions in conception, design and interpretation of data. TA and FN wrote the manuscript. TD, SIw, SIIt and SH made substantial contributions in interpretation and acquisition of data. SIIt performed the histological examination. TA and FN were responsible for confirming the authenticity of all raw data. All the authors read and approved the final manuscript.

## Ethics approval and consent to participate

Not applicable.

## Patient consent for publication

The patient provided written informed consent for the publication of his data.

## Competing interests

The authors declare that they have no competing interests.

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