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A Rare Case of Primary Squamous Cell Carcinoma of the Urinary Bladder Associated With a Large Bladder Diverticulum

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Abstract

Carcinoma of the urinary bladder is one of the most frequently encountered malignancies of the genitourinary tract, with urothelial carcinoma constituting the predominant histological subtype. Primary squamous cell carcinoma (SCC) of the urinary bladder is an uncommon entity, accounting for only a small proportion (1-3%) of bladder cancers. It is usually associated with chronic irritation and inflammation of the bladder mucosa and is often diagnosed at an advanced stage, leading to an unfavorable prognosis. We report a rare case of primary SCC of the urinary bladder in a 69-year-old male patient who presented with long-standing irritative lower urinary tract symptoms, recurrent urinary tract infections, and intermittent hematuria. Radiological evaluation revealed an irregular bladder mass associated with a large bladder diverticulum. Cystoscopy, biopsy, and immunohistochemistry confirmed the diagnosis of moderately differentiated keratinizing SCC, stage pT1N0M0. The patient was managed with neoadjuvant chemotherapy and immunotherapy, followed by radical cystectomy, with histopathology showing SCC of the urinary bladder and negative lymph nodes (ypT1N0M0). This case highlights the importance of early suspicion, histopathological confirmation, and a multidisciplinary treatment approach in managing this rare and aggressive bladder malignancy.

Categories: Urology, Public Health, Oncology
Keywords: bladder diverticulum, chronic irritation, radical cystectomy, squamous cell carcinoma, urinary bladder

Introduction

Malignancies of the urinary bladder represent a significant proportion of urological cancers worldwide and predominantly affect the elderly population [1]. The incidence is higher in males, with a male-to-female ratio ranging from 3:1 to 4:1. Urothelial carcinoma, previously referred to as transitional cell carcinoma, accounts for approximately 90-95% of all bladder tumors [2]. The remaining cases comprise non-urothelial malignancies, including squamous cell carcinoma (SCC), adenocarcinoma, and various mesenchymal tumors.

Primary SCC of the urinary bladder is rare in non-endemic regions and accounts for only 1-3% of bladder cancers [3]. In contrast, in areas endemic for schistosomiasis, SCC constitutes a much higher proportion of bladder malignancies. Non-bilharzial SCC of the bladder is typically associated with chronic irritation of the urothelium caused by recurrent urinary tract infections, bladder calculi, long-term catheterization, neurogenic bladder, and bladder diverticula [4]. Persistent inflammation may lead to squamous metaplasia, dysplasia, and eventual malignant transformation.

SCC of the bladder is characterized by aggressive local behavior, advanced stage at presentation, and relatively poor survival outcomes compared to urothelial carcinoma [2,3]. Due to its rarity, there is a lack of standardized treatment guidelines, and management is largely based on small retrospective series and expert opinion. Radical cystectomy with pelvic lymphadenectomy is generally considered the treatment of choice for localized disease, while the role of chemotherapy, radiotherapy, and immunotherapy remains uncertain.

In this report, we describe a rare case of primary SCC of the urinary bladder arising in association with a large bladder diverticulum in an elderly male patient, emphasizing the clinical presentation, diagnostic workup, histopathological findings, and multidisciplinary management.

Case Presentation

A 69-year-old male presented to the urology outpatient department with complaints of progressively worsening lower urinary tract symptoms over the past several months. His primary symptoms included increased urinary frequency during the daytime, with voiding approximately 15-20 times per day, nocturia occurring four to five times per night, urinary urgency, and a poor urinary stream. He also reported intermittent painless hematuria for the past nine months and recurrent episodes of urinary tract infection

over the preceding year. The patient had undergone multiple short-term urethral catheterizations during episodes of acute urinary retention.

The patient was a non-smoker but had a history of tobacco chewing for approximately 15 years. There was no history of occupational exposure to industrial chemicals, dyes, or carcinogens. He had no significant medical comorbidities such as diabetes mellitus or hypertension. There was no personal or family history of malignancy. Physical examination was unremarkable, and abdominal examination did not reveal any palpable mass.

Routine hematological investigations, including complete blood count and renal function tests, were within normal limits. Urinalysis performed on multiple occasions revealed persistent pyuria and microscopic hematuria. Urine culture reports were suggestive of recurrent bacterial infections, for which the patient had received multiple courses of antibiotics.

Contrast-enhanced computed tomography (CECT) of the pelvis demonstrated an ill-defined, irregular, enhancing mass-like thickening involving the superior aspect of the urinary bladder extending to the left posterolateral wall, measuring approximately 7.5 × 4.9 cm. In addition, a large cystic structure measuring 10.5 × 9.6 cm was noted along the right lateral wall of the bladder. This structure was seen communicating with the bladder lumen through a defect measuring approximately 14 mm, consistent with a large bladder diverticulum. No obvious pelvic lymphadenopathy or distant metastasis was noted on imaging (Figure *1a*). Magnetic resonance imaging (MRI) of the pelvis showed an irregular, lobulated infiltrative endoluminal heterogeneous soft tissue lesion (6.5 x 6.2 cm) noted along the superior aspect of the bladder with involvement of the adjoining left lateral and anterior wall of the bladder. The lesion involves the left vesicoureteral junction (VUJ) with resultant luminal narrowing. A large diverticulum measuring about 11.3 x 9.0 cm is noted adjacent to the right VUJ (Figure *1b*).

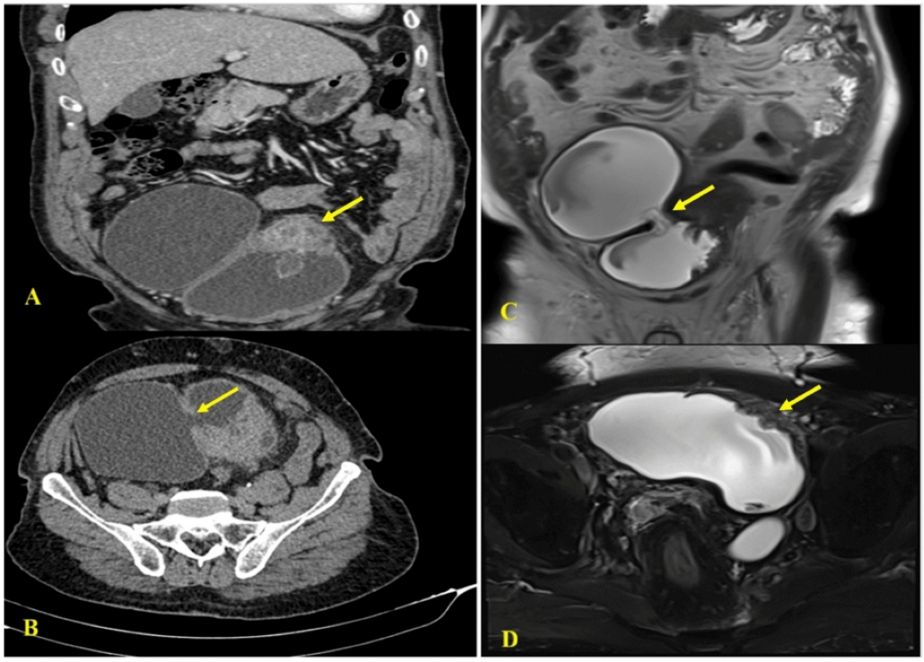


FIGURE 1: Radiological findings of the urinary bladder lesion with diverticulum

(A) Coronal contrast-enhanced CT image showing an irregular enhancing soft-tissue lesion involving the urinary bladder wall (yellow arrow). (B) Axial contrast-enhanced CT image demonstrating the bladder wall lesion with heterogeneous enhancement and a narrow-mouth diverticulum (yellow arrow). (C) Sagittal MRI showing a narrow-mouth diverticulum (yellow arrow). (D) Coronal MRI demonstrating the corresponding irregular bladder wall lesion (yellow arrow).

Cystoscopic evaluation revealed a large, warty, exophytic mass measuring approximately 6 × 5 cm located over the left posterolateral wall of the urinary bladder, extending to the anterior wall, with surrounding inflammatory and cystitis-like changes. A large-mouthed diverticulum was identified on the right lateral wall, while another smaller diverticulum with a narrow neck was observed on the left posterolateral wall (Figure *2*). Transurethral resection of bladder tumor was done, and biopsy samples were obtained from the bladder mass and suspicious areas. Complete clearance of the tumor could not be achieved.

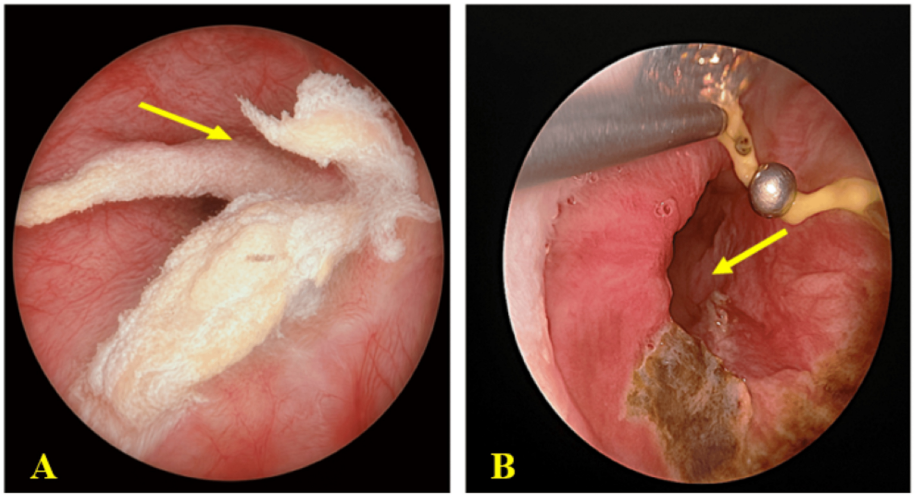


FIGURE 2: Cystoscopic findings of the squamous cell carcinoma of the urinary bladder with the bladder diverticulum

(A) Cystoscopic view showing an irregular whitish papillary lesion involving the urinary bladder mucosa, corresponding to the squamous cell carcinoma (yellow arrow). (B) Cystoscopic view demonstrating the opening of the bladder diverticulum adjacent to the bladder lesion (yellow arrow).

Histopathological examination revealed bladder mucosal tissue lined focally by normal to hyperplastic urothelium. The lamina propria showed reactive lymphoid follicles. Multiple nests and sheets of malignant squamous cells with keratin pearl formation and intercellular bridges were identified, consistent with moderately differentiated keratinizing SCC. Tumor infiltration into the lamina propria was noted. The deep muscle fragments largely showed reactive changes, including von Brunn's nests (stage pT1N0M0).

Immunohistochemical analysis demonstrated focal positivity for p40 and p63, supporting squamous differentiation. Markers typically associated with urothelial carcinoma, including uroplakin, CK7, CK20, and GATA-3, were negative. The Ki-67 proliferation index was approximately 40-45%, indicating high proliferative activity. These findings confirmed the diagnosis of primary SCC of the urinary bladder.

The case was discussed in a multidisciplinary tumor board involving urologists, medical oncologists, radiation oncologists, and pathologists. Considering the locally advanced nature of the disease and absence of distant metastasis, the patient was planned for neoadjuvant systemic therapy followed by definitive surgical management.

The patient received four cycles of combination chemotherapy with gemcitabine and cisplatin, administered as eight doses, along with two cycles of immunotherapy using pembrolizumab at a dose of 200 mg, given every three weeks. The treatment was well tolerated, with no significant adverse events.

Following completion of neoadjuvant therapy, the patient underwent radical cystectomy with pelvic lymph node dissection (Figure *3*). The postoperative period was uneventful. Histopathological examination of the cystectomy specimen revealed residual keratinizing SCC with significant treatment response. All surgical margins were free of tumor, and all dissected pelvic lymph nodes (0/17) showed reactive changes with no evidence of metastatic involvement (ypT1N0M0).

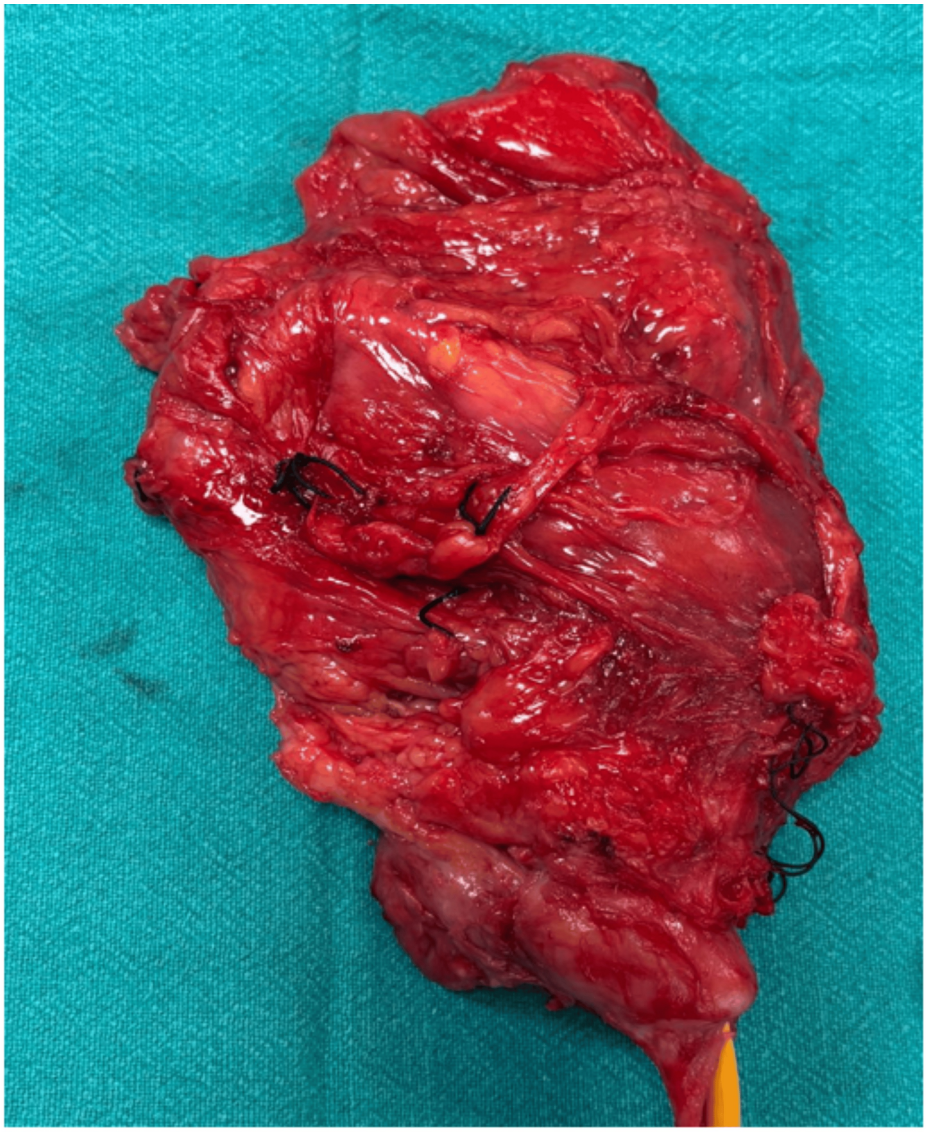


FIGURE 3: Gross photograph of the intact radical cysto-prostatectomy specimen showing the urinary bladder with attached prostate and Foley catheter in situ

The patient was followed up at regular intervals with clinical examination and imaging. At one-year follow-up, he remained asymptomatic with complete resolution of preoperative urinary symptoms. Follow-up MRI showed no evidence of local recurrence or distant metastasis.

Discussion

Primary SCC of the urinary bladder is a rare and aggressive malignancy, particularly in non-endemic regions [2]. It predominantly affects elderly males and is commonly associated with chronic inflammatory conditions of the bladder. Recurrent urinary tract infections, urinary stasis, bladder diverticula, bladder stones, and prolonged catheterization are well-recognized risk factors that contribute to chronic irritation of the urothelium [3].

Chronic inflammation leads to squamous metaplasia of the transitional epithelium, which may progress through dysplasia to invasive SCC. Unlike urothelial carcinoma, SCC of the bladder is usually muscle-invasive at the time of diagnosis and tends to exhibit aggressive local behavior with early invasion of surrounding structures [3].

Clinically, patients often present with hematuria, irritative voiding symptoms, and recurrent urinary tract infections [1]. Radiological findings are non-specific, and definitive diagnosis relies on histopathological examination and immunohistochemistry to differentiate SCC from urothelial carcinoma with squamous

differentiation.

Radical cystectomy with pelvic lymphadenectomy remains the cornerstone of treatment for localized SCC of the bladder [5,6]. Partial cystectomy is generally not recommended due to the high risk of local recurrence. The role of neoadjuvant or adjuvant chemotherapy remains controversial, and current guidelines do not establish a definitive benefit. However, selected patients may derive benefit from multimodal therapy, particularly in advanced or high-risk cases.

Galsky et al. conducted the first prospective study evaluating patients with unresectable non-transitional cell carcinoma, which included eight individuals with pure SCC. They demonstrated that a combination regimen of ifosfamide, paclitaxel, and cisplatin showed activity in SCC, with a median overall survival of 8.9 months and complete response observed in two patients [7]. Richie et al. initially reported a five-year survival rate of 48% in patients with non-bilharzial SCC (NB-SCC) treated with radical cystectomy; however, later reanalysis suggested that the actual survival outcomes were less favourable [8]. In a more recent retrospective study, Kassouf et al. found that radical cystectomy was associated with improved recurrence-free survival, and notably, all patients who survived beyond two years had undergone this surgical intervention [9].

The prognosis of bladder SCC remains poor, with reported five-year survival rates ranging from 27% to 33% [10]. Early diagnosis and aggressive surgical management offer the best chance for disease control. The present case demonstrates a favorable outcome with a multidisciplinary approach, including neoadjuvant chemotherapy and immunotherapy followed by radical surgery.

Conclusions

This case underscores the importance of considering primary SCC in the differential diagnosis of bladder masses, particularly in the presence of predisposing chronic inflammatory conditions. Reporting such rare cases may enhance clinical awareness and improve understanding of the disease spectrum. Radical cystectomy remains the standard of care for localized disease, while the role of systemic therapy continues to evolve. Early recognition, accurate histopathological diagnosis, and a multidisciplinary treatment strategy are crucial for improving patient outcomes. Larger prospective studies are needed to establish optimal management protocols for this uncommon tumor.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Anshu Kumar, Himanshu Shekhar, Ratnadip Deb

Acquisition, analysis, or interpretation of data: Anshu Kumar, Himanshu Shekhar, Manish Kumar, Ratnadip Deb

Drafting of the manuscript: Anshu Kumar, Himanshu Shekhar, Ratnadip Deb

Critical review of the manuscript for important intellectual content: Anshu Kumar, Himanshu Shekhar, Manish Kumar, Ratnadip Deb

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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