Case Report

JHSMR Journal of Health Science and Medical Research

Non-Bilharzial Squamous Cell Carcinoma of Urinary Bladder – Tailored Management Yields Better Outcomes: A Single Centre Experience

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Received 6 August 2024 ● Accepted 9 December 2024 ● Published online 13 May 2025

Abstract:

Urothelial carcinoma constitutes 90.0% to 95.0% of bladder malignancies and the rest are associated with epithelial and mesenchymal tumors. Squamous cell carcinoma (SCC) can be either bilharzial or non-bilharzial in origin; 2.0% to 5.0% of individuals with bladder cancer have non-bilharzial SCC, an unusual diagnosis. Here we report 3 cases of non-bilharzial SCC in males. Hematuria was the most common presenting symptom. Transurethral resection of the bladder tumor was performed and the histopathological study confirmed SCC in all 3 cases. Radical cystectomy was done in 2 patients and the third patient underwent partial cystectomy.

Keywords: carcinoma, cystectomy, squamous cell, urinary bladder

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J Health Sci Med Res 2025;43(6):e20251203
doi: 10.31584/jhsmr.20251203
www.jhsmr.org

Introduction

The most frequent cancer of the urinary tract, bladder cancer, is divided into 3 categories: nonurothelial cancer, urothelial carcinoma with divergent differentiation, and conventional urothelial carcinoma[1]. Of bladder cancers, 90.0% to 95.0% are urothelial carcinomas; the remaining 5.0% to 10.0% are mesenchymal and other epithelial tumors. Adenocarcinoma, squamous cell carcinoma (SCC), carcinosarcoma, and neuroendocrine tumors are the non-urothelial types of bladder cancer. SCC of the bladder is rare and usually associated with bilharziasis. Only 2.0% to 5.0% of individuals with bladder cancer have non-bilharzial SCC (NB-SCC)[2]. This series contributes by analyzing the clinicopathological traits, probable causative factors, and patient outcomes of SCC bladder treated at our facility.

Case reports

Case 1

A 62-year-old man, who is a known case of recurrent stricture urethra with a history of urethroplasty, presented with difficulty in voiding for one month. Blood investigations and urine analysis were within normal limits. A short segment bulbar urethral stricture was noted on the ascending urethrogram. Ultrasonography (USG) of the abdomen revealed renal cysts and focal irregular thickening in the right lateral wall of the bladder. The patient underwent an optical internal urethrotomy. On cystoscopy, a papilliferous growth was noted in the right posterolateral wall, after which transurethral resection (TUR) of the growth was undertaken. A muscle-invasive SCC was confirmed with the following histology report: pT2, high grade. Immunohistochemistry (IHC) markers revealed P40 positivity and GATA3 negativity. Contrast-enhanced computed tomography (CECT) KUB did not show tumors elsewhere. CT chest was done as a part of the metastasis workup, but no lesions were revealed. As the patient wanted to retain the normal voiding function, radical cystectomy (RC) with orthotopic neobladder construction and pelvic lymphadenectomy was performed. The histopathological report came out as pT2bN0M0 with negative margins. At the 3-year follow-up, the patient is doing well and no local recurrence was detected (Figure 1).

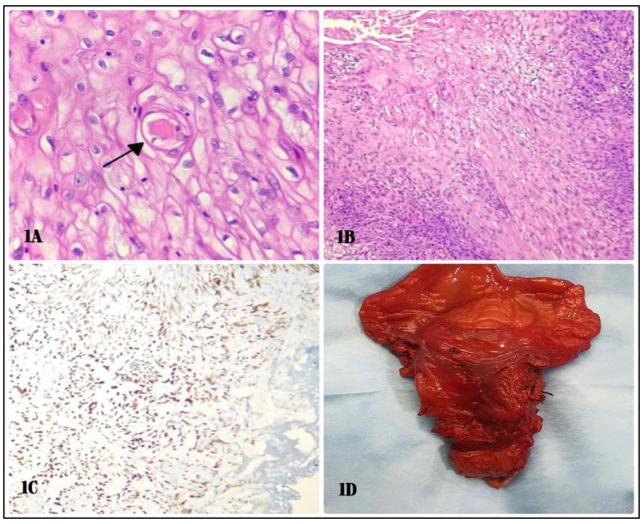

Figure 1 Histopathological study of bladder tumor with IHC staining and RC. 1A-Keratin pearl (black arrow) [Haematoxylin and Eosin stain 40x]. 1B-Squamous cells arranged in nests and sheets [Haematoxylin and Eosin stain 10x]. 1C-IHC staining showing nucleus positivity for P40 [10x]. 1D-RC specimen.

Case 2

A 71-year-old man who is a chronic smoker presented with total painless hematuria for 4 months. Routine blood investigations were done which revealed hemoglobin of 7.7 gm/dl and creatinine of 1.3 mg/dl. Urine analysis displayed plenty of red blood cells. Squamous cells were seen on urine cytology. USG abdomen revealed multiple heterogenous hyperechoic lesions in the bladder. CECT abdomen and pelvis showed multiple irregular polypoidal lesions, with the largest measuring approximately 5.5x5 cm in the bladder with left vesicoureteric junction (VUJ) infiltration causing moderate left hydroureteronephrosis (HUN). No abnormality was detected on the CT chest. TUR of the bladder tumor was done, and a diagnosis of muscle-invasive SCC was made. RC with ileal conduit and bilateral pelvic lymphadenectomy was performed. The pathologist reported a moderately differentiated SCC of the bladder with seminal vesicle infiltration and multiple regional lymph nodes - pT4aN2M0. Adjuvant radiotherapy (RT) was offered. Positron emission tomography-computed tomography was done after 3 months, and no residual disease or metastases were seen. Later, the patient was lost to follow-up (Figure 2).

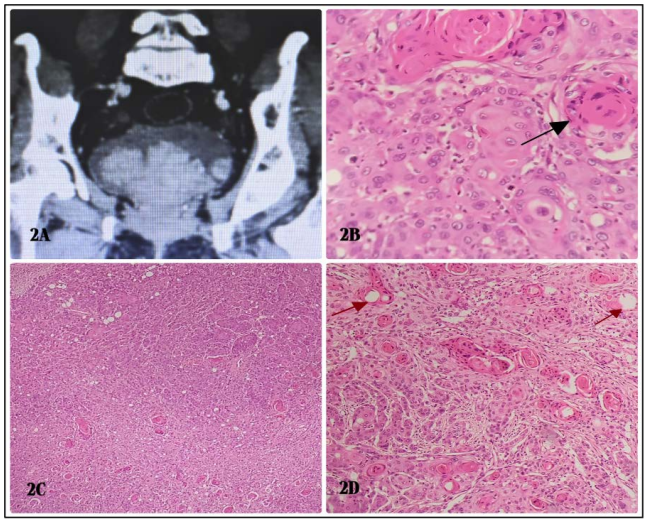

Figure 2 CECT abdomen – coronal imaging with the photomicrographic study of bladder tumor. 2A-CECT abdomen showing multiple irregular polypoidal lesions in the bladder. 2B-Keratin pearl (black arrow) [Haematoxylin & Eosin stain 40x]. 2C-Malignant squamous cells arranged in nests and sheets [Haematoxylin & Eosin stain 10x]. 2D-Squamous cells infiltrating the adjacent adipose tissue (red arrows) [Haematoxylin & Eosin stain 10x].

Case 3

A 66-year-old man presented with painless hematuria for 2 months. He had a history of recurrent episodes of cystitis and stones in the bladder. He is a known diabetic and hypertensive. Routine blood tests revealed hemoglobin of 12.4 gm/dl and creatinine of 3.2 mg/dl. USG of the abdomen showed a hyper-echoic lesion inside the diverticulum in the left lateral wall of the bladder. Magnetic resonance urography imaging demonstrated a solitary intra-diverticular lesion of size 2.5 x 2 cm in the left posterolateral wall of the bladder. Urine cytology was negative. TUR of the bladder tumor was done, and tissue diagnosis of SCC was obtained. The performance status of the patient was not satisfactory. Hence, by considering the patient-related and disease-related factors, partial cystectomy with pelvic lymphadenectomy was performed. The resected portion included a bladder diverticulum with the tumor and a margin of 2 cm of normal bladder wall. The final histopathological report was well-differentiated SCC – G1, pT3aN0M0 with negative surgical margins. Radiation therapy was offered as adjuvant treatment. Postoperatively, cystoscopy with urine cytology was undertaken at regular intervals and found to be normal. No recurrence or metastases were seen at the 5-year follow-up.

Discussion

Our patients did not live in places of endemicity for schistosomiasis infection and had no history of visiting such areas. The following are common etiologies of non-bilharzial SCC: bladder calculus, spinal cord injury, long-term indwelling catheters, foreign substances, and urinary tract infection. They form a platform for the growth factors and cytokines to promote cell proliferation, angiogenesis, and inhibition of apoptosis, leading to squamous metaplasia, dysplasia, and cancer. In our series, case 1 had a history of urethral surgery and recurrent urethral catheterizations. Case 2 had a prior history of smoking. Case 3 had a history of vesical calculus and cystitis. RC with urinary diversion and pelvic lymphadenectomy was done in the first 2 cases. Adjuvant radiation therapy was given in case 2, where the disease was locally advanced with the involvement of multiple regional nodes. In case 3, since the tumor was solitary and inside the diverticulum of the bladder, partial cystectomy with pelvic lymphadenectomy was done, followed by a course of adjuvant radiation therapy. Bladder SCC typically appears as painless hematuria. Urinary blockage and symptoms of an irritable bladder are the other unusual presentations. SCC usually manifests at a more advanced stage, even if nodal and metastatic disease frequency is lower. HUN, advanced age (70 years and above), lymph node metastasis, and higher T-stage were reported as negative prognostic factors for SCC, among which HUN is considered an independent risk factor. The majority of bladder squamous cell carcinomas are aggressive, of a higher grade, and have a poor prognosis due to muscle involvement. They are also sessile, nodular, ulcerating, and infiltrating, in contrast to transitional cell carcinomas, which are primarily papillary and non-ulcerating.

SCC is categorized as well, moderately, or poorly differentiated based on histology[3]. According to research, the majority of individuals with atypical squamous cells in their urine were found to have vaginal contamination in females and distal urethral exfoliation in males; only 25.0% of these patients had squamous cell bladder cancer[4]. Following the transurethral removal of the bladder tumor, the primary SCC diagnosis was made after the entire specimen was examined in order to rule out any focus of transitional cell carcinoma. Studies on histology have revealed a 24.0% frequency of lymph node metastases, highlighting the significant role of pelvic lymphadenectomy[5]. Because bladder SCC is chemo-refractory, RC and urinary diversion with or without radiation therapy based on the extent of the

disease and nodal involvement is the preferred treatment of choice[6]. After reviewing the effectiveness of neoadjuvant and adjuvant methods, Rausch et al. advised that pre-operative RT can be taken into consideration only in locally advanced cases[7]. In patients with operable muscle-invasive bladder cancer, European urological guidelines suggest that pre-operative RT is not offered, as it shows no improvement in survival. The combination of RC and adjuvant RT improves 5-year disease-free survival and decreases the chances of recurrence, supporting the use of RT in reducing the pelvic failures[8]. The use of neoadjuvant chemotherapy is currently ambiguous for squamous histology, as no regime has demonstrated a persistent, successful response[9].

For partial cystectomy, the Memorial Sloan Kettering Cancer Centre and MD Anderson study developed stringent criteria, including solitary tumor away from VUJ that would allow for 2 cm margins, no carcinoma in situ (CIS), no tumors in the bladder neck or trigone and a complete TUR. Variant histology should also be considered in patient selection[10]. Kassouf et al. did a study on 37 patients with no CIS disease undergoing partial cystectomy and concluded that 5-year overall survival and disease-specific survival were 67.0% and 87.0%[11]. Capitanio et al. did a comparative analysis between radical and partial cystectomy and reported that partial cystectomy provided similar overall and cancer-specific survival[12]. Na yin et al. reported a case of localized SCC bladder with disease-free survival of 10 years following partial cystectomy[13]. SCC is associated with poor prognosis; the reported 5-year survival rate is 33.0% to 48.0%[14].

Conclusion

The majority of bladder squamous cell carcinomas are aggressive and exhibit muscle involvement with a worse prognosis than urothelial carcinoma. RC with ileal conduit is the ideal procedure of choice in patients with SCC of the urinary bladder. Orthotopic neobladder construction can be an alternative technique option in plausible scenarios. Partial cystectomy can be an alternative management option for solitary SCC tumors located in the bladder diverticulum, irrespective of any histological pattern. Adjuvant RT should be considered following partial cystectomy in patients with pathological evidence of extravesical involvement or pelvic lymph node metastases as it helps in decreasing local recurrence. Since SCC bladder spreads rapidly and has a high recurrence rate and different clinical outcomes when compared to urothelial carcinoma, early diagnosis and management with regular follow-up are the key factors to improving prognosis. Finally, personalized management plans are mandatory in order to achieve the best possible outcomes in these cases.

Conflict of interest

There are no potential conflicts of interest to declare.

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