



## Case Report

# Squamous Cell Carcinoma of the Urinary Bladder Associated with Large Vesical Calculus

Sankalp Singh<sup>1\*</sup>, Niharika Bisht<sup>2</sup>, Samir Gupta<sup>2</sup>, Arijit Sen<sup>3</sup>, Richa Joshi<sup>2</sup>

<sup>1</sup>Department of Radiation Oncology, Command Hospital (CC), Lucknow, Uttar Pradesh, India

<sup>2</sup>Malignant Disease Treatment Centre, Command Hospital (SC), Pune, Maharashtra, India

<sup>3</sup>Department of Pathology, Armed Forces Medical College, Pune, Maharashtra, India

## Abstract

Squamous cell carcinoma is a histological diagnosis rarely seen in bladder cancers. It is classically associated with chronic mucosal inflammation or urinary retention. Very few studies have clearly defined the management guidelines, however multimodality treatment is frequently offered along the lines of more common transitional cell cancer. We report the case of a 50-year-old male who presented with obstructive urinary symptoms and on evaluation was found to have a large vesical calculus associated with squamous cell cancer of the bladder. He was treated with surgery in the form of radical cystectomy followed by adjuvant locoregional radiotherapy. He has remained on regular follow-up for the last 2 years and has been disease free.

**Keywords:** Radical cystectomy, squamous cell carcinoma, urinary bladder, vesical calculus

## INTRODUCTION

The urinary bladder is the most common site of malignancy of the urinary tract,<sup>[1]</sup> with transitional cell carcinoma (TCC) being the most common histology. Squamous cell carcinoma (SCC) is a rare histopathological diagnosis in the urinary bladder, accounting for only 2%–3% of all cancers at this site. It is often associated with chronic inflammation or urinary retention and is divided into two main subtypes based on the presence or absence of associated bilharziasis (schistosomiasis). The mainstay of treatment remains radical cystectomy (RC), while the role of adjuvant and neoadjuvant therapy (radiation or chemotherapy) is still debatable.

Received: 19-Mar-2019 Revised: 15-Sep-2019

Accepted: 27-Nov-2019 Published: 02-Mar-2020

### Access this article online

#### Quick Response Code:



Website:  
[www.ejcrp.org](http://www.ejcrp.org)

DOI:  
10.4103/JCRP.JCRP\_29\_19

## CASE REPORT

A 50-year-old male presented to the outpatient department of our hospital with complaints of difficulty in passing urine and urinary urgency for a period of 1 month. He had a history of occasional pain on passing urine as well as a history of unquantified weight loss over the previous month. There was no history of passing blood in urine or of burning micturition, no change in appetite, and no fever or other systemic symptoms. He was a nonsmoker with no known comorbidities.

**Address for correspondence:** Dr. Sankalp Singh,  
Command Hospital (CC), Lucknow - 226 002, Uttar Pradesh, India.  
E-mail: [sankalpsingh9@gmail.com](mailto:sankalpsingh9@gmail.com)

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** [reprints@medknow.com](mailto:reprints@medknow.com)

**How to cite this article:** Singh S, Bisht N, Gupta S, Sen A, Joshi R. Squamous cell carcinoma of the urinary bladder associated with large vesical calculus. *J Cancer Res Pract* 2020;7:45-8.

On examination, he had an excellent performance status (Eastern Cooperative Oncology Group Score 0) with a soft abdomen without any generalized tenderness or palpable lumps. A digital rectal examination did not reveal any enlargement of the prostate. A routine urine examination was unremarkable. A Kidneys, Ureters, Bladder (KUB) radiograph showed a pelvic calcification, which was likely to be calcific vesical calculus. With the diagnosis of a vesicular calculus, he was further evaluated with cystoscopy which showed a large vesicular calculus, about 8 cm in the largest dimension, occupying two-thirds of the bladder. The cystoscopy also detected a proliferative mass lesion, about 5 cm × 5 cm in size, over the right lateral wall of the urinary bladder.

The patient then underwent a computed tomography (CT) scan of the abdomen and pelvis [Figure 1a], which was suggestive of an enhancing soft-tissue mass lesion, 77 mm × 21 mm in size, involving the right anterolateral wall of the urinary bladder with an enlarged right iliac lymph node, 16 mm × 9 mm in size. A large calculus, 65 mm × 47 mm × 45 mm in size, was also noted in the urinary bladder. A magnetic resonance imaging (MRI) scan of his pelvis [Figure 1b] corroborated the findings of the CT scan. A whole-body positron emission tomography CT scan showed the lesion in the right lateral wall of the urinary bladder to be highly metabolically active ( $SUV_{max}$ : 16.5), with the right iliac node showing very mild fluorodeoxyglucose activity ( $SUV_{max}$ : 3.2). No distant metastases were detected.

A transurethral resection of bladder tumor biopsy was taken from the growth, which showed numerous tumor islands composed of malignant squamous cells in the subepithelial stroma [Figure 2]. The malignant cells were large with abundant eosinophilic cytoplasm, large vesicular nuclei, and prominent nucleoli. Foci of keratin pearls and individual cell keratinization were also noted. The appearance was consistent with a moderately differentiated SCC.

The case was discussed at a multimodality tumor board meeting where the management was decided as upfront surgery. The patient was treated with a radical cystoprostatectomy along with pelvic lymph node dissection and formation of an ileal conduit. Intra-operatively, the urinary bladder showed a growth over the right lateral wall as well as a smooth round calculus measuring 8 cm within. Uretero-ileal anastomosis was done over feeding

tube stents, and the stoma was brought out over the anterior abdominal wall.

The postoperative histopathology report showed an SCC arising in the lateral wall of the bladder and extending through the full thickness of the bladder wall and infiltrating the prostate with extension into the perivesical tissue. One right external iliac lymph node was positive for tumor deposits. Surgical margins of the neck of the bladder, ureter, and vas deferens were free of tumor cells. The tumor was staged as pT4aN1M0 as per the AJCC 7<sup>th</sup> edition staging system. The case was again discussed at a multimodality tumor board meeting and in view of the adverse factors of locally advanced stage and nodal positivity of the bladder carcinoma, it was decided to treat the patient with adjuvant radiotherapy.

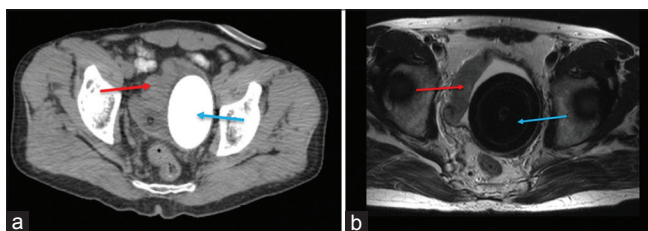
The patient was treated with a dose of 5040 cGy in 28 fractions to the cystectomy bed and pelvic lymph nodes with 6 MV photons on a “ÜNIQUE” medical linear accelerator of Varian Medical Systems, Inc. of Palo Alto, CA, United States using the RapidArc technique of rotational intensity-modulated radiotherapy (IMRT). During the treatment, he developed Grade II radiation dermatitis, but otherwise he tolerated the treatment well with no major adverse reactions or treatment breaks.

The patient has remained on regular 3-month follow-up since completion of the treatment. He has remained asymptomatic, and MRI scans of his pelvis done at 6-month intervals post surgery have shown no evidence of any residual or recurrent disease. He has now achieved a disease-free period of 2 years.

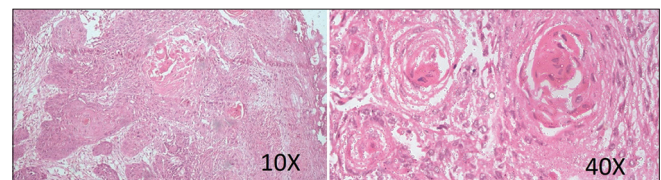
Informed consent was obtained from the patient for publication of this case report. Approval of the MDTC Institutional Ethical Committee was also acquired for this study vide case number RO/07/2019 dated February 19, 2019.

## DISCUSSION

Bladder cancer is a leading cause of mortality, however SCC accounts for only a small percentage (<5%) of cancers at this site. The two subtypes of SCC, namely bilharzia SCC (B-SCC) and non-Bilharzia SCC (NB-SCC), present as two distinct etiological, epidemiological, and clinicopathological entities.<sup>[2]</sup>



**Figure 1:** Computed tomography (a) and magnetic resonance imaging (b) scans showing large vesical calculus (blue arrow) with soft-tissue mass lesion in the right lateral wall of the urinary bladder (red arrow)



**Figure 2:** Microscopic view of the transurethral resection of bladder tumor specimen. Low-power view (×10) shows tumor islands composed of malignant squamous cells in the subepithelial stroma. High-power view (×40) shows large neoplastic cells with abundant eosinophilic cytoplasm, large vesicular nuclei, and prominent nucleoli. Foci of keratin pearls and individual cell keratinization were also noted

B-SCC is predominantly found in the Middle East, Southeast Asia, and South America, where schistosomiasis is endemic.<sup>[3]</sup> NB-SCC, on the other hand, is the more common variant in Western countries and is often associated with the long-term use of an indwelling catheter<sup>[4]</sup> and other causes of chronic bladder irritation.

B-SCC occurs at an average age at diagnosis in the fifth decade with a male-to-female ratio of about 5:1, and is probably related to the increased exposure of male farmers to schistosome infestation in fields.<sup>[3]</sup> Patients with NB-SCC are generally diagnosed in the seventh decade with a slight male-to-female preponderance (3:2). Patients are often diagnosed in a locally advanced stage and are associated with a poorer prognosis and survival compared to B-SCC.<sup>[2]</sup> The patient in our report had NB-SCC which developed as squamous carcinoma of the urinary bladder, probably as a result of long-standing irritation from the large vesical calculus.

Smoking remains the main etiological factor for all bladder cancer variants with chronic inflammation due to long-term indwelling catheters, recurrent urinary tract infections, and other bladder irritants also contributing to squamous metaplasia, dysplasia, and cancer.<sup>[5]</sup> The risk of bladder cancer development following squamous metaplasia is 21%–42%, although the precise pathway is unclear.<sup>[6]</sup> Vitamin A deficiency and systemic cyclophosphamide use are other factors implicated in the causation of SCC of the urinary bladder. Interestingly, our patient has never used tobacco in any form.

A search of published literature revealed that a few cases of SCC of the urinary bladder associated with vesical calculi have been reported.<sup>[7–9]</sup> The association of vesical calculi and other foreign bodies causing chronic mucosal injury leading to the development of SCC has been well established, and an almost two-fold increase in the risk of SCC with the presence of bladder stones<sup>[9]</sup> has been reported. However, no previous studies have reported what percentage of SCCs are found with bladder stones or *vice versa*, and further studies are needed to clarify this issue. Although no size classification is currently used for bladder stones, a stone is referred to as being large if the patient is unable to pass it per urethra. At 8 cm in diameter, the stone found in our patient's bladder was possibly the largest ever reported in association with SCC.

SCC is defined as an epithelial cancer exclusively displaying histological features such as squamous pearls, intercellular bridges, and keratohyalin granules,<sup>[10]</sup> without any evidence of urothelial components.

Most of the data available in the literature come from small retrospective studies. The mainstay of treatment for both variants remains RC.<sup>[11]</sup> Kassouf *et al.*<sup>[12]</sup> reported that treatment with RC was associated with recurrence-free survival, and noted that all of their cases surviving for more than 2 years had undergone RC. Even though the role of RC is now established as the cornerstone of management, the rates of recurrence and local failure resulting in death remain high.

Radiotherapy alone has poor local control in the management of this disease,<sup>[13]</sup> however it has been shown to improve locoregional control when used in association with surgery. Swanson *et al.* reported that combining preoperative radiotherapy with RC enhanced the 5-year disease-free survival (DFS) (40%) over radiotherapy alone (16%) and lowered the rates of recurrence.<sup>[14]</sup> In a more recent study of patients with B-SCC, it was determined that those not receiving adjuvant radiotherapy after surgery had a DFS of 29% compared to 48% for those who received it.<sup>[15]</sup> Although radiotherapy is traditionally associated with high rates of late complications, these are likely to be significantly reduced with the modern techniques of radiation delivery such as IMRT. The use of systemic chemotherapy (methotrexate, vinblastine, doxorubicin, and cisplatin) has proven to be ineffective in patients with a non-TCC histology both in neoadjuvant and adjuvant settings.<sup>[16]</sup>

## CONCLUSION

This case report highlights the etiology of SCC of the bladder and its association with long-standing vesical calculi. Our patient remained asymptomatic to mildly symptomatic but did not seek medical help until the stone reached the size of 8 cm and almost completely filled his urinary bladder. This is characteristic of the Indian subcontinent where late presentation of malignancies in advanced stages is the norm and has a negative effect on survival outcomes. This study also highlights the importance of skilled and multimodality management of such cases, with surgery offering the best curative option. This case was managed successfully with surgery and adjuvant radiotherapy, and the patient remains disease free at 24-month post treatment. The role of radiotherapy, although still not well defined, has shown promise in improving the locoregional control of SCC of the urinary bladder and merits further exploration.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

## Acknowledgments

The authors would like to acknowledge:

1. Malignant Disease Treatment Centre, Command Hospital (SC), Pune
2. Department of Pathology, Armed Forces Medical College, Pune.

## Financial support and sponsorship

This study was financially supported by Command Hospital (SC), Pune - 411 040.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin* 2016;66:7-30.
2. Martin JW, Carballido EM, Ahmed A, Farhan B, Dutta R, Smith C, *et al.* Squamous cell carcinoma of the urinary bladder: Systematic review of clinical characteristics and therapeutic approaches. *Arab J Urol* 2016;14:183-91.
3. Shokeir AA. Squamous cell carcinoma of the bladder: Pathology, diagnosis and treatment. *BJU Int* 2004;93:216-20.
4. Welk B, McIntyre A, Teasell R, Potter P, Loh E. Bladder cancer in individuals with spinal cord injuries. *Spinal Cord* 2013;51:516-21.
5. Youssef R, Kapur P, Kabbani W, Shariat SF, Mosbah A, Abol-Enein H, *et al.* Bilharzial vs. non-Bilharzial related bladder cancer: Pathological characteristics and value of cyclooxygenase-2 expression. *BJU Int* 2011;108:31-7.
6. Khan MS, Thornhill JA, Gaffney E, Loftus B, Butler MR. Keratinising squamous metaplasia of the bladder: Natural history and rationalization of management based on review of 54 years experience. *Eur Urol* 2002;42:469-74.
7. Hirata N, Maruyama Y, Tanaka N, Hirayama A, Samma S, Ozono S, *et al.* A case of squamous cell carcinoma of the urinary bladder associated with bladder calculi. *Hinyokika Kiyo* 1991;37:77-81.
8. Cho JH, Holley JL. Squamous cell carcinoma of the bladder in a female associated with multiple bladder stones. *BMC Res Notes* 2013;6:354.
9. Fernando MH, Jayarajah U, Herath KB, de Silva MV, Goonewardena SA. Aggressive squamous cell carcinoma of the bladder associated with a history of large bladder stone – A case report. *Clin Case Rep* 2017;5:1616-9.
10. Manunta A, Vincendeau S, Kiriakou G, Lobel B, Guillé F. Non-transitional cell bladder carcinomas. *BJU Int* 2005;95:497-502.
11. Izard JP, Siemens DR, Mackillop WJ, Wei X, Leveridge MJ, Berman DM, *et al.* Outcomes of squamous histology in bladder cancer: A population-based study. *Urol Oncol* 2015;33:425.e7-13.
12. Kassouf W, Spiess PE, Siefker-Radtke A, Swanson D, Grossman HB, Kamat AM, *et al.* Outcome and patterns of recurrence of non-Bilharzial pure squamous cell carcinoma of the bladder: A contemporary review of The University of Texas M D Anderson Cancer Center experience. *Cancer* 2007;110:764-9.
13. Quilty PM, Duncan W. Radiotherapy for squamous carcinoma of the urinary bladder. *Int J Radiat Oncol Biol Phys* 1986;12:861-5.
14. Swanson DA, Liles A, Zagars GK. Preoperative irradiation and radical cystectomy for stages T2 and T3 squamous cell carcinoma of the bladder. *J Urol* 1990;143:37-40.
15. El-Monim HA, El-Baradie MM, Younis A, Ragab Y, Labib A, El-Attar I. A prospective randomized trial for postoperative vs. preoperative adjuvant radiotherapy for muscle-invasive bladder cancer. *Urol Oncol* 2013;31:359-65.
16. Rausch S, Hofmann R, von Knobloch R. Non-Bilharzial squamous cell carcinoma and transitional cell carcinoma with squamous differentiation of the lower and upper urinary tract. *Urol Ann* 2012;4:14-8.