

**SQUAMOUS CELL CARCINOMA OF THE URINARY BLADDER: PATHOLOGY,
DIAGNOSIS AND TREATMENT**Dr. Yeshwant Ganpatrao Kale¹ and Dr. Karan Singh Chandrakar^{2*}¹Professor Dept. of Surgery CCM Medical College Durg 490024.²Assistant Professor Dept. of Pathology CCM Medical College Durg 490024.***Corresponding Author: Dr. Karan Singh Chandrakar**

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ABSTRACT

*Squamous Cell Carcinoma of the Bladder is a rare type of bladder cancer. The majority of bladder cancers are transitional cell carcinomas that arise in the urinary tract epithelium and can also occur in parts of the kidney, ureter and urethra. The majority of cases are transitional cell carcinomas affecting the tall epithelial cells lining the bladder. Squamous cell carcinoma accounts for only 3 to 7% of bladder cancers in Western countries, but in certain countries where parasites are very common (especially schistosomiasis) it is found much more. **Material and Methods:** Total 29 patients were included in the studies that were diagnosed. All patients underwent ultrasound examination prior to their surgery and histopathological analysis Detailed history of the patient was taken. Demographic data was recorded. **Results:** Out of 29 patients, 9 patients were in the high-risk category, which included TaHG, T1LG, and T1HG. And 20 patients received Bacillus Calmette-Guérin (BCG) as induction therapy. A total of 6 patients received 40 mg, 12 patients received 80 mg, and 11 patients received 120 mg of BCG. Each patient received BCG weekly for 6 weeks. Of the 12 patients with muscle-invasive bladder cancer, 17 patients underwent a radical cystectomy and standard pelvic lymph node dissection with urinary diversion. Of the 17 patients, 11 patients had orthotopic neobladder while the remaining 6 underwent ileal conduit. A total of 5 patients died during the study period. **Conclusion:** EUA is a valuable staging tool that is readily available to all physicians Radical cystoprostatectomy is the treatment of choice with lymph node dissection. In case of muscle is not involved, the intravesical immunotherapy with Bacillus Calmette-Guerin is given with regular surveillance cystoscopies. Given recent advances in radiotherapy and previous studies suggesting improved outcomes with radiotherapy, the role of neoadjuvant/adjuvant radiation should be re-evaluated. Immunotherapy may also improve clinical outcomes. Biomarkers and pathological prognostic factors such as staging, grading also help in improving prognosis.*

KEYWORDS: SCC, Urinary bladder, schistosomiasis, BCG, TaHG, T1LG, and T1HG.**INTRODUCTION**

Squamous Cell Carcinoma (SCC) of the Bladder is a rare type of bladder cancer. The majority of bladder carcinomas are transitional cell carcinomas that arise in the urinary tract and can also occur in other parts like kidney, ureter and urethra. The urinary bladder is a waste storage system for urine. The urinary bladder is lined with epithelium called transitional cells which are tall, thin cells that protect the underlying bladder from the urine contained therein. Because the bladder is lined with transitional epithelium, the usual type of cancer affecting the bladder is transitional cell carcinoma.^[1]

Urinary Bladder carcinoma is the most common malignancy affecting the urinary system. The most of cases are transitional cell carcinomas affecting the urinary bladder epithelial cell. In Western countries only 3-7%, urinary bladder squamous cell carcinoma accounts but in many countries where schistosomiasis parasites

are very common in these countries it accounts up to 70%. The schistosomiasis parasites cause chronic irritation of the bladder causing the cells to change their shape to try to protect the bladder after over time the cells can change to become neoplastic or cancerous. The incidence of bladder carcinoma increases with age and it accounts near about 80% of patients are found to be between 50 - 80 years.^[2]

Currently practices for the initial diagnosis, staging and evaluation of bladder cancer includes: transurethral resection of bladder tumors (TURBT), bimanual exam under anesthesia (EUA), abdominal and pelvic imaging, baseline laboratory studies, and chest imaging. The EUA is performed to determine local tumor extent outside the bladder and imaging is performed to assess regional lymph nodes for tumor involvement. The EUA can be performed after complete tumor resection by placing one hand on the anterior abdomen and a finger of the other

hand in the rectal vault when the patient in the dorsal lithotomy position. In a female patient, two fingers of the other hand are placed in the vagina. This procedure allows direct palpation of the bladder between the two hands to manually determine if the tumor is palpable on the outer surface of the bladder and whether it is a mobile or fixed mass, distinguishing clinical stage T3 and T4 disease respectively.^[3]

There are only a few centers in India where a high volume of bladder carcinoma is being treated. Most of the data come from these tertiary centers. Two large series from different parts of the country have looked into the epidemiological aspects of bladder carcinoma. Gupta *et al.*^[4] published a series of 561 bladder carcinoma patients treated between 2001 and 2008 at SGPGI, Lucknow. In this series, 97% of the patients presented with painless haematuria.

SCC can occur in two types i.e. nonbilharzial and bilharzial infection (schistosomiasis) bladders. These are differing from each other in epidemiology, pathogenesis and clinicopathological features. The nonbilharzial type occurs in Western countries and represents < 5% of all vesical tumours. The principal predisposing factor is spinal cord injury and the main symptom is haematuria. Patients are usually diagnosed at an advanced stage and most of the tumours are of moderate and high grades. At cystoscopy tumours are predominantly ulcerative and commonly involve the trigone and lateral walls. Although distant metastasis is infrequent (8-10%) the

prognosis is grave and most patients die after failure of loco regional control; radical cystectomy provides the best therapy. To avoid nonbilharzial SCC, patients with spinal cord injury should be free of catheterization if possible. The outcome can be improved by early detection with frequent cytology, cystoscopy and biopsy.^[5]

Bilharzial SCC occurs commonly in the Middle East, South-east Asia and South America where schistosomiasis is endemic.^[6] In an Egyptian series SCC represented 59% of 1026 cystectomy specimens. The tumour is diagnosed in the fifth decade, and five times more common in men than women. Bladder carcinogenesis is probably related to bacterial and viral infections, commonly associated with bilharzial infestation rather than the parasite itself.

The presentation is often with irritative bladder symptoms and haematuria. Many patients present at an advanced stage, although most tumours are of low and moderate grades. At cystoscopy tumours are predominantly nodular and usually arise from the upper vesical hemisphere. Lymph-node metastasis occurs in approximately 19% and significantly decreases survival; radical cystectomy remains the main treatment, giving a 5-year survival rate of 50%. Early detection improves the therapeutic yield and prevention is possible by combining snail control and mass therapy of the infested rural population by oral antibilharzial drugs.^[5]

B-SCC and NB-SCC differ in their epidemiology, natural history, and clinicopathological features.^[7]

	B-SCC	NB-SCC
Geography	Middle East, Southeast Asia, South America	Western countries
% of bladder tumours	20–30 (>50 in the past)	2–5
Age	Fifth decade	Seventh decade
Male:Female	5:1	3:2
Major predisposing factors	Bilharzial cystitis, UTIs	Indwelling catheters, chronic inflammation, bladder irritants, UTIs
Principal symptoms	Haematuria, irritative bladder symptoms	Haematuria
Stage	Mostly advanced	Mostly advanced
Grade	50% low grade	Mostly high grade
LN metastasis, %	18	8–10
Standard treatment	RC	RC
Prognosis (5-year survival), %	~50–60	33–48
Recurrence	Mostly local	Mostly local
Prevention	Snail control and anti-bilharzial drugs	Avoidance of bladder irritants, including prolonged indwelling catheterisation

In urinary bladder carcinoma there is normally little to find on examination, unless the bladder tumour is widespread. Your doctor will carefully examine your abdomen, pelvis and urinary tract. Haematuria or microscopic haematuria on urinalysis may be the only sign in 2% of incidents.^[8]

Urinary bladder cancer investigations tend to involve basic blood tests such as full blood test which may reveal anaemia due to chronic blood loss. A urine sample may reveal red blood cells or malignant cells. Pictures of the urinary tract will be performed such as Ultrasound and intravenous pyelogram which are followed by CT or MRI. Rule out pathology of other parts of the urinary tract and its use to visualise the urothelial. Biopsy and Cystoscopy

are important investigations for diagnosis of urinary bladder carcinoma.^[9]

MATERIAL AND METHODS

The present study was carried out in the department of Surgery in collaboration with Dept. of Pathology at CCM Medical College and Hospital over a period of 3 years from Oct 2014 to May 2017 and. An exclusion criterion was patients who were not willing for study, seriously ill patients and patients with deranged renal functions.

Total 29 patients were included in the studies that were diagnosed. All patients underwent ultrasound examination prior to their surgery and histopathological analysis Detailed history of the patient was taken. Demographic data was recorded.

OBSERVATIONS AND RESULTS

Clinicopathological Features

Urinary Bladder carcinoma is related to bacterial and viral infections, commonly associated with bilharzial infestation. Urinary bacteria secretes the of β -glucuronidase enzyme which may clear conjugated carcinogens, yielding free carcinogenic products, and the production of carcinogenic nitrosamines from their precursors in urine, e.g. nitrates and secondary amines.^[10]

Haematuria is the major symptom and it is observed in nearly all cases of carcinoma and some patients having irritative bladder symptoms. Symptoms of pelvic pain, back pain and hydronephrosis are showing the progression of disease. Inflammation from chronic urinary tract irritation, either from bacterial infections, foreign bodies and bladder calculi, or chronic BOO, have been implicated in the pathogenesis of SCC. Many of these factors are present in patients with SCI and long-term indwelling catheters. It has been reported that at the time of diagnosis up to 94.91% of patients suffer with UTI.^[6] These symptoms are often present for protracted intervals before the definitive diagnosis.

A population-based analysis conducted by Abdollah F et.al. They examine 614 patients with NB-SCC using the Surveillance, Epidemiology, and End Results (SEER) programme showed that the most frequent stage was T3 (42.3%), and the most common histological grades were II (37.3%) and III (42.5%).^[11]

Treatment

Out of 29 patients, 9 patients were in the high-risk category, which included TaHG, T1LG, and T1HG. And 20 patients received Bacillus Calmette-Guérin (BCG) as induction therapy. A total of 6 patients received 40 mg, 12 patients received 80 mg, and 11 patients received 120 mg of BCG. Each patient received BCG weekly for 6 weeks.

Of the 12 patients with muscle-invasive bladder cancer, 17 patients underwent a radical cystectomy and standard

pelvic lymph node dissection with urinary diversion. Of the 17 patients, 11 patients had orthotopic neobladder while the remaining 6 underwent ileal conduit. A total of 5 patients died during the study period.

The tumor is found to be muscle-invasive and then radical cystoprostatectomy is the treatment of choice with lymph node dissection. In case of muscle is not involved, the intravesical immunotherapy with Bacillus Calmette-Guérin is given with regular surveillance cystoscopies. A transurethral resection of the bladder tumor (TURBT) was performed using Glycine (1.5%) as an irrigant. A random biopsy was not performed as per the protocol and only suspicious lesions were biopsied. None of the patients had repeated a TURBT. The biopsy specimen in which there was no evidence of detrusor muscle was recorded separately.

DISCUSSION

For bladder cancer, precise determination of tumor stage is a key or determining the most appropriate treatment strategy. As per the cancer statistics the bladder cancer incidence is variable in geographic areas which stated that in developed countries incidence is 16.6%, while in less developed countries incidence is 5.4%.^[12] It is the most common malignant tumour in male where infection with schistosomiasis.^[13] The association between chronic bladder irritation and squamous cell carcinoma has been postulated, which include chronic or recurrent urinary tract infection, chronic in dwelling urinary devices, neurogenic bladder, bladder stone, foreign bodies in the bladder and prolonged exposure to cyclophosphamide.^[14]

Examination under anesthesia (EUA) has been done in the clinical staging of bladder cancer, with a palpable mass indicating more advanced disease with higher rates of lymph node positive disease and poorer overall survival.^[15] Wijkstrom et al in their study found that patients with a palpable bladder mass had survival rates of 53% and 45% at 5 and 10 years respectively, compared to 80% and 70% without palpable masses at 5 and 10 years respectively. In our study out of 29 patients, 9 patients were in the high-risk category and having palpable bladder mass.^[16] In this study we want to demonstrate the importance of EUA in the clinical staging of bladder cancer, and that it should not be ignored as part of the preoperative staging evaluation of muscle invasive bladder cancer, and it was correctly diagnosed in all our cases. In our study EUA was performed by the two experienced surgeons and also anesthesia was given by the experienced anesthetist, thereby reducing inter-observer variability in our staging. The focus of our analysis was to characterize the impact of EUA on clinical staging of bladder cancer. These pathologic characteristic to assess their importance in predicting extra-vesical disease by independent and in combination with EUA can confirmed by further studies.

CONCLUSION

The incidence rate of SCC is decreasing but the clinical staging of bladder cancer is critical because of its impact on management. Due to lack of research and rarity of the disease, there is a lack of Level I evidence guiding management of SCC. EUA is a valuable staging tool that is readily available to all physicians. Radical cystoprostatectomy is the treatment of choice with lymph node dissection. In case of muscle is not involved, the intravesical immunotherapy with Bacillus Calmette–Guerin is given with regular surveillance cystoscopies. Given recent advances in radiotherapy and previous studies suggesting improved outcomes with radiotherapy, the role of neoadjuvant/adjuvant radiation should be re-evaluated. Immunotherapy may also improve clinical outcomes. Biomarkers and pathological prognostic factors such as staging, grading also help in improving prognosis.

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