

Superficial Bladder Cancer Recurrence on First Check Cystoscopy after Transurethral Resection (TURBT).

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Abstract

Background: To determine the frequency of recurrence of superficial tumours on first check cystoscopy i.e. 3 months after complete resection of tumour.

Methods: In this descriptive study adult male and female patients (n=41) presenting with a superficial transitional cell carcinoma of urinary bladder were included and complete resection of the tumour was done and tissue sent for histopathology. Patients with Superficial T.C.C (confirmed by histopathology) were followed up, after three months by cystoscopy and findings noted. Any tumour growth on the same or new location was resected again and sent to the same histopathologist for examination and confirmation of TCC. All the above information was recorded and entered into a structured proforma.

Results: Majority (80.5%) were male. The age of patients ranged from 28 to 85 years with a mean of 59 ± 11.5 yrs.. The T-stage at presentation was pTa in 11 (27%) patients and pT1 in 30 (73%) patients. The histological grade of tumour at presentation was G-I in 16 (39%), G-II in 10 (24%) and G-III in 15 (37%) patients. First check cystoscopy was done 3 months after TURBT. In which 28 (68%) patients showed recurrence of tumour while the rest, i.e. 13 (32%) showed disease free status. Out of 28 cases with recurrence of tumour, 2 (5%) cases showed pTa and 26 (63%) showed pT1. The recurrent histological G-I, G-II and G-III were 5, 8 and 15 respectively.

Conclusion: Recurrence of superficial transitional cell carcinoma at first check cystoscopy is high and has a predictive value for future recurrence of the disease.

Key Word: Transitional Cell Carcinoma (T.C.C), Transurethral resection of bladder tumour (TURBT), Cystoscopy

Introduction

Transitional Cell Carcinoma (T.C.C) is the most common tumour of urinary bladder. White light cystoscopy is the standard tool for diagnosis.

Treatment of choice for superficial T.C.C is transurethral resection of bladder tumour (TURBT). Superficial T.C.C has a natural history of recurrence and disease progression. The risk of tumour recurrence can be minimized by using intravesical chemo/immunotherapy. It represents 70%-80% of all bladder neoplasms.¹ More than 90% of urothelial cancers in the bladder TCC. Other important histological types include squamous cell carcinoma and adenocarcinoma.² Urinary bladder neoplasm can be grouped into three different categories i.e., superficial, invasive and metastatic. At presentation, 75% of the tumours are superficial, 20% are invasive and up to 5% have de novo metastasis¹. TCC is the seventh most common cause of death in men and tenth most common cause of death in women. It can occur anywhere along the urinary tract which is lined by transitional cell epithelium (urothelium) but its presence in the bladder, in majority of cases points to a cause related to pooling of urine/mucosal contact with urine. Superficial bladder cancers, which include papillary carcinoma (Ta), Carcinoma in Situ (C.I.S or Tis), which are flat, and on cystoscopy appear as red (hyperemic), raised, velvety areas which bleed readily on touch, and tumors that invade Lamina Propria (T1).³ Superficial TCC is the most common form of transitional cell carcinoma of the bladder, and accounts for 90% of cases. Of the superficial variety, pTa accounts for about 70% of cases and pT1 for 30% of cases.⁴ Carcinoma in situ, like T.C.C, can be found anywhere along the urinary tract. It is considered to be a very highly aggressive form of the disease as it has the ability to invade deeper layers of the bladder rapidly and can progress to more invasive forms of T.C.C. Various etiological/risk factors for T.C.C bladder are identified including environmental factors and genetic factors. The most common environmental factors responsible for T.C.C bladder are the aromatic amines (Arylamines), Benzidine, 4-Aminobiphenyl, Beta- Nephthylamines, found in various industrial products. The occupational hazards include working in paints, petroleum, rubber or leather, coal, printing industries and barbers.⁵ Smokers have up to four fold

higher incidence of bladder cancer than non smokers.⁶ The risk correlates with the number of cigarettes smoked, the duration of smoking and the degree of inhalation of smoke. Causative agents in cigarette smoke are thought to be alpha and beta naphthylamine, which are secreted in the urine of smokers.⁷ Various infections, such as Human Papilloma Virus (HPV), are also considered to have an etiological effect.⁸ National Cancer Institute Surveillance Epidemiology and End Results (SEER) programme estimates that 89% of bladder carcinoma patients are 55 years of age or older at the time of diagnosis and that the median age at the time of diagnosis for both men and women.⁹ Painless, intermittent, gross haematuria with passage of clots is the most common form of presentation of superficial T.C.C.¹⁰ Symptoms such as frequency, urgency, nocturia, supra pubic discomfort and flank pain, are usually not a feature of superficial T.C.C. Their presence at times would indicate a more invasive form or carcinoma in situ (CIS). Intravenous urogram is done to identify a filling defect in the bladder. However, the main aim of intravenous urography is to identify the presence of any synchronous tumour of ureter and renal pelvis on either side. With the availability of more sophisticated ultrasonographic probes and advances in experience, bladder tumours can be fairly picked up by sonography as it is easy to identify any increased vascularity in the bladder mass to differentiate it from a blood clot in a patient with frank haematuria.¹¹

T.C.C is known to have a varied response to treatment. The disease has a natural course of multiple recurrences and progression in terms of histological grade and T-stage. About 70% of superficial T.C.C recur after T.U.R.B.T and about 25% will progress to more invasive forms.¹² Intravesical chemotherapy is known to be effective in preventing cancer recurrence by suppressing implantation of the postoperative tumor cells wandering in the bladder after the surgery. On the other hand, in the case of non-muscle-invasive bladder cancer patients in the intermediate risk group (TaG1 with multifocal or >3 cm diameter, TaG2, T1G1, T1G2).¹³ The rates of recurrence and progression can be minimized by intravesical chemo or immunotherapy in the form of Mitomycin-C or BCG respectively.¹⁴ Various factors are considered for the prediction of future recurrence and progression of the disease, according to EORTC risk tables, including tumour diameter, multiplicity, prior recurrence, presence of concomitant C.I.S, T-stage and histological grade.¹⁵ Every patient should have a check cystoscopy

three months after the initial T.U.R.B.T. This first check cystoscopy is of utmost importance as it has a predictive value regarding the future recurrences of the disease. Patients who have a recurrence at first check cystoscopy, are at a higher risk of further future recurrences as compared to those with no recurrence at first check cystoscopy.¹⁶

Patients and Methods

This descriptive/observational study of total duration of 06 months from June 2011 to December 2011 was carried out at the department of Urology, Shaheed Zulfiqar Ali Bhutto Medical University, PIMS, Islamabad. The total number of patients were 41 of either sex with a clinical suspicion of bladder tumour presenting at OPD and ER Department were included in study. We included all patients who fulfilled our inclusion/exclusion criteria. All patients underwent cystoscopy and if there was papillary growth in bladder it was completely resected (TURBT). If there is any suspicion of concomitant Carcinoma in situ, a biopsy was taken to rule it out. All operations were performed or supervised by single surgeon and the resected tissue was sent to single histopathologist for examination (To control bias). The exclusion criteria was followed up, after three months with cystoscopy preferably by the same operator and findings noted. Any tumour growth on the same or new location was resected again and sent to the same histopathologist for examination and confirmation of recurrence of TCC. (Diagnosis Criteria for recurrence was seeing the growth at the same or other sides, resecting the growth and further confirmed on histopathology.

Results

Total number of patients included in the study were 41. Majority were male (n= 33; (80.5%) and females were 8 (19.5%) with a male to female ratio of 4:1. The mean age at presentation was 59 years (28-85 years) with majority of patients (n = 30), 73.12% falling in the age range of 50-70 years. The most common T-stage at presentation was pT1 (73%)(Table 1). The most common histological grade at presentation was G-I (39%) (Table 2). The frequency of recurrence, 3 months after TURBT, at first check cystoscopy was 68.3% (Table 3). In the group without recurrence 61.5% (8) of cases belonged to pTa stage and 38.5% (5) to pT1 stage. Majority of cases, in no recurrence group, were histologically G-I (61.5%, 8), while 3 and 2 cases were G-II and G-III respectively. In recurrence group majority were pT1 (89%)(Table 4). Histologically majority recurred in G 3(46.4%) (Table 5).T-stage

progression was noted in only one case from pTa to pT1. Progression of histological grade was noted in 3 cases from G-I to G-II, 3 cases from G-I to G-III and 5 cases from G-II to G-III. Down grading occurred in 2 cases from G-II to G-I, 4 cases from G-III to G-II and one case from G-III to G-I. In recurrence group, there were 11 (39%) cases of pT1G-III (T1G3) tumours.

Table 1: Frequencies of T-stage at presentation
(n = 41)

Stage	Frequency	Percent
PTa	11	26.8
pT1	30	73.2

Table 2: Frequencies of various histological grades at presentation

Histological grade	No(%)
G-I	16(39)
G- II	10(24.4)
G -III	15(36.6)

Table3: Frequency of recurrence on first check cystoscopy after TURBT

	No (%)
Yes	28 (68.3)
No	13 (13.7)

Table 4: Frequencies of recurrent T-stage (n=28)

	No	Percentage
pTa	3	11
pT1	25	89

Table 5: Recurrent histological grades (n=28)

Histological grade	No(%)
G-I	8 (28.5%)
G-II	7 (25%)
G-III	13 (46.4%)

Discussion

Transitional cell carcinoma of urinary bladder is the second most common cause of death in males.¹⁷ It is considered to be disease of the elderly, with the most common age at presentation being in the 5th and 6th decade. Males being affected in predominance as compared to females, i.e. 3:1, it is considered that factors responsible for the disease may be more common in males. The single most important risk factor for the disease is cigarette smoking. Smokers are considered to have β-naphthylamines in their urine, which usually stagnates in urinary bladder leading to events responsible for cancerous change in the bladder transitional epithelium (urothelium).^{18,19} As the whole urinary tract is lined by transitional cell epithelium,

TCC can occur anywhere from the calyces down to fossa navicularis of the penile urethra, as the rest is lined by squamous epithelium. Frequency at which the disease affects urinary bladder shows the effect of pooling of urine and its hazardous contents in it as it functions as a reservoir for urine. Other risk factors include chemicals used in industries such as coal, paints, printing, leather, plastic, and many more. Even the artificial sweeteners used in various beverages have been condemned. Infections with Human Papilloma Virus (HPV) have also been reported as the etiological/risk factor.

Every patient was followed up every 3 months with cystoscopy in order to detect any recurrence, if so, any progression in T-stage or histological grade. The first check cystoscopy after TURBT is of utmost importance, as a recurrent disease at first check cystoscopy has a bright chance of further future recurrences and progression. Gupta SK et al conducted a research in United Kingdom and their findings have strongly supported these results with a recurrence rate of 68%.²⁵ Trinchieri et al have further solidified and supported our study by analyzing high grade superficial TCC of bladder and have confirmed recurrence in 69% of cases under TURBT alone.²⁶ Gudjonsson et al found frequency of recurrence of superficial TCC after TURBT to be 77% in group of patients receiving no intra-vesical chemotherapy supporting our results.²⁷ YANG et al have contradicted our findings in that their study showed a recurrence in 33.3% of cases. In addition their patient population was also younger (52.98+/- 11.28 years).²⁸ The age factor may be responsible for a low recurrence frequency in YANG's work. In addition, a high population of G-3 tumours may be responsible for high recurrence in our study.

Larsson et al had findings in their research which also supported our evidence of recurrence more than 60%. Their study showed a 62% recurrence frequency in superficial bladder TCC and also showed that pT1 recur earlier as compared to pTa tumours.²⁹ Present study showed that pT1 tumours were more common accounting for 73.2% of cases while pTa was found in 26.8% of cases.

In our study the additional findings were that no-recurrence group had 8 pTa tumours and 5 pT1 tumours. In no-recurrence group there were 8 G-1 tumours, 3 G-2 tumours and 2 G-3 tumours. It is important to note here that in no-recurrence group pTa G-1 tumours are in abundance. These are considered to be low risk tumours and usually have low potential for recurrence and progression. Thus their

management needs less aggressive therapy. This debate in our study is supported by Gofrit and colleagues in their study which concluded the low-grade pTa tumours to be minimal risk for the patient after resection and approved conservative management.³⁰

In our study, the group with recurrence had majority of the patients in pT1 variety and G-3 variety. pTa was found in 3 cases (n=28) while pT1 in 25 cases (n=28). G-1, G-2 and G-3 were found in 8, 7 and 13 cases respectively. Our study has shown that recurrence is more common in patients with pT1G-III (T1G3) tumours. This evidence is supported by Kulkarni et al by recommending a more aggressive treatment regimen for T1G3 tumours.³¹ Shinohara et al also recognized a virulent nature of G-III tumours and confirmed that G-III was more aggressive in recurrence and progression as compared to G-I and G-II tumours, in support of our findings.³² In order to reduce the frequencies of recurrence and, especially, progression, these high risk groups should receive intra-vesical BCG according to Irani J.³³ In addition, primary T1G3 tumours have a more significant risk of recurrence and progression as compared to non-primary T1G3 despite multifocality of the latter.³⁴ On the other hand,

Present study has additionally highlighted the evidence of disease progression in the recurrent tumours. There was only 1 case (n=3) which progressed from pTa to pT1. However, 3 cases progressed from G-1 to G-2 and 3 cases from G-I to G-3 (n=8). Progression from G-2 to G-3 was noted in 5 cases (n=7). Downgrading was also noted in some cases from G-3 to G-2 (4/13) and to G-I (1/13). Only 2 cases (n=7) downgraded from G-II to G-I in the recurrent tumour. It is noteworthy here that, after TURBT alone, there are chances of T-stage and histological grade progression in some cases and hence such patients are prone to further recurrences in future. Such cases are high risk cases and will need some adjuvant therapy for the reduction of tumour recurrence and more importantly progression. Different treatment regimens, including Mitomycin-C, BCG, second look TURBT and radical cystectomy should be compared regarding their efficacy and safety, especially in pT1 and GIII tumours

Conclusions

1. Superficial TCC of the bladder is a common condition affecting elderly male population. Recurrence is common after TURBT and is more so in

T1 G-III tumours. Progression was also noted in certain cases of recurrence.

2. TURBT alone is the preferred mode of treatment for patients with pTa and G-I tumours whereas tumours of pT1 stage and higher grades require immediate instillation of Mitomycin-C and then 6 weekly intravesical BCG course.

3. Radical cystectomy should be considered early if the disease is organ confined and there is failure of BCG.

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