Our Experience with the Management of Superficial Bladder Cancer (Transitional Cell Ca), the Role of Adjuvant Intravesical BCG Therapy

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We present our experience of 52 patients with bladder cancer. 47 patients (90%) were having superficial bladder disease (Ta, T1) who underwent TURBT followed by intravesical BCG postoperatively, 35 patients (67.3%) completed 6 weeks. Course of intravesical BCG with 10 patients (19.3%) showed recurrence of disease after six month of follow-up. 4 patients (7.6%) left after 2 weeks of intravesical BCG and 3 patients (5.76%) did not take BCG therapy. These patients hade invasive disease and underwent radical cystectomy and two patients had metastatic bladder cancer disease which were advised systemic palliative treatment. We found intravesical BCG as effective and successful adjuvant therapy for superficial bladder cancer.
Key words: Transitional cell ca, BCG, Bladder cancer

In western countries, the incidence of bladder carcinoma is rising; this is the case in both the USA and Europe. Bladder cancer is the fourth leading cause of cancer in Americans accounting for 12000 death annually[1]. It was one of the first malignancy in which carcinogens were identified as an important factor in its cause[2]. Currently cigarette smoking is by far the most common cause of bladder cancer. Although occupational exposure to Arylamine is most common[2] the majority of patients with bladder cancer have superficial disease meaning that the lesion is confined to the mucosa (stage – Ta or submucosa T1)1 and superficial tumors have a tendency to recur after transurethral resection[3].

Superficial bladder cancer is a heterogeneous disease and it is difficult to predict which patient will develop a recurrence[3]. Gross or microscopic hematuria is the most common sign at presentation[4].

The best management currently is controversial[5]. The transurethral resection remains the first treatment of choice, there is however a considerable risk of recurrence of tumor (50-70%) and a low risk (10-15%) of progression to muscle invasive disease[5]. Adjuvant, intravesical immunotherapy and chemotherapy significantly decrease the recurrence of bladder cancer when compared in controlled trials to surgical resection alone[6]. Immunotherapy with bacillus Calmette Guerin (BCG) has resulted in long term protection from bladder tumor recurrence and many controlled studies have demonstrated that BCG reduces tumor recurrence to greater extent than intravesical chemotherapy[7, 8].

The present study constitutes a management of superficial bladder cancer by surgery (TURBT) followed by BCG therapy.

Material & methods

The present study was carried out in the department of urology. It was prospective follow-up study. A total of 52 patients with bladder cancer were admitted through urology OPD in the department of urology / Kidney transplantation Mayo Hospital Lahore during January 2005 to February 2006 (13 months). The diagnosis of the disease was made on clinical history and cystoscopy .Routine investigations like CBC, serum urea and creatinine, abdominal USG, IVU were performed in all patients. The imaging studies like CT-scan was done in selected patients. We used intravesical BCG after ten days of TURBT in a dose of 120 mg / 200 ml of normal saline and continued weekly for 6 weeks. A second course of BCG therapy was given to patients showing recurrence of primary disease on follow-up cystoscopy.

Results

The total of 52 patients were included in the study project with bladder cancer disease, 34(65%) patients were male and 18(34.6%) patients were female, the age range is shown in (Table I) the mean age of presentation of disease in all patients was 45 years, the chief presenting complaints are listed in (Table II), they were the painless hematuria, irritative bladder symptoms & difficulty in micturition.

Table-1: Age distribution

Age Range	No. of patients	%age
20-30	10	19.2
31-40	5	9.6
41-50	16	30.76
51-60	15	28.84
61-70	6	11.53

Table 2: Distribution of patients according to symptoms

Presenting Complaint	=n	%age
Painless Hematuria	30	57
Irritative Bladder symptoms	11	21.1
Retention/ Difficulty in micturition	7	13.4
B/L Renal pain	2	3.84
Chronic Renal Failure	2	3.84
Bone Pain	2	3.84

All the patients underwent cystoscopy, TUR (BT) was done in all the patients. 3 patients (5.7%) had invasive (T2

– T3) disease and were managed by radical cystectomy followed by ileal conduit in 2 patients and uretero-sigmoidostomy in one patient. 47 patients underwent TUR of growth bladder. The area of involvement of bladder on cystoscopy in various patients is shown in (Table III)

Table 3: Distribution according to site of tumor

Area of bladder wall involved	=n	%age
Right posterior wall	10	20
Left posterior wall	15	30
Both posterior walls	9	18
Right lateral wall	2	4
Left lateral wall	1	2
Anterior wall	4	8
Floor of the bladder	9	18

42 patients were diagnosed to have T1 (G1-G2) disease, 5 patients had Ta (G1) disease.

Table-4 represents the distribution of patients according to histopathology report. We used intravesical BCG therapy in 42 patients with T1/G1-G2 disease, ten days after resection of primary tumor; out of 42 patients only 35 patients completed the six weeks course of intravesical BCG therapy, while 4 patients left the protocol after second week of BCG therapy while 3 patients refused to take BCG treatment – postoperatively. After one year of follow-up 35 patients out of 42 patients completed the four follow-up after every 3-monthly visit after BCG therapy with check cystoscopy every three monthly, but did not report any recurrence of disease or progression of superficial disease to invasive one. Whereas ten patients showed recurrence of primary disease at six month of follow-up and were put on for second six weekly course of induction BCG therapy.

Table-4

Clinical stage	Histological Grade	=n	%age
Ta	G1	5	9.61
T1	G1-G2	42	80.76
T2	G3	2	3.84
T3	G3	1	1.92
T4	G3	2	3.84

Discussion

Bladder cancer is a heterogeneous disease with variable natural history. Low grade Ta tumors have a low progression rate and require initial endoscopic treatment and surveillance but rarely present a threat to the patient[9].

At the other extreme, high grade tumors have a high malignant potential associated with significant progression and cancer death rate[9]. The risk of developing bladder cancer at <75years of age is 2% to 4% for men and 0.5% to 1% in women as compared with the risk of lung cancer[10]. Patients with high grade Ta tumor represent a relatively small subgroups of patients and they have 20% to 25% chance of progression to muscle invasive disease, which warrants a proper treatment after TUR (BT)[11]. While patients with tumor appearing to be high grade Ta should receive a single immediate postoperative instillation of chemotherapy[12], they should go second look TUR (BT) and bladder mapping biopsies two to four weeks later if residual tumor is found, resection should be followed with single post operative instillation of BCG[13,14].

Diagnosis of the disease was made by abdominal ultrasound, IVU and cystoscopy. The reported incidence of solitary lesions on cystoscopy is 70% while that of multiple lesions is 30%. Among these 70% of tumors are confined to mucosa (Ta) while 30% are T1 disease[15]. In our study 34 cases had solitary papillary growth and 13 cases had multiple papillary growths. The lesions were confined to lamina propria T1 (G1-G2) in 42 cases, only 5 patients had Ta (G1) disease which is contrary to other studies done where most of the tumors were confined to mucosa only (Ta)[15,16].

We used BCG intravesical immunotherapy for all 42 patients after resection which came out to be T1 (G1-G2) on histopathology. But only 35 patients completed the six week course of BCG therapy.

At six month of follow-up after BCG therapy 25 patients showed a complete success of treatment which means there was no active lesion on cystoscopy and on biopsy there was no tumor which gave them more control over various parameters. But our follow-up was only one year which also demanded further extension of follow-up in these patients. So far as the progression of superficial disease is concerned, we could not see any one f case out of 35 cases within a period of one year which could prove that superficial disease had progressed to muscle invasive. Disease progression of superficial bladder transitional carcinoma has been reported to reduce from 30% to 6% after BCG therapy[16, 17].

While ten patients showed a partial success in treatment e.g. on cystoscopy there was no active lesion but on histology there was T1 (G1-G2) histopathology.

At one year of follow-up, we found complete success of BCG therapy in 35 patients. Again in various studies like Morales & Wilson[18], Lamm et al[19], Brosman[20], there was 67,61,60% of success rate when used for T1(G1-G2) disease as adjuvant BCG therapy while Martinez-Pinero et al[21] and Sarosdy[22] found 87% & 91% success of intravesical BCG after TUR (BT) in superficial bladder disease (T1). So our results are comparable to other researchers but due to shortage of cases included in our study (35 patients) compared to large size of the sample in other studies; high success rate 67% is still comparable to 70% in other studies mentioned above. Moreover their follow-up was over several years.

Conclusions

1. Superficial bladder transitional cell carcinoma is a treatable disease with excellent result after endoscopic resection followed by intravesical BCG immunotherapy.

2. Cohort type of study is needed where one can perfectly define other parameters of superficial bladder tumors and role of BCG postoperatively to treat the disease.
3. Due to high cost of BCG vaccine and low socioeconomic condition of patients need is felt to have a funds from government health care agencies or a program of free delivery of medications in such patients so that we could cater more cases with longer follow-up.

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