RESEARCH COMMUNICATION

Clinicopathological Features of Bladder Tumours in a Single Institution in Malaysia

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Abstract

Objective: To determine the clinicopathological features of bladder tumours encountered over a five year period in Universiti Kebangsaan Malaysia Medical Centre. Methods: Medical records of bladder tumour cases from 2005 till 2009 were retrospectively reviewed and tabulated. Results: A total of 83 cases were recorded. The incidence was highest among the Chinese (56.6%), followed by Malays (34.9%), Indians (6%) and other races (2.4%). The male-to-female ratio was 9.4:1. The median age was 65 years (range 30-91 years) and median duration of follow up was 17.2 months (range 2-60 months). The main histopathology was transitional cell carcinoma (TCC) (90.4%), followed by adenocarcinoma (6%), squamous cell carcinoma (1.2%), leiomyoma (1.2%) and myeloid sarcoma (1.2%). For the TCCs, 58.6% were superficial while 41.4% were muscle invasive, and 13.3% had nodal metastasis with distant metastasis in 8%. Of the total, 5.3% were papillary urothelial tumours of low malignant potential, 33.3% pTa, 20% pT1, 10.7% pT2, 12.0% pT3 and 18.7% pT4. Of the superficial tumours, 32.5% were high grade tumours. There were ten radical cystectomies performed for transitional cell carcinomas; two had neobladder reconstruction whereas the other eight had ileal conduits. All the adenocarcinomas and squamous cell carcinomas were treated by radiotherapy due to the advanced stage of the disease while the myeloid sarcoma received chemotherapy. Mean survival of patients with muscle invasive cancer was 33±5 months. By the end of the study, 18.1% of patients had died of their cancer. Conclusion: The incidence of bladder tumours is highest among the Chinese. When compared to other studies, the incidence of muscle invasive and high-grade superficial tumours was greater.

Key Words: Urinary bladder neoplasm - tumour- bladder - demography - survival

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Introduction

Bladder tumours constitute one of the most common urological conditions, where in United States alone, an estimated 70,980 new cases were diagnosed with an estimated 14,330 deaths in 2009 (Jemal et al., 2009). In Malaysia, it is the 6th most common cancer among males, with an incidence of 4.7% (Zainal et al., 2006). To our knowledge, there have been no data published reporting on the clinical or pathological features of bladder cancer in Malaysia. Therefore, an audit was done on bladder tumour seen over a five year period in Universiti Kebangsaan Malaysia Medical Centre in order to give a background knowledge of the clinicopathological features of this disease in this country.

Materials and Methods

This is a retrospective study in which all cases of bladder tumours diagnosed between the years 2005 and 2009 were included. The study group consisted only of incident cases of bladder carcinoma, all prevalent cases being excluded. The medical records of these patients were reviewed and included in the present study.

All patients were initially evaluated by history-taking, clinical examination, standard laboratory investigations, chest radiographs, excretory urography and/or abdominal ultrasonography. The tumours were assessed by bimanual examination under anaesthesia, cystoscopy and biopsy. Abdominal and pelvic computed tomography and radioisotope bone scan were performed for patients with evidence of advanced disease.

Clinicopathological data (size, site, morphology, multiplicity, stage, grade of tumour, etc.), epidemiological data (age, sex, occupation and smoking habit), investigations, treatment and follow-up data from the case notes were entered on a standard data collection sheet. The histopathology results were recorded just as they appeared in the notes as reported by different pathologists.

The tumours were graded histologically, and staged pathologically according to World Health Organization (WHO)/International Society of Urological Pathology consensus classification of urothelial (transitional cell) neoplasms of the urinary bladder into low- and high-grade

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tumours (Epstein et al., 1998). Pathological staging was also done according to the TNM system with the following stages: pTa: limited to mucosa; pT1: invasion of the lamina propria; pT2: invasion of the muscularis propria; pT3: invasion of the perivesical fat; and pT4: invasion of organs in the vicinity (Sobin et al., 2002).

Data were analyzed using SPSS software version 12.0.1(SPSS, Chicago, IL, USA) and chi-square test was used to compare the variables. A p-value of 0.05 was taken as significant. Kaplan Meier survival analysis was used to calculate the mean survival time. This study had been approved by the Universiti Kebangsaan Malaysia (National University of Malaysia) Research Ethics Committee.

Results

A total of 83 cases of bladder tumours were recorded. Incidence was highest among the Chinese (56.6%), followed by Malays (34.9%), Indians (6%) and other races (2.4%). 90.4% of bladder tumours involved men with a male-to-female ratio of 9.4:1. The median age was 65 years (range 30-91 years). The median for the duration of follow up was 17.2 months (range 2-60 months). The main histopathology was transitional cell carcinoma (90.4%), followed by adenocarcinoma (6%), squamous cell carcinoma (1.2%), leiomyoma (1.2%) and myeloid sarcoma (1.2%) (Table 1).

For the transitional cell tumours, 58.6% were superficial tumours while 41.4% were muscle invasive. 5.3% were papillary urothelial tumours of low malignant potential (PUNLMP), 33.3% pTa, 20% pT1, 10.7% pT2, 12.0% pT3 and 18.7% pT4 (Table 2). 13.3% of these transitional cell carcinomas had nodal metastasis while 8% had distant metastasis. Of the superficial tumours, 32.5% were high grade tumours. There was no difference in terms of muscle invasiveness between those below 65 years or those 65 years and above, at 15 (48.4%) and16 (51.6%), respectively. All the adenocarcinomas, squamous cell carcinoma and myeloid sarcoma were muscle invasive. Age group distribution by stage for urothelial tumours are given in Table 4.

There were ten radical cystectomies done for transitional cell carcinomas; two had neobladder reconstructions whereas the other eight had ileal conduit. All the adenocarcinomas and squamous cell carcinomas were treated by radiotherapy due to the advanced stage of the disease while the myeloid sarcoma had chemotherapy. Mean survival time of patients with muscle invasive cancer was 33±5 months (Figure 1). By the end of the study, 18.1% of patients died of cancer.

Table 1. Clinicopathological Features of the Bladder Tumour Cases

Features		No (%) of patients
Gender	Male	75 (90.4)
	Female	8 (9.6)
Male-to-female ratio		9.4:1
Histological type	TCC	75 (90.4)
	Adenocarcinoma	5 (6.0)
	Squamous cell	1 (1.2)
	Leiomyoma	1 (1.2)
	Myeloid sarcoma	1 (1.2)

TCC: Transitional Cell Carcinoma

Table 2. Clinical Stage of Transitional Cell Carcinoma Cases

Stage	No.	(%)
PUNLMP	4	(5.3)
pTa	25	(33.3)
pT1	15	(20.0)
pT2	8	(10.7)
pT3	9	(12.0)
pT4	14	(18.7)

PUNLMP: Papillary urothelial neoplasm of low malignant potential

Table 3. Age group Distribution by Stage

Age group	30-45	46-60	61-75	76-91	Total
PUNLMP	0	2	1	1	4
Ta	2	8	13	2	25
T1	2	3	7	3	15
T2	1	2	4	1	8
T3	0	0	7	2	9
T4	1	7	4	2	14
Total	6	22	36	11	75

PUNLMP: Papillary urothelial neoplasm of low malignant potential

Discussion

The incidence of bladder cancer is higher among males as compared to females. Our study showed a ratio of 9.4:1 which is comparable to that reported in Jordan (Matalka et al., 2008) and India (Gupta et al., 2009), but was higher than the United States (Johansson et al., 1997). There are various possible explanations for the observed preponderance of bladder tumours in males. Among them are environment and dietary exposures not yet identified and innate sexual characteristics such as anatomic

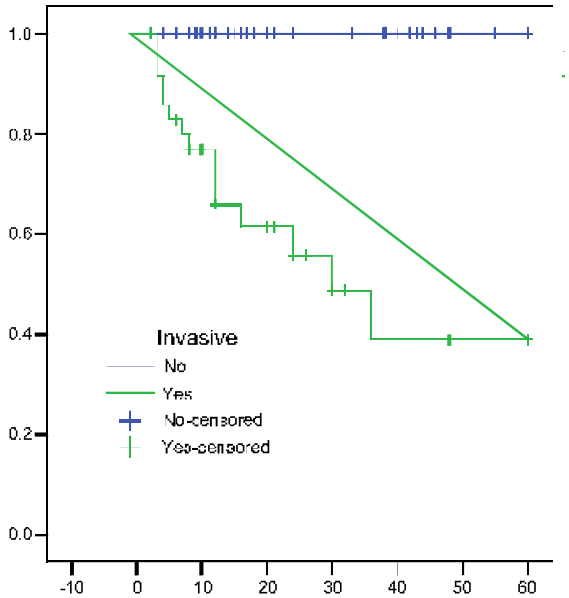

Figure 1. Kaplan-Meier Curves of Cumulative Survival in Patients with Muscle-invasive Tumours

differences, urination habits or hormonal factors (Hartge et al., 1990; Horn et al., 1995). Besides that, the lower incidence of bladder tumours in females could be attributed to the decreased exposure to the industrial carcinogens as there are fewer women working outside the home. In addition to that, there are fewer women who smoke as compared to men, which is a major predisposing factor for bladder tumours (Gupta et al., 2009).

The median age was 65 years which is almost similar to that reported in Jordan and United States (Matalka et al., 2008). There is also a higher preponderance amongst the Chinese. Whether this is due to genetic predisposition, remains to be seen. Further studies need to be done to elucidate this. Transitional cell carcinoma was the commonest variant, which is similarly reported by the world literature at 90% (Rabbani et al., 2000). The prevalence of squamous cell carcinoma varies in different parts of the world. The incidence of 1.2% seen in this study was similar to that reported in England (1%), United States (3-7%), but differed from the reported 75% in Egypt. Adenocarcinoma was also reported to be about 2% in other parts of the world, which is slightly lower compared to that seen in our study (Matalka et al., 2008).

Numerous studies have shown statistically-significant survival differences between patients with non-invasive tumours (pTa), invasive tumours confined to the lamina propria (pT1) and tumours with muscle invasion. Our superficial tumours which comprised of 58.6% were very much lower compared to that reported in the literature (71.8-75%) (Messing et al., 1995). Amongst the superficial tumours, high grades were seen in 32.5%, which is double of that reported in Jordan (15.5%) (Matalka et al., 2008). This shows that the bladder tumours seen in our centre were at a more advanced stage as compared to other parts of the world. This could be due to the lack of awareness among patients and also their propensity to seek traditional medications before subjecting themselves to modern medicine.

The mean survival time for our patients was also worse compared to that reported in the literature. Our mean survival time for muscle invasive bladder tumours at 33 months was almost half of that reported in Turkey (77.8 months) (Turkolmez et al., 2007). This could be attributed to the fact that a large number of our patients present at an advanced stage (pT3 and pT4) and were of high grade tumours.

There are many options of treatment for bladder tumours. In an attempt to reduce functional complications, partial cystectomy has been tried at many centres but local recurrence is high. For advanced transitional cell carcinoma and recurrent refractory cases of superficial high-grade transitional cell carcinoma, radical cystectomy with urinary diversion is the treatment of choice (Carrion et al., 2002). The downside is, radical cystectomy has a high morbidity rate, as it results in many changes in the quality of life, including sexual and social functions. A modified technique of radical cystectomy with prostate and seminal vesicle sparing in selected patients with bladder cancer was introduced in 2002. In this technique, the functional results with regard to continence and potency with cancer control were comparable to the standard procedure (Vallancien et al., 2002). Preoperative radiotherapy and adjuvant chemotherapy, may reduce deaths from localized disease in transitional cell carcinoma, but not in squamous tumours (Sternberg et al., 1989; Logothetis et al., 1989; Skinner 1991). The acceptance of patients for surgical treatment had improved with the introduction of orthotopic bladder replacement. However, the current treatment modalities do not alter the dismal prognosis of .patients diagnosed with advanced stage of cancer. Thus, newer therapeutic approaches that improve the patient survival and enhance the quality of life need to be explored.

In conclusion, the incidence of bladder tumours was highest among the Chinese. When compared to other studies, the incidence of muscle invasive and high-grade superficial tumours was higher.

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