To the Editors:

A clinico-pathological study of non-urothelial bladder cancers in a cohort of patients from a tertiary care urology unit in Sri Lanka

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Introduction

Bladder cancer is the ninth most commonest cancer worldwide. The spectrum of bladder cancer is quite diverse and the majority (90-95%) of cancers are urothelial in origin [1]. Non-urothelial bladder cancers are known to occur in around 5% of all bladder cancers [1]. Due to the rarity of non-urothelial bladder cancers, understanding of the clinico-pathological characteristics and effective management strategies are poor, particularly in the South Asian region [2]. Therefore, this study aimed to describe the clinico-pathological characteristics of non-urothelial bladder cancers.

Methods

All patients with newly diagnosed bladder cancer referred to a urology unit of the National Hospital of Sri Lanka from January 2007 to December 2016 were recorded in a database and were analysed retrospectively. Staging and categorisation of tumours were done according to the World Health Organization (WHO) classification guidelines [3]. During the study period 312 patients presented with primary bladder tumours. Histology was available in 310 (99.4%) patients of which 25 (8.0%) were non-urothelial malignancies. All data were recorded prospectively at the operating theatre, before discharge and during clinic visits to ensure accuracy. Urothelial bladder cancers containing non-urothelial elements or mixed tumours were considered as variants of urothelial bladder cancers and were not analysed as non-urothelial bladder cancers. Ethical approval was obtained from the Ethics review committee of the National Hospital of Sri Lanka.

Data were analysed using SPSS 17.0 statistical software. Comparison between non-urothelial bladder cancers and urothelial bladder cancers were done using chi square tests.

Results

Of the 25 patients with non-urothelial bladder cancers, 14 (56%) were male (male: female=1.27:1). The median age was 64 years (range: 17-84). Seventeen patients (68%) presented with haematuria and 24% (n=6) were detected incidentally. The majority were squamous cell carcinoma (n=10, 40%) followed by adenocarcinoma (n=9, 36.0%). All adenocarcinomas were non-urachal in origin. The characteristics of squamous and adeno-carcinoma is summarised in Table 1. Other types were sarcomatoid carcinoma (n=4, 16%), poorly differentiated carcinoma (n=1, 4%) and leiomyosarcoma (n=1, 4%).

The tumour size was estimated during cystoscopy and classified as ≤3 cm and >3 cm. The majority (n=15,60%) were >3cm in size at cystoscopy.

The commonest site of tumour origin was the lateral walls (n=11, 44%), followed by anterior wall (n=9, 36%), posterior wall (n=7, [28%), trigone (n=6, 24%), bladder neck (n=3, 12%), and dome (n=3, 12%).

Nineteen (76%) were solitary tumours. The majority (n=15, 60%) were solid tumours while 6 (24%) had papillary and 4 (16%) had mixed configurations. Eighteen patients (72%) had muscle invasion while pT1 tumours were seen in 5 (20%) and pTa in 2 (8%) patients.

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Table 1. Characteristics of squamous and adenocarcinoma of the bladder

	Squamous Cell Carcinoma		*Adenocarcinoma*	
	Number	*Percentage*	*Number*	Percentage
Age	median 70.5		median 59.0	
Gender				
Male	7	70.0	5	55.6
Female	3	30.0	4	44.4
Size				
≤3cm	2	20.0	5	55.6
>3cm	8	80.0	4	44.4
Multiplicity				
1	7	70.0	7	77.8
>1	3	30.0	2	22.2
Tumour morphology at cystoscopy				
Papillary	2	20.0	3	33.3
Solid	8	80.0	3	33.3
Papillary with solid base	0	0.0	3	33.3
Tumour stage				
pTa	0	0.0	1	11.1
pT1	2	20.0	1	11.1
pT2	8	80.0	7	77.8
Tumour grade				
High Grade	7	70.0	7	77.8
Low Grade	3	30.0	2	22.2

We compared the non-urothelial bladder cancers (n=25) with urothelial bladder cancers (n=285). Compared to urothelial bladder cancers, non-urothelial bladder cancers were more in females (n=11; 44%, vs. n=45; 15.7%; p=0.004). The proportion of solid and mixed tumours were significantly higher among non-urothelial bladder cancers (n=19; 76% vs. n=123; 44%; p=0.002). A significantly higher proportion of non-urothelial bladder cancers were muscle invasive (18; 72% vs. n=102; 36%; p<0.001) at the time of diagnosis.

Discussion

Non-urothelial bladder cancers are rare bladder tumours consisting of 5% of all bladder tumours [1]. Due to its rarity, there is no consensus regarding treatment. Studies have reported a wide variety of non-urothelial bladder cancer tumour types. The different histological types are briefly described below.

Squamous cell carcinoma of the bladder

Squamous cell carcinoma accounts for 2.7% of bladder cancers in the developed world [4]. It is the second most common primary bladder cancer next to urothelial cancers. In a study by Kassouf et al 27 patients of nonbilharzial squamous cell carcinoma were described [5]. Of the participants, 13 had cT2, 9 had cT3, 5 had cT4 lesions. Thus, this series showed that this group had aggressive tumours with poor outcome. In a study by Dahm *et al* squamous cell carcinoma was the commonest type of non-urothelial bladder cancer with an incidence of 3 to 5 %, followed by adenocarcinoma (0.5-2 %) [1]. In the present study, majority of squamous cell carcinomas were large (n=8; 80%,), solid tumours (n=8; 80%,), muscle invasive (n=8; 80%,) and high grade (n=7; 70%,), which are well known characteristics of aggressive tumours.

Adenocarcinoma of the bladder

Primary adenocarcinoma of the bladder is seen in 1.4% of bladder cancers undergoing radical cystectomy in the developed world [4]. The prevalence is reported to be considerably higher in the developing world, accounting for up to 11% [6]. In a series by Ravi *et al* from India, out of 21 non-urothelial tumours, 9 (42.8 %) were adenocarcinoma with a mean age of 49.33 years [2]. Male to female ratio was 2: 1. Two (22.2%) were urachal tumours and 4 (44.44%) were moderately differentiated while 5 (55.55%) were poorly differentiated [2]. In a study by Grignon, out of 72 patients with adenocarcinoma 24 patients had urachal and 48 patients had non urachal

adenocarcinoma [7]. The study concluded that variations in the histological type did not show a significant difference in the outcome. In the present study, all were non-urachal in origin and around 78% (n=7) were muscle invasive and high grade tumours.

Sarcomatoid carcinoma

This is a rare biphasic variant of urothelial carcinoma with a reported incidence of 0.2% to 4.3%. It is known to be associated with poor outcome [8]. There are only a few studies regarding the treatment for this type. In the present study, of the 4 patients with, three had solid tumours and one patient had muscle invasive disease.

In this series, we found that the non-urothelial bladder cancers in general were more aggressive with higher rates of muscle invasion and solid tumours compared to the urothelial bladder cancers. Furthermore, a female preponderance was seen among non-urothelial bladder cancer. There were several limitations to this study. Even though we collected data from patients over a 10 year period, due to the rarity of the disease we had only small number of patients. Furthermore, it was a retrospective analysis of a single tertiary care referral centre.

Conclusion

In our study, characteristics of non-urothelial bladder cancers were different and more aggressive compared to urothelial bladder cancers. The current evidence of non-urothelial bladder cancers in the South Asian region is restricted to a few case series and studies including a small sample size. A collective effort by multiple institutions to form a national or regional registry is necessary to advance our understanding, which will enable us to evaluate and optimise management strategies in future.

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