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

U Jayarajah\textsuperscript{1}, K B Herath\textsuperscript{1}, M H Fernando\textsuperscript{1}, S N Kuruppu\textsuperscript{1}, U L Wickramanayaka\textsuperscript{1}, I U Fernando\textsuperscript{1}, D S Lokuhetty\textsuperscript{2}, V C de Silva\textsuperscript{2}, S A S Goonewardena\textsuperscript{1}

\textit{Ceylon Medical Journal} 2018; 63: 92-94

DOI: http://doi.org/10.4038/cmj.v63i2.8680

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 \cite{1}. Non-urothelial bladder cancers are known to occur in around 5% of all bladder cancers \cite{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 \cite{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 \cite{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 \( \leq \)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.

---

\textsuperscript{1}Department of Urology, National Hospital of Sri Lanka, \textsuperscript{2}Department of Pathology, Faculty of Medicine, University of Colombo, Sri Lanka.

Correspondence: UJ, e-mail: <umeshe.jaya@gmail.com>. Received 09 May 2017 and revised version accepted 06 June 2018.

This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
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 nonblahrzial 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
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.

**References**