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HISTOPATHOLOGICAL VARIANTS OF UROTHELIAL CARCINOMA ACCORDING TO WHO CLASSIFICATION AND GRADING IN A TERTIARY CARE HOSPITAL.

Dr. Danish Sagheer[1], Dr. Abdullah[2], Dr. Urooj Aamir[3], Dr. Muhammad Saad[4].

[1]M.B.B.S., Medical Officer, Asia General Hospital, G.T. road, Rawalpindi., [2] M.B.B.S., Medical Officer, THQ Hospital, Murree., [3]M.B.B.S., Fauji Foundation Hospital, Rawalpindi., [4] M.B.B.S., Medical Officer, Asia General Hospital, G.T. Road, Rawalpindi.

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Abstract:

Introduction: *Urinary bladder carcinoma is the ninth most common malignancy worldwide. Many risk factors have been established, most notably the use of industrial carcinogens and dyes. Papillary Urothelial carcinoma accounts for most of the cases followed by squamous cell and then adenocarcinoma.*

Objective: *To find out various histopathological variants, grading according to WHO, muscle invasion, Lymphovascular Invasion (LVI) and geographical necrosis in patients presenting in Fauji Foundation Hospital, Rawalpindi (FFH, Rwp).*

Methods: *This was a case series study, conducted in FFH Rwp, from January to December 2016. Patients with definitive diagnosis of bladder carcinoma were included in the study. Histopathology report and various demographic variables were recorded. Data was analyzed by using SPS v25.*

Results: *A total of 19 patients presented with bladder carcinoma. Out of 19, 4 were males and 15 were females showing female predominance. Papillary Urothelial carcinoma was the most common finding. 17 patients (89.4%) had low grade Papillary Urothelial tumor whereas 2 (10.6%) patients had a high-grade tumor. Peak age of presentation was in the 6th decade of life. Muscle invasion was seen in 10 patients (52.6%). The muscle was not involved in 9 (47.4%) patients who had a low-grade tumor, indicating most patients present at early or noninvasive stage. Lymphovascular invasion (LVI) and geographical necrosis were found in 4 (21.05%) patients. Lymphovascular invasion was seen more in low grade tumor.*

Conclusion: *Low grade Papillary Urothelial carcinoma was the most common variant encountered in our setting. Almost half i.e. 47.4% patients were in sixth decade of life. Geographic necrosis was associated with high-grade tumors (p-value 0.004) as well as a high incidence of Lymphovascular Invasion (p- value 0.003).*

Keyword: *Bladder cancer, papillary, necrosis, urology, histopathology.*

Corresponding author:

Dr. Danish Sagheer,

M.B.B.S., Medical Officer, Asia General Hospital, G.T. road, Rawalpindi.

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INTRODUCTION:

Urothelial carcinoma or carcinoma of urinary bladder is the ninth most common carcinoma in the world affecting nearly 429 per 100,000 per year combined for both sexes, according to GLOBOCAN. However, the incidence is higher in males as compared to females, affecting nearly 330 males and 99 females per 1,00,000. Official data reports a total of 165000 deaths from bladder cancer emphasizing on better diagnosis modalities, treatment plans, and follow up. Bladder cancer is common after 55 years of age and the average age at the time of diagnosis is 73 [1,2]. Many risk factors have already been established, including smoking, opium use; as well as occupational hazards as seen in painters, motor exhaust related jobs such as truck drivers and drill press operators [3,4]. Radiation exposure to pelvis, cyclophosphamide use for lymphoma and long term diabetes medication such as thiazolidinedione for type 2 DM are associated with increased incidence of bladder cancer [5,6]. For decades, it is known that parasitic infection such as schistosomiasis which is more common in Africa and Middle East causes bladder cancer [7]. There are three types of bladder cancer, with transitional cell carcinoma being the most common. Other types include squamous cell carcinoma and adenocarcinoma. Transitional cell carcinoma arises from the inner lining of bladder and is also known as Urothelial carcinoma [1,8]. The stage of bladder carcinoma depends upon the degree of invasion. Two broad categories are defined, non-muscle invasive bladder carcinoma (NMIBC) and muscle invasive bladder carcinoma (MIBC). NMIBC includes Tis, Ta and T1 whereas MIBC includes T2, T3 and T4. Stage T2 is when tumor has invaded into the muscle layer [9]. In Pakistan, it is among the top ten malignancies in men and the most common urological carcinoma in both sexes. Precise data related to this cancer is not available in our setting. Karachi Cancer Registry (KCR) and Shaukat Khanum Hospital are the only cancer registries available but their work is limited. The incidence study was published in 2000 in Karachi, South district, showing a crude rate of 4.5 and 1.6 for male and female respectively [10] . A study conducted at Shaukat Khanum reports 607 patients of urinary bladder cancer from 1994 to 2004 [11]. Current data is lacking, which prompted us to perform a study in our hospital to study its incidence in relation to various demographics.

METHODS:

It is a case series study performed in Fauji Foundation Hospital, Rawalpindi from January to December 2016. It is a tertiary care hospital that deals with entitled, panel and private patients. All the patients who had a definitive diagnosis of bladder carcinoma were included. Definitive diagnosis was made with the help of cystoscopy guided biopsy. TURBT (transurethral resection of bladder tumor) was performed and the specimen was sent for histopathology. All the consecutive cases in 2016 were included in the study. Histopathology result along with various demographic data was recorded using self-administered proforma. Data was analyzed using SPSS v25 and descriptive statistics like frequencies and percentages were calculated. Data was converted into tables where necessary.

RESULTS:

The aim of this study to find the incidence of bladder carcinoma and its histopathological variants with relation to age, gender, site of lesion, grade of lesion, and involvement of various layers. Nineteen patients were included in the study and their data was collected.

Table no. 1: Age of study participants.

Age of patients	n (%)
51-60 years	6 (31.6%)
61-70 years	9 (47.4%)
71-80 years	4 (21.1%)
Total	19 (100%)

Mostly patients belonged to 61-70 years of age. No patient presented before the age of 50 years or after the age of 80 years.

Table no. 2: Gender of study participants.

Gender	n (%)
Male	4 (21.1%)
Female	15 (78.9%)
Total	19 (100%)

Out of nineteen patients, only four were males. It showed female predominance

Table no. 3: Histological variants of transitional cell carcinoma.

Histology type of transitional cell carcinoma	n (%)
Papilloma	0
Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP)	0
Low grade papillary Urothelial carcinoma	17 (89.4%)
High grade papillary Urothelial carcinoma	2 (10.6%)
Total	19 (100%)

Only papillary Urothelial carcinoma was found in our research with no case of squamous or adenocarcinoma. Out of nineteen (100%) patients, seventeen (89.4%) had a low-grade tumor whereas two (10.6%) patients had high-grade tumors according to WHO/ISUP. No case of papilloma or Papillary Urothelial neoplasm of low malignant potential (PUNLMP) was found. Peak age of presentation was 6th decade of life.

Out of 19 patients, Lymphovascular involvement was seen in 4 (21.05%) patients with involvement of muscle layer.
4 (21.05%) patients had geographic necrosis on histology. 2 (50%) of them were low grade and 2 (50%) were grade tumor. The incidence of geographic necrosis was noted higher in 7th decade of life.

DISCUSSION:

A study conducted in FFH, Rwp to study different variants of Urothelial carcinoma is relation with various demographic variables. 19 (100%) patients had a definitive diagnosis of Urothelial carcinoma. Out of 19 patients, 4(21.1%) were male and 15 (78.9%) were females. This suggests female predominance in our clinical setting. The earlier results demonstrated there is male predominance in urinary bladder carcinoma [12]. This varied result can be due hospitals policy of dealing mostly with entitled patient' families.

Many of the patients i.e. 9(47.3%) belonged to the sixth decade of life followed by the fifth decade as see in 6 patients (31.5%) and seventh decade in 4 patients (21.05%). This showed the incidence increases in old age and peaks around the sixth and seventh decade. Various reasons have been proposed behind this age predominance, prominently increased carcinogens exposure as one ages, inability to empty bladder effectively in old age resulting in increased contact time between lining and carcinogens, and dehydration in old age which concentrates the carcinogens in bladder and exerts toxic effects. This is in accordance with these published articles [12,13].

WHO proposed classification of urinary bladder tumors. It includes 4 categories i.e. Papilloma, Papillary Urothelial Neoplasm of Low Malignant Potential (PUNLMP), low grade carcinoma, and high grade carcinoma. This classification is used worldwide and results are shown accordingly. Commonest histology type found was Papillary Urothelial carcinoma. Predominantly low grade carcinoma i.e. 17 (89.4%) out of total 19 patents was reported more frequently than high grade. No case of papilloma or PUNLMP was found in this study. In majority of the patients i.e. 9 (52.9%) out of 17 patients who had low grade tumor, the muscularis layer was not involved in low grade tumor indicating most patients present at an early stage/noninvasive stage. Muscle invasion was seen in 10 (52.6%) patients most prominently in the sixth decade. This shows the when incidence of bladder carcinoma peaks, it usually presents with muscle involvement. This indicates that using better modalities may detect a disease at an earlier stage, when the muscle is not involved. In that case, the survival and prognosis becomes favorable. Similar findings have been published by a recent study performed in Rawalpindi [15].

In the 7th decade of life, 2(10.5%) patients had high-grade tumor. Our study showed that old age was associated with high grade tumor and muscle invasion. This finding was supported by a research conducted in India. In this study, non-invasive carcinoma was found in young adults whereas muscle invasive tumors i.e. detrusor muscle involvement was found to be more common among patients older than 60 years [16].

Lymphovascular Invasion (LVI) was in found in 4 (21.05%) patients, peak incidence in 7th decade of life and with muscular layer involvement. Therefore, it also supports the results; as age advances, the disease progression occurs resulting increased morbidity and mortality [17,18]. Geographical necrosis or tissue necrosis is often commented and reported separately in pathology report owing to its association with high stage and high grade disease. In our study, 4(21.05%) patients had geographic

necrosis in which two had high grade tumor (p-value 0.004). It was mostly seen in seventh decade of life with high incidence of Lymphovascular Invasion (p-value 0.003). Presence of geographic necrosis or tissue necrosis decreases metastasis-free survival rates and therefore, is an important histological variable which influences metastasis-free interval.

Early diagnosis, categorizing the disease into low-grade or high-grade, and degree of muscular invasion remain the most valuable factors when diagnosing and treating urinary bladder carcinoma.

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