Histoprognostic Factors in Bladder Cancer: A Case Series of 156 Patients

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Abstract

Introduction: Bladder cancer is the second most common cancer of the genitourinary tract. The transitional cell carcinoma accounts for nearly 90% of all primary tumors of the bladder. Although the majority of patients have superficial tumors, 20% or 40% have invasive disease develops. The pathologist plays a crucial role in determining the histological type, as well as determining factors for a histoprognostic proper care of patients.

Objectives: The purpose of this study is to provide an epidemiological overview of bladder cancer and to find an association between tumor grade and other histoprognostic factors.

Materials and Methods: We conducted a retrospective study of 156 bladder tumor listed in the laboratory of pathology of CHU Hassan II Fez over a period of 6 years from 2009 to 2014.

Results: Median age was 62 years with a sex ratio M/F=8.7. Transitional cell carcinoma (TCC) was the most common histological type (87.8%). 36.8% of TCC were classified as low grade and 63.2% in high grade according to WHO in 2004. The tumor was superficial in 23.7%. It has been classified as pT1 in 22.4%, 36.2% in pT2, pT3 in 9.9% and 7.2% in pT4. In this series, 64.4% of patients over age 50 had high-grade tumors compared with 45% of patients younger than 50 years (p=0.08). We found a significant association between sex and grade of the tumor. In fact, 85.7% of women had a high-grade tumor (p=0.05). 85.6% of TCC were in localized stage, compared to 58% in other histological types (p=0.01). This study showed a significant association between the grade and stage of the tumor (p=0.006). It was also noted a significant association between tumor grade and the presence of vascular emboli (p=0.002).

Conclusion: In conclusion, the presence of a high-grade tumor is strongly associated with factors of poor prognosis, such as advanced tumor stage and vascular emboli. Urothelial tumors of the bladder are far more common in men than in women buthey are more aggressive in women than in men.

Keywords: Bladder cancer; WHO classification; TNM staging; Vascular emboli; Transitional Cell Carcinoma (TCC)

Introduction

Bladder cancer is the second most common cancer of the genitourinary tract [1]. The transitional cell carcinoma accounts for nearly 90% of all primary tumors of the bladder [2]. According to hospital cancer register of Fez [3], it was estimated of all cancer and 85.3% of urologic cancer. In nearly every country bladder cancer predominates in men [4], suggesting etiological factors that occur more in men than in women. Although the majority of patients have superficial tumors, 20 to 40% either present with or develop invasive disease. At one of the spectrum, low-grade tumors have a low progression rate and require initial endoscopic

treatment and surveillance bat rarely present a threat to the patient. At the other extreme, high-grade tumors have a high malignant potential associated with a significant progression and cancer death rates. The pathologists play a crucial role in determining the histological type, as well as determining histoprognostic factors for proper care of patients.

Patient and Methods

Between 2009 and 2014, 156 patients with bladder cancer were enrolled at laboratory of surgical pathology of hospital teaching Hassan II of Fez. Eligibility required histological confirmation of the diagnosis by core biopsy, transurethral resection and cystectomy. All specimens were examined by the same pathologic protocol. Histologic type was determined according to WHO classification of tumors of urinary system. Tumors are graded as high and low grade according to WHO classification 2004 and concomitantly are graded according to the 1973 classifications of high, low and intermediate grade carcinoma. Pathologic staging of the primary bladder tumor was performed using the 2009 tumor-node-metastasis (TNM) classification. We distinguee superficial tumors who were classified as pTa, pT1 and invasive tumors who were classified as pT2, pT3 and pT4. Statistical analysis was performed using Epi-info 3.5.3 of the determination of significance of differences between patients groups; p values less than 0.05 were considered significant.

Results

Characteristics for all 156 patients are showed in **Table 1**. The median age was 62 years (range 30-88years) and 89.7% of patients were male. All cases were reviewed and interpreted according to the WHO classification 2004 of bladder tumors. Transitional cell carcinoma was the most frequent (87.8%), followed by squamous cell carcinoma in 8.3%of cases. The other types of bladder cancer are relatively uncommon, including small cell carcinoma, sarcomatoid carcinoma and poorly differentiated carcinoma in 0.6% of cases. Tumor grade according to WHO classification 1973 was as follows: grade 1 in 2.9% of tumors, grade 2in 43.4% and grade 3 in 53.7% of cases. According to WHO classification 2004, 36.8% of tumors were classified as low grade and 63.2% were high grade. In this cohort, we have used TNM staging system. Non-invasive disease was diagnosed in 23.7% of cases (pTa). Tumors that invade the chorion of the bladder are classified as pT1 in 22.4%, pT2 in 36.2%, pT3 in 9.9% and pT4 in 7.2% of cases. Sex of patients, TNM staging and vascular emboli for the entire cohort were significantly related to the WHO classification 2004 (p=0.05, p=0.006, p=0.002 respectively) although age of patients was not statistically correlated with WHO classification 2004 (p=0.08), but more than half of patients are over 60 years. Patients with transitional cell carcinoma demonstrated significantly more superficial tumor, compared with those with other histologic types (p=0.01). There is no differences in age and

Table 1 Characteristics of patients.

Characteristics	Percentage
Age	
<60 years	44.20%
≥60 years	55.80%
Sex	
Men	89.70%
Women	10.30%
Histologic type	
Transitional Cell Carcinoma	87.80%
Squamous Cell Carcinoma	8.30%
Others	1.80%
WHO classification (1973)	
Grade I	2.90%
Grade II	43.40%
Grade III	53.70%
WHO classification (2004)	
Low grade	36.80%
High grade	63.20%
TNM staging	
pTa	23.70%
pT1	22.40%
pT2	36.20%
pT3	9.90%
pT4	7.20%
Vascular emboli	13.10%
Perineural invasion	3.90%

Series	CHU Hassan II	Para Jerome [14]	Lebret [15]	Senegal [16]	Togo [17]
	n=156	**[14] n=1825**	**n=504**	**n=428**	**n=678**
Average age	62.3 years	58.8 years	62 years	45.5 years	65 years

Table 2 Comparison of the average age in different series.

Series	CHU Hassan II	Para Jerome [14]	Lebret [15]	Senegal [16]	Togo [17]
	n=156	**n=1825**	**n=504**	**n=428**	**n=678**
Sex-ratio (M/W)	8.7	3	7.4	1.25	9.27

Table 3 Comparison of the sex-ratio in different series.

Histological type	CHU Hassan II	Para Jerome [14]	Dangou [18]	Senegal [16]	Togo [17]
	n=156	**n=1825**	**n=82**	**n=428**	**n=678**
Transitional cell. C	87.8%	50.0%	26.6%	38.4%	26.0%
Squamous cell. C	8.3%	37.5%	62.2%	58.4%	37.5%
Others	2.4%	12.5%	11.0%	3.2%	33.3%

Table 4 Comparison of the histological type between different series.

sex between superficial and invasive tumor, but there is a strong association between TNM staging and the presence of vascular emboli (p=0.00003).

Discussion

Bladder cancer is the most common urinary tract malignancy in Fez [3]. Bladder cancer incidence is strongly related to age, with the highest incidence rates being in older men and women. In this series, the mean age was 62 years, similar to that of the literature (**Table 2**). The age of our patients seem plays no role in TNM staging ant tumor grade (p=non-significant) worldwide, bladder cancer is seen mainly in men (**Table 3**). It was 8 times more frequent in our men than in our women. Female patients with bladder cancer have a worse prognosis than in male patients. It is unlikely that the difference can explained entirely by the more frequent diagnosis of higher stage at first presentation among women [5,6]. According to a report published by the National Cancer Institute, the survival rate for women with bladder cancer lags behind that of men at all stage of the disease [7]. Among our women, the tumor grade was significantly more high compared to male patients (p=0.05). Transional cell carcinoma is the most common primary pathologic subtype of bladder cancer in our series. It was observed in >80% of tumors. Squamous cell carcinoma is less common and occurs in approximately 8% of our cases. Our data are similar to epidemiological results from several countries (**Table 4**). But, in some regions of the world where schistosomias infection is endemic, squamous cell carcinoma can account for up to 75% of bladder cancer [8,9]. Transitional cell carcinomas are classified as high or low grade according to WHO classification 2004. 36.8% of patients were presented with low grade tumor and 63.2% with high grade tumor. Our cohort demonstrated a significant association between tumor grade and tumor stage (p=0.006). The findings on grade are contradictory. For Lebert et

al. [10], tumor grade does not appear as independent prognostic factors. The vast majority of invasive tumors are classified as high grade. In addition, for recurrent superficial tumors, it does not appear prognostic difference between low-grade and high-grade tumors. Kaubisch et al. [11] found that the tumor grade is only the significant factor in predicting for invasive disease (p=0.005). In the literature, the frequency of vascular emboli ranges from 13 to 42% of urinary tract tumors [12]. In our series, we observed 13.1% of vascular emboli. They were strongly associated with worse prognostic factors such as advanced stage (p=0.0003) and high tumor grade (p=0.002). Colin et al. [12] demonstrated in a retrospective study of 83 patients that the presence of vascular emboli is strongly correlated with advanced stage and high grade of tumor. Eiji Kikuchi [13] found that vascular emboli an independent predictor of disease recurrence and survival (p=0.001 for both).

Conclusion

In our cohort, bladder cancer is predominantly transitional cell carcinoma and more than 60% of patients are over 50 years. Male preponderance is frequent in our population as well as in other series. Although these tumors are more common in men than in women. They are more aggressive in women than in men. The presence of high-grade tumor is strongly associated with worse prognosis factors such as advanced stage and vascular emboli [14-18].

Conflict of Interest

Authors declared that they had no conflict of interest.

Author's Contribution

All authors read and approved the final manuscript.

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