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Original Article

Clinical Characteristics of Urinary Bladder Cancer in the Sudan; Evidence of Pathoetiology Changes

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Abstract

Introduction: Bladder cancer (BC) is highly heterogeneous with regard to clinical course, etiology, histology, and geographic distribution. Recent clinical observations suggest changes in the pattern of BC in the Sudan perhaps due to lifestyle change following the massive displacement from rural to urban areas.

The present study aimed to characterize the clinical profile of the BC among Sudanese patients and compare it with what has been previous reported.

Material and Methods: Demographic, habitual, clinical, and histopathology information of 1610 patients with BC were obtained from the hospital record of Ibn Sina specialized hospital, Soba University hospital, Khartoum North hospital and Khartoum teaching hospital during the period 2007–2019. The data was analyzed using SPSS program version 23.

Results: Of the 1610 cases of BC, 1480 cases (91.9%) were males and 130 cases (8.1%) were females. The most affected patients (39.3%) were those with age group ranging between 61–75 year–old. The vast majority of the patients (73%) were from urban and/or metropolitan areas of the capital Khartoum, whereas the remaining (27%) were farmers coming from rural areas. Although, smoking habits information were missed in 410 patients, 44% of the patients were smokers. History of hematuria was present in almost all cases (99.4%), whereas history of urinary bilharziasis was mentioned in 40.9% of the patients' records.

The TCC histology type was seen in 77.4% of the cases, SCC in 21.1%, and adenocarcinoma in only 1.5% of all cases. The vast majority of the tumors were poorly differentiated tumors (700/52.6%), followed by moderately differentiated tumors (430/32.3%) and well differentiated ones (200/15.1%). Of the total tumors, 346/26% were Ta–T1, 456/34% were T2, and 528/40% were T3–T4a,b. Most of tumors were solid ones, accounting for 74% compared with the papillary ones (26%) with most (54.9%) of the tumor located in the lateral wall of the bladder.

Although in 620 (38.5%) patients, the follow up information were missing from the records, still the recurrence of the tumors were recorded in 890 (55.3%) of the patients 6 month after the initial therapy.

Discussion: The results showed that poorly differentiated, muscle invasive, and high recurrent TCCs tumors dominate BC profile of Sudanese patients. It revealed also that the most affected population are those between 61–75 year–old. These findings are in clear contrast with BC profile, previously, reported in which solitary muscle invasive Bilharzia–associated SCCs tumors affecting younger population was the dominated patterns as reported by Daoud el al (1968), Malik et al., (1975) and later by Sharfi et al., (1992). Thus clear change in BC profile in Sudan is evident, perhaps due to increased urbanization and style of life that led to change in the causative etiology, and eventually the histology type.

Key words: Bladder cancer, Squamous cell carcinoma, Transitional Cell Carcinoma, Post–bilharzial carcinoma.

Introduction

Bladder cancer (BC) is a common malignancy, especially among men in whom it holds the 6th place after cancer of the lung, prostate, non–melanoma of skin, rectum, colon, stomach and the liver[(1)]. In areas where urinary bilharziasis is endemic it is even more common especially in those

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working in agriculture field[2]. In such setting it represent the commonest malignancy among males[3].

Several etiologic factors have been associated with the development of uroepithelial carcinomas of which occupational exposure to chemicals, cigarette smoking, ionizing radiation and chronic parasitic infections are the most important[4]. In particular, smoking increases the risk as well as the aggressiveness of the disease[5]. These various carcinogenetic factors have been translated in different geographical, etiological, histology types, and even in heterogeneous natural history of the disease. Two main types of uroepithelial tumors exist in Europe and the USA are the transitional cell carcinoma (TCC) which accounts for 90% of the cases, whereas squamous cell carcinoma (SCC) is rare. This picture is reversed in Africa, where SCC dominates[6]. Histology variations may be seen even within the same country. Al–Husseini *et al.*, reported that during the period 1973–2014, 91.3% of the TCC cases were among Caucasians in USA versus 4.3% in African American[7]. DeDeugd e*t al.*, (2015) reported that the incidence of SCC was double in African American compared to Caucasian in USA[8].

According to the geographical distribution, BC can be classified into two distinct types; the first one is present in industrialized countries like Europe and USA and is known to be associated with dyes industry exposures and cigarette smoking. It is dominated by the TCC and the vast majority of the cases are superficial at diagnosis and can be managed well by transurethral resection of the tumors. The second type is present in the areas where urinary bilharziasis is endemic and is dominated by the SCC. In contrast to the *TCC* type, most *SCC* tumors are muscle infiltrating at the time of the initial diagnosis and thus require radical cystectomy[9]. Although both histological (TCC, SCC), and etiological (post–bilharzial and chemical exposure) types of BC are present in Sudan, clear domination of post–bilharzial squamous cell differentiation has been repeatedly reported[10–12]. Unfortunately since 1992 few, if any, large studies have been performed, although clinical observation indicates changing in the BC characteristics in this country. So the aims of the present study were to investigate the clinical changes in bladder–cancer profile including causative etiology, histology, and natural history of the disease in contrast to what have been reported early[10–12]. This information may lead to better understanding of the present etiology, histology, and the natural history and hence help to improve disease management and outcome.

Material and Methods

Demographic and clinical data of 1610 patients diagnosed as carcinoma of the bladder based on histopathology examination, were collected from the patients records of Ibn Sina specialized hospital, Soba University hospital, Khartoum North hospital and Khartoum teaching hospital during the period 2007–2019. The data were collected in predesigned questionnaires and analyzed using SPSS program version 23.

The classification and tumor grading were done according to the World Health Organization (WHO) classification system for uroepithelial tumors[13], and the staging was performed in accordance with the Union for International Cancer Control (UICC) tumor–node–metastasis (TNM) system[14]. The diagnosis of postbilharzial SCC of the bladder was based on the positive past history of urinary bilharziasis and the presence of calcified ovum in tumor tissue sections (Figure 1).
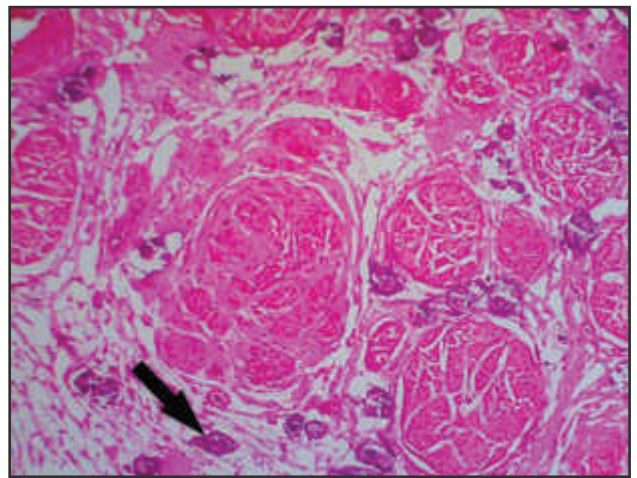
Figure 1: Squamous cell carcinoma of the bladder. Arrowhead indicates calcified Schistosoma eggs.

The ethical clearance for conducting this study was obtained from the Ethical Committee Board of Assafa College. Patients were not contacted directly; data and laboratory results were obtained from hospitals archive and kept anonymous.

Results

Of the 1610 cases of BC, 1480 (91.9%) were males and 130 (8.1%) were females with Male: female ratio of 9:1. Ages of patients ranged between 17–100 year–old with the mean age of 59–year–old. The most affected age group ranged between 61–75 years (39.3%) followed by the one ranged between 46–60 years (31%), and the one ranged between 31–45 years (11.7%).

Smoking habits information has been missing in the records of 410 patients (25.5%). However, in the remaining 1200 patients, 44% were smokers and 30.5% were nonsmokers. History of urinary bilharziasis was positive in 660 (40.9%) of the patients records, negative in 720 (44.7%), and missed in 230 (14.3%) of the cases.

Hematuria was the main complaint in almost all the cases, present in 99.4% and absent in only one case, which had symptoms other than hematuria (Table 1).

		Number	Percentage %
Gender	Male	1480	91.9%
	Female	130	8.1%
Age	31 – 45 years	188	11.7%
	46 – 60 years	499	31%
	61 – 75 years	633	39.3%
Rresidence	Urban areas	1175	73%
	Rural areas	435	27%
Smoking habits	Smokers	708	44%
	Non smokers	491	30.5%
	Missing data	410	25.5%
History of urinary bilharzias	Positive	660	40.9%
	Negative	720	44.7%
	Missing data	230	14.3%
Haematuria	Present	1600	99.4%
	Absent	10	0.6%

Table 1: Demographic characteristics of bladder cancer patients

Of the 1610 cases, histopathology information were available for 1330 cases only, and miss for the remaining 280 tumors. The histology results showed that 1030 (77.4%) of the cases were TCC histology type, 280 (21.1%) were SCC type (Figure 1 and 2), and 20 (1.5%) were adenocarcinoma. The staging and grading results revealed that 346 tumors (26%) were Ta–T1, 456 tumors (34%) were T2, and 528 tumors (40%) were T3–T4. Regarding grade of the tumors, 700 (52.6%) tumors were poorly differentiated, 430 (32.3%) tumors were moderately differentiated, and only 200 (15.1%) were well differentiated.

Solid tumors seem to be the most common gross morphology type and was seen in 984 (74%) of the tumors, while the papillary ones were seen in 346 (26%) (Figure 2). The most frequent location of the tumor was the lateral wall, seen in 890 tumors (54.9%), followed by 300 (20.4%) tumors located on the dome of the bladder, and 150 (9.3%) in the trigone region (Table 2). Recurrence
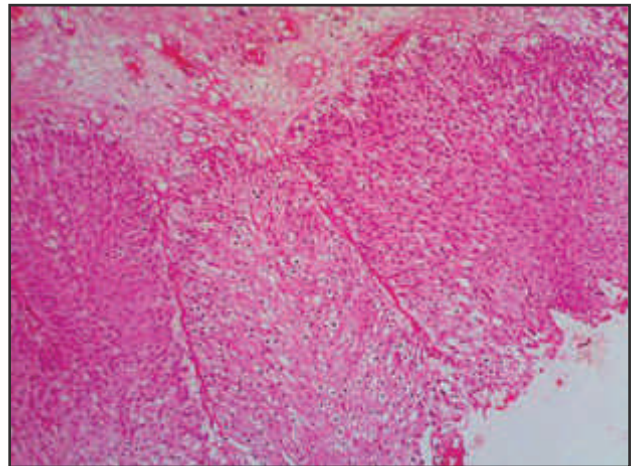
Figure 2: Papillary urothelial carcinoma

		Number	Percentage %
Histology type	TCC	1030	77.4%
	SCC	280	21.1%
	adenocarcinoma	20	1.5%
Stage	Ta–T1	346	26%
	T2	456	34%
	T3– T4	528	40%
Grade	G I	700	52.6%
	G II	430	32.3%
	G III	200	15.1%
Morphology Type	Solid tumors	984	74%
	Papillary	346	26
Tumor location	Lateral wall	890	54.9
	Dome of the bladder	300	20.4
	Trigone region	150	9.3

Table 2: Histopathology results of 1330 patients with bladder cancer

of the tumor occurred in 890 (55.3) of patients, whereas 100 (6.2%) of patients showed no recurrence 6 month after the initial therapy. Unfortunately, in the 620 (38.5%) of the patients' records, no information regarding the recurrence were not available or they did not show for follow–up.

Discussion

The data in the present study contrast strongly with what has been reported about clinical characteristics of BC in this country[10–12]. The data in this study suggest basic changes in the epidemiology, pathoetiology and clinical aspects of BC in the Sudan.

Worldwide, BC is 3 times more common in men than in women[15]. Our data showed even higher gender ratio (9:1) compared to the international figures. However, the sex discrepancy may be explained by the fact that men are more exposed to carcinogens than women i.e., smoking and urinary bilharziasis. Another interesting finding is the relation between the gender and the histology type and again this may have something to do with the type of the carcinogens the males are exposed to.

Although BC is a disease of elderly patients at 7th decade in TCC (16), post–bilharzial SCC sub–type peak incidence takes place at 5th decade[17]. In our study, the mean age was 59 and the peak incidence for BC has been found in patients aged between 61 and 75 years (45%). This is in complete agreement with the steady increase in number of TCC of the BC and decreases of SCC type in which the peak of incidence ranges between 31 and 45 years.

Several epidemiological studies incriminate cigarette smoking in pathogenesis and natural history of BC[4]. In USA 17.5% and 13.5% of males and females smoke, respectively[18]. According, to the WHO, prevalence of smoking among Sudanese is 23.5%, 1.5%, 20.3% and 12.9% among adult males, adult females, young males and young females respectively[19]. Although smoking habits is important information, this was missing from the records in 25.5% since the study was a retrospective one. Nevertheless, the available data revealed that 709 patient (44%) were smokers and 491 (30.5%) were nonsmokers. As aforementioned smoking increases the aggressiveness of the disease[5], as our data showed strong association between smoking and high grade advance tumor.

The association of bladder SCC with *S. haematobium* infection among Sudanese has been supported and reported by many authors[12, 20]. The present study showed evidence of histology profile changing in form of decreased SCC differentiation and increased TCC differentiation cases. The data suggest also less association between BC and urinary bilharzias which declined to 40.7%, in contrast to the previously report in which 69% of cases showed evidence of bilharzial ova in the tumors. The successful control program of urinary bilharziasis i.e., Blue Nile project may decreased the incidence of the urinary bilharziasis and hence SCC differentiation

cases[11]. Urbanization and change in the style of life may have also played important factor in this dramatic change. During the last 4 decades, internal displacement was widespread in Sudan forcing many farmers and their families to abandon their farms and homes in search of a better live in urban areas[21].

The vast majority of the tumors were poorly differentiated tumors (52.6%), the moderately differentiated were 32.3% and the well differentiated were only 15.1%. Globally, more than 70% of newly diagnosed BC are superficial and papillary tumors i.e., the tumor is confined to the lamina propria[22, 23]. Our data showed distinct pattern as 52.6% of the tumors were poorly differentiated tumors (G3), of which 74% were muscle invasive carcinomas (≤T2). This finding may reflect a late presentation of the patients, and scarcity of trained medical personnel and health services, all of which lead to delay in the initial diagnosis.

Recurrences after initial treatment occurred in 890 (55.3%) of the cases. This figure is far less than the international figures where more than 70% of the tumors relapse in form of recurrence[23]. The discrepancies can be explained by the fact that only 61.5% of the cases showed up for follow–up cystoscopy and that the modality of treatment differs because most of the tumors are muscle invasive and they required radical surgery rather than simple transurethral resection of superficial noninvasive tumors.

Although, the present study showed changed in the pathoetiology profile of the BC in the Sudan, the clinical profile is dominated by advanced grade and/or stage of TCC at the time of diagnosis. The vast majority of the tumors were poorly differentiated and muscle invasive even at the time of first diagnosis. The improvement of diagnosis and management of BC in Sudan require more facilities than the present ones, and perhaps even a better distribution of the limited resources and medical personnel in a more fair, just, and reasonable way. Until this comes true, the diagnosis and management of BC in Sudan will remain hampered resulting in poor treatment outcome.

Conflict of Interest

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