BLADDER CANCER: INCIDENCE, ASSOCIATION, BASIS, GEOGRAPHY AND RISK FACTORS

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Abstract

Objectives: The purpose of the study are to formulate an idea about the number of patients with bladder cancer in Missan city and those of them that are on treatment by the oncology center of the province. Also to point towards the most prevalent histo-pathologic finding and to put our hands on the probable effect of some risk factors on the incidence which indicate to the noticed association between the endemicity of schistosomiasis in the rural areas of Missan with bladder cancer.

Methods: A descriptive study was conducted in Al-Shafaa oncology center. The total numbers of patients involved in the study were 55, through period from July 2014 to April 2015.

Results: Men were most affected 78.18% (43) than women 21.82% (12).Most of patients were smokers 80% (44). The mean age affected was between 60-70 years 34.55% (19). The urban peoples were most present 65.45% (36). Among most histopathology, the transitional cell carcinoma was the most type 87.27% (48), which mostly invasive 63.64% (35), while the most grading was grade III 47.28% (26) and the most staging was T2 45.45% (25).

Conclusion: The incidence of squamous cell carcinoma was, 12.73% of the subjects of the study, which is associated with schistosomiasis.

Keywords: Bladder cancer**,** Transitional cell carcinoma, Schistosomiasis**,** Hematuria**,** Squamous cell carcinoma**,** Urinary obstruction

Introduction:

Bladder cancer is the fourth most common cancer in men and the tenth in women (Goldman, et al 2003). A transitional cell epithelium lines the urinary tract, cancers can occur at any point: 90% of malignancies develop in the bladder, 8% in the renal pelvis and the remaining 2% in the ureter or urethra (Fauci, et al 2008). Transitional cell carcinomas in these

various locations share a similar natural history; they tend to be multifocal and carry a high recurrence rate (Goldman, et al 2003). The incidence is three times higher in men than in women and twofold higher in whites than blacks, with a median age at diagnosis of 65 years (Fauci, et al 2008). The development of bladder cancer is closely related to the length of exposure to a variety of environmental carcinogens. In the Western world, cigarette smoking is the leading cause for bladder cancer, and smokers have about ten-fold increased risk for development of bladder cancer. That risk decreases but remains elevated up to 10 years after smoking cessation (Goldman, et al 2003). Exposure to Schistosoma haematobium, a parasite found in many developing countries, is associated with an increase in both squamous and transitional cell carcinomas of the bladder (Fauci, et al 2008). It is estimated that over 200 million people are currently infected worldwide, mainly in rural agricultural and peri-urban areas. It is spread intensely in the Nile delta north of Cairo and in one belt across Africa south of the Sahara from Mali to Ethiopia and in another belt south to Mozambique. The worms live in the venous plexus around the lower ends of the ureters and the urinary bladder, where they shed their eggs.

The acute granulomatous response to parasite eggs in the early stages causes urinary tract disease, such as urethral ulceration and bladder polyposis. Up to 50 to 70% of infected individuals have hematuria, dysuria, or frequency. An increased incidence of squamous cell carcinoma of the bladder has been reported in endemic areas of S. haematobium infection, but the mechanism of carcinogenesis is unknown. In schistosome-infected populations, intensity of infection increases during the first two decades of life, as children accumulate worms, and then declines (WHO, 1993). Other implicated agents include the aniline dyes, the drugs phenacetin and chlornaphazine, and external beam radiation. Chronic cyclophosphamide exposure may also increase risk, whereas vitamin A supplements appear to be protective (Fauci, et al 2008 and Matthew, et al 2012). In the Western world, more than 90% of tumors in the urinary bladder are transitional cell carcinomas (Thompson, 1954). Pure squamous cell tumors constitute 3% of the cases and are strongly associated with chronic bladder infection (Goldman, et al 2003) with Schistosoma and it occurs in developing countries (Thompson, 1954). Adenocarcinomas, which represent 2 to 3% of tumors, usually develop at the dome of the bladder (urachal carcinomas) or in the peri-urethral tissues (Fauci, et al 2008). The predominant presenting symptom is painless hematuria, either gross or microscopic (Colledge, et al 2010). The hematuria typically occurs throughout urination, indicating that the blood is from the bladder or above it, not the urethra (Goldman, et al 2003). The irritative symptoms are the next most common presentation (Matthew, et al 2012), which may reflect in situ disease manifest as

increased urinary frequency, urgency, or dysuria (Thompson, 1954). A tumor at the lower end of a ureter or a bladder tumor involving the ureteric orifice may cause obstructive symptoms (Yun-Ling, et al 2012). Obstruction of the ureters may cause flank pain. Symptoms of metastatic disease are rarely the first presenting sign (Fauci, et al 2008). Examination is usually unhelpful. Rectal examination detects only very advanced tumors (Talib, 2008). In patients with painless hematuria, the diagnostic evaluation should begin with a CT scan to locate or exclude any tumor above the bladder (Goldman, et al 2003). Urine cytology is helpful to confirm the diagnosis, but it is unable to determine the location of the tumor. Flexible cystoscopy, which is the single most important test in diagnosing bladder cancer, is required in adults with unexplained hematuria. If a bladder tumor or a suspicious lesion is found, the patient should then undergo transurethral resection of the tumor with a resectoscope and have biopsies of the underlying muscle under general anesthesia to ensure that the entire bladder interior is optimally visualized and examined, especially the proximal urethra and bladder neck regions. The locations of the tumors should be recorded (Al-Fouadi and Parkin, 2006). Ultrasonography, CT, and/or MRI may help to determine whether a tumor extends to peri-vesical fat (T3) and to document nodal spread. Distant metastases are assessed by CT of the chest and abdomen, MRI, or radionuclide imaging of the skeleton (Fauci, et al 2008).

Patients and Methods

A descriptive study was conducted in Al-Shafaa Oncology Center, Missan city, Iraq. The data was collected from the statistics department of the center. The study was performed by percentage calculation and frequency. The total number of subjects involved in the study is 55 patient and they are the total number of patients diagnosed and treated of bladder carcinoma in Al-Shafaa oncology center from July 2014 to April 2015.

Results and Discussion

From the study we noticed the obvious prevalence of male gender among the diagnosed patients with a 78.18% and this quite resembles the association of smoking with the incidence of bladder carcinoma with an 80%. In comparison with a similar research done for bladder cancer patients in Egypt that was conducted from 2006 to 2010. It found that there was a high association between cigarette smoking and urothelial carcinoma but not SCC, and that among nonsmokers; environmental tobacco smoking was associated with an increased risk of urothelial carcinoma (Gelfand, et al 1967). While in the age discrepancy, the most elevated percentage was in those in their sixtieth, with 34.55% of the patients, followed by a 25.45%

made of those in their seventieth. Only one was below 30 years old and 5 above the age 80.

Whereas for the occupation of the subjects, all the females were housewives and half of the males were self-employees so we couldn't link them to a precise occupation that may be related and the other half were mostly governmental employees.

The residency of those patients is a key environmental factor in our study since it implicates on the still risk of the development of bladder cancer among our citizens due to the resident infection with schistosomiasis, this is mostly noticed in the rural areas which, although only 34.55% of those involved are currently residing in rural areas, but certainly this was not the condition several years prior. As for the histo-pathologic findings of the study 48 of the subjects were diagnosed with transitional cell carcinoma and seven patients with squamous cell carcinoma, and here we must ponder, since the relationship between SCC and schistosomiasis is the focus of our study.

All of those 7 patients reported a history of bilharziasis lived in rural areas when they were younger (history of painless hematuria). All of them were males and were smoking.

In a study done in Iraq from 1960 to 1969 by Talib, 2008: mention that the impact of bilharziasis in Iraq and found higher association at its time period than we have found now, which gives an optimistic sigh (Rambau, et al 2013). While a study conducted in 2006 in Baghdad by Al-Fouadi and Parkin, 2006: there was a high association but it is lower than that reported in other endemic areas (Al-Fouadi and Parkin, 2006). In comparison with a neighboring country, Egypt, 55% was the prevalence of ever being diagnosed with schistosomiasis (Gelfand, et al 1967). Such studies were also performed in Africa (Gelfand, et al 1967).

In a study in north western Tanzania, 44.9% of the subjects were found to have schistosome eggs (Rambau, et al 2013). In several researches published in NEJM, strong reference to the fact that it no longer exist outside of the developing countries and china after the efforts of its eradication in the 1980s , by the introduction of the highly effective anti-schistosomal drug praziquantel (King, 2009).

Back to the histo-pathologic findings of our study, 63.64% of the patients were at an invasive stage , as merely 9 of them were in grade I, 20 of them were in grade II and 26 in grade III, 34.55% of them were Ta and 20.00% were T1 while the remaining 45.45% were T2 and thus metastatic. As we have mentioned earlier, most metastasis are to the bones and prostate and pelvic lymph nodes, but rare was the finding of metastasis elsewhere.

Table. Variables of the studied among gender, smoker status, age, occupation, residence, histopathology, invasion, grading and staging in 55 bladder cancer patients in Missan city.

Variable		No. (*n=55*)	%
Gender	Male	43	78.18
	Female	12	21.82
Chi-square = 0.0007, P value = 0.009719			
Smoker	Yes	44	80.00
	No	11	20.00
Chi-square = 0.0341, P value = 0.01			
Age discrepancy	Below 30	1	1.81
	30 - 40	2	3.64
	40 - 50	4	7.27
	50 - 60	10	18.18
	60 - 70	19	34.55
	70 - 80	14	25.45
	Above 80	5	9.10
Chi-square = 0.0226, P-Value = 0.009937			
Occupation	Housewives	12	21.82
	Self-employees	22	40.00
	Others	21	38.18
Chi-square = 0.0073, P value = 0.009328			
Residency	Rural	19	34.55
	Urban	36	65.45
Chi-square = 0.0032, P value = 0.009582			
Histopathology (Type of bladder cancer)	Transitional cell carcinoma	48	87.27
	Squamous cell carcinoma	7	12.73
Chi-square = 0.0023, P value = 0.009649			
Invasiveness	invasive	35	63.64
	noninvasive	20	36.36
Chi-square = 0.0021, P value = 0.009604			
Grading	Grade I	9	16.36
	Grade II	20	36.36
	Grade III	26	47.28
Chi-square = 0.0012, P value = 0.009743			
Staging	Ta	19	34.55
	T1	11	20.00
	T2	25	45.45
Chi-square = 0.0037, P value 0.009535			

Conclusion

Our aim here mainly is to refer to the fact that there is still incidence of squamous cell carcinoma, 12.73% of the subjects of the study, which is associated with schistosomiasis. But it is important to point to the fact of

decreased incidence of bladder cancer due to schistosomiasis in Iraq, which is a good sign forward.

Acknowledgements

Great thankful for Dr. Rasha K. Al-Saad, M. Sc. Parasitology, Veterinary Medicine College / Basrah University and Dr. Ahmed S. Al-Shewered, Permanent Doctor, Missan Oncology Centre for their helping.

References:

Al-Fouadi, A., and Parkin, D. (2006). Cancer in Iraq: Seven years' data from the Baghdad tumour registry. International journal of cancer, 34(2): 207-213.

Colledge, N.R., Walker, B.R. and Ralston, S.H. (2010). Davidson's Principles & Practice of Medicine. 21st ed. Elsevier, Churchill Livingstone, China.

Fauci, A.S., Braunwald, E., Kasper, D.L., Hauser, S.L., Longo, D.L. and Jameson, J.L. (2008). HARRISON`s a Principles of Internal Medicine: Bladder and Renal Cell Carcinomas. 17th edition. The McGraw-Hill Companies, Inc. USA.

Gelfand, M., Weinberg, R., and Castle, W. (1967). Relation between carcinoma of the bladder and infestation with schistosoma haematobium. The Lancet,1(7502): 1249-1251.

Goldman, L., Ausiello, D., Bennett, C., and Russell L. (2003). Cecil Textbook of Medicine, (22nded.). Elsevier Health Sciences. Oncology, pp: 1228-1230.

King, C.H. (2009). Toward the Elimination of Schistosomiasis. The new England journal of medicine, 360: 106-109.

Matthew, E.N., Angela, B.S., Raj, S.P., Thomas, J.G., Gilad, A., Neal, S., and Yair, L. (2012). Reported use of intra-vesical therapy for non-muscle-invasive bladder cancer (NMIBC): results from the Bladder Cancer Advocacy Network (BCAN) survey. British journal of urology international, 110(7): 967-972.

Rambau, P.F., Philipo, L.C. and Jackson, K. (2013). Schistosomiasis and urinary bladder cancer in North Western Tanzania: a retrospective review of 185 patients. Infectious Agents and Cancer, 8:19.

Talib, H. (2008).The problem of carcinoma of bilharzial bladder in Iraq. British journal of urology, 42(5): 571-579.

Thompson, J.H. (1954). Host-parasite relationships of *Schistosoma mansoni*. Experimental Parasitology, 3(2): 140–160.

World Health Organization (1993). The Control of Schistosomiasis. Description of the epidemiology, morbidity, and methods of control of schistosomiasis. Technical Report Series 728, pp: 1-86. Geneva.

Yun-Ling, Z., Sania, A., Doa'a, A., Chiranjeev, D., Sameera, E., Nabiel, N., Iman, G., Iman, L., Tamer, H., Mohamed, A., Hussein, K., Beverly, W., Mohamed A., and Christopher, A. (2012). Urinary bladder cancer risk factors in Egypt: a multi-center case-control study. Cancer Epidemiology Biomarkers Preview, 21(3): 537–546.