Schistosoma – Associated Bladder Cancer: is There a Change in The Trend of Cell Type?

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ABSTRACT:

OBJECTIVE:

To compare the contribution of squamous cell and transitional cell types to the schistosoma – related and schistosoma – unrelated bladder cancer among Egyptian patients and to evaluate any significant association of carcinoma in situ (CIS) and stage T1 – TCC in schistosomiasis.

MATERIALS AND METHODS:

A retrospective study in which the histopathologic records of 196 patients who underwent radical or salvage cystectomy for bladder cancer from August 1994 to December 2000 in Urology and Nephrology Center/ Mansoura University – Egypt, had been carried out.

RESULTS:

The age range of patients was (29 – 75) with a mean of (55.82 ± 8.81) years. Histopathologic examinations of cystectomy specimens showed schistosomiasis in 81(41.32%) patients while in 115 (58.67%) patients; bladder cancer was schistosoma – unrelated. The cell type of cancer in (80) patients with schistosomiasis, was transitional cell carcinoma (TCC) in 40 (50%), squamous cell carcinoma (SCC) in 37 (46.25%), and adenocarcinoma in 3 (3.75%) patients. In schistosoma – unrelated bladder cancer, TCC was reported in 76 (66.08%), SCC in 34 (29.56%), undifferentiated carcinoma in 4 (3.47%) and adenocarcinoma in 1 (0.86%) patients. CIS associated with (stage T1 – TCC) was reported in 2 (15.38 %) out of 13 patients with schitosoma – related bladder cancer, while it was reported in 3 (14.28%) out of 21 patients with schistosoma – unrelated bladder cancer. There was no significant statistical difference between the two groups.

CONCLUSION:

Schistosoma – related bladder cancer is still a problem in countries endemic with schistsomiasis. Although the major histological cell type in such cancer is SCC, there is a trend of increasing frequency of schistosoma – related TCC.

KEYWORDS: Schistosomiasis, Bladder cancer, Squamous cell carcinoma, Transitional cell carcinoma.

INTRODUCTION:

Schistosomiasis is the second most common parasitic infection of humans after malaria. Approximately 200 million people are infected globally in 76 countries and about 600 million are exposed to infection in tropical and subtropical regions of Africa, Asia, South America and the Caribbean [1, 2]. Epidemiological data support a positive correlation between schistosomal infection and the risk to develop specific malignancies such as liver and bladder carcinomas and other tumors of the genitourinary tract [3].

In schistosomiasis chronic bladder infection and inflammation would produce squamous metaplsia and leukoplakia of the urothelium, which are considered pre – cancerous lesions. However the role of leukoplakia and squamous metaplasia has been questioned [4]. Bladder carcinogenesis is probably related to bacterial and viral infections,commonly associated with bilharzial infestation, rather than the parasite itself [5].

The major histological cell type of bladder cancer associated with schistosomiasis of the urinary tract is squamous cell carcinoma (SCC). In many areas of endemic schistosome infection, a much higher proportion SCC of the bladder was seen compared to those occurring in Europe or North America [6], in which more than 90% of primary bladder carcinomas are transitional cell carcinoma (TCC), whereas squamous cell carcinoma (SCC) comprises less than 10% [7]. However in the last decade some studies reported a relative increase in the frequency of transitional cell type in schistosoma – associated bladder cancer [8, 9].

In this study evaluation of the contribution of squamous and transitional cell types to the schistosoma – related and schistosoma – unrelated bladder cancer among Egyptian patients was carried out. Carcinoma in situ (CIS) associated

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with stage T1 – TCC was compared in schistosoma – related and schistosoma – unrelated bladder cancer patients.

MATERIALS AND METHODS:

196 patients who underwent radical or salvage cystectomy for bladder cancer from August 1994 to December 2000 in Urology and Nephrology Center / Mansoura University – Egypt, were included in the present study. A retrospective review of the histopathologic records of cystectomy specimens was carried out. Tumor stage and grade were defined according to UICC [10] and World Health organization classifications [11]. All samples were from formalin – fixed, paraffin – embedded archival specimens. Representative 5 µm H & E – stained sections from each tumor were reviewed by a pathologist to identify the histological type of tumor. Since focal squamous cell changes are common in high grade TCC, the term squamous cell carcinoma in this study was reserved for those tumors that are squamous throughout [12]. Mixed tumors were excluded from the study. Schistosomiasis infection was confirmed histopathologically by the presence of schistosoma – ova in every case.

Statistical analysis:

Data were analyzed using mean ± standard deviation (SD), frequency and percentage. Chi – square and Fisher's exact tests were used for statistical analysis. P value < 0.05 was considered statistically significant.

RESULTS:

In this study 196 patients aged (29 – 75) with a mean age (55.82 ± 8.81) years had radical or salvage cystectomy for bladder cancer. They were 167 (85.2%) men and 29 (14.79%) women. Histopathologic examinations of specimens examined showed schistosoma – related bladder cancer in 81(41.32%) patients. In one of those patients, the cell type of bladder cancer was not recorded. Thus, the cell type of cancer in 80 patients with schistosomiasis was TCC in 40 (50%) patients, SCC in 37 (46.25%) patients, and adenocarcinoma in 3 (3.75%) patients. Schistosoma – unrelated bladder cancer was reported in 115 (58.67%) patients. The cell type of such cancer was TCC in 76 (66.08%), SCC in 34 (29.56%), undifferentiated in 4 (3.47%) and adenocarcinoma in 1 (0.86%) patients.

The number of patients with bladder adenocarcinoma and undifferentiated cancer was small, so they were excluded from the statistical analysis. There was statistically significant association between TCC and schistosoma related bladder cancer (P=0.017).

Table (1) shows that the total number of TCC accounts for 116 (59.18%) of bladder cancer patients, while SCC accounts for 71 (36.22%) patients.

Pathological staging and grading criteria of bladder cancer patients were shown by table (2). Statistical analysis of possible specific association of schistosoma related or unrelated bladder cancer with certain pathological stage and grade was invalid. The association of TCC and certain tumor grade in both schistosoma related and unrelated groups, was not significant.

Carcinoma in situ (CIS) was studied in stage (T1 – TCC) in both schistosoma related and unrelated bladder cancer patients. CIS was reported in 2 (15.38 %) out of 13 patients with schitosoma – related bladder cancer, while it was reported in 3 (14.28%) out of 21 patients with schistosoma – unrelated bladder cancer. There was no significant statistical difference between the two groups, as shown by table (3).

DISCUSSION:

Egypt has the highest frequency of bladder cancer in the world [3, 7]. The Egyptian bladder cancer is of great clinical significance because its etiology, pathology and biological behavior differ considerably from that seen in Europe and the United States. From the pathologic point of view, bladder cancer in Egyptian patients is characterized by high frequency of SCC [8, 9]. Indeed the highest incidence of SCC of the bilharzial bladder is in Egypt [5]. Schistosoma – related bladder SCC was reported in (50 – 70%) followed by TCC (30 – 50%) and adenocarcinoma (2%) of Egyptian patients [13]. Ghoneim et al. **[14]** reported that SCC constituted (59%) of 1026 cystectomy specimens at the Mansoura Urology and Nephrology Centre. Thereafter Khaled et al [15] reported SCC in (53.3%) of 180 schistosoma – related bladder cancer. Other countries in the Middle East with a high incidence of SCC of the bilharzial bladder include Iraq [16], southern province of Saudi Arabia from which SCC was reported in 20% of 60 patients with bladder cancer [17], Yemen and Sudan. In Africa a high frequency of bladder cancer was reported from the Gold Coast and South Africa, but the reported incidence of SCC in these countries is much less than in Egypt because bilharziasis is less endemic and less severe [5].

The gradual change in the trend of pathological cell type of schistosoma – related bladder cancer in Egypt from SCC to TCC was recognized and reported by some literatures [8, 9]. Mostafa et al compared the periods 1962 to 1967 and 1987 to 1992, there was a decrease in the incidence of

nodular tumors (83.4 to 58.7%) and of SCC (65.8 to 54.0%) but an increase in the incidence of papillary tumors (4.3 to 34.8%) and TCC (31.0 to 42.0%); all changes were statistically significant [6].

This study reported an increasing frequency of schitosoma – related TCC in 40 (50%) patients to the extent that it exceeded schitosoma – related SCC which was reported in 37 (46.25%) patients. The explanation of this phenomenon may be multifactorial. The extent of Schistosoma infection apparently plays a significant role in the induction of different types of carcinoma, since SCC is usually associated with moderate or high worm burdens whereas TCC occurs more commonly in areas associated with lower degrees of infection [6]. We think that other patients' factors such as smoking, immunological status, dietary habits, and other possible environmental factors may affect the change of the cell type in schistosoma – related bladder cancer.

CIS is one of the most significant clinical and pathological factors to predict recurrence and progression of Ta T1 bladder cancers [18]. CIS association with stage (T1 – TCC) in schistosoma related and unrelated bladder cancer was compared. The comparison was not statistically significant. To our knowledge, few literatures, if any, had focused on the possible significant association of CIS with schistosoma related early stage TCC (Ta T1), probably because the concept of SCC dominance in schistosoma – related bladder cancer is still having a broad background.

The increase in the frequency of schistosoma related bladder TCC which is confirmed in the present study necessitates further assessment with larger number of patients to evaluate whether this change in the trend of cell type of schistosoma – related bladder cancer is confined to Egyptian patients or it involves other endemic areas of schistosomiasis. Besides, it is interesting to study the criteria of schistosoma related stage T1 – TCC, including any possible significant association with pathological factors such as CIS that affect its recurrence and progression.

CONCLUSION:

Schistosoma – related bladder cancer is still a problem in countries endemic with schistsomiasis. Although the major histological cell type in such cancer is SCC, there is a trend of increasing frequency of schistosoma – related TCC.

Table (1) Histopathologic criteria of bladder cancer patients

Bladder cancer	TCC * N=116	SCC † N=71
Schistosoma -Related	40	37
Schistosoma -Unrelated	76	34
* : Transitional cell carcinoma, † : Squamous cell carcinoma, N: Number $X^2 = 5.65$ P=0.017 (significant)		

Table (2) Staging and grading criteria of bladder cancer patients

Pathological tumor stage	Schistosoma – related TCC N= 40	Schistosoma – unrelated TCC N= 76	Schistosoma – related SCC N= 37	Schistosoma – unrelated SCC N= 34
pT1	13	20	6	7
pT2	6	21	9	9
pT3	20	32	18	16
pT4	1	3	4	2
Tumor grade				
Grade I	0	2	23	22
Grade II	29	58	10	12
Grade III	11	16	4	0
	P=0.46 (not significant)			

Table (3) CIS associated stage T1 – TCC in bladder cancer

Bladder cancer	Stage T1 – TCC (N=34)	CIS (N= 5)
Schistosoma -Related	13	2
Schistosoma -Unrelated	21	3
P=0.65 (not significant)		

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