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PATTERN OF TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER AS SEEN AT KENYATTA NATIONAL HOSPITAL, NAIROBI
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C. G. WAIHENYA and P. N. MUNGAI

ABSTRACT

Objective: **To highlight the pattern of patients with transitional cell carcinoma of the urinary bladder with regards to age, sex, ethnic origin and histopathological classification.**
Design: **A ten year retrospective study.**
Setting: **Kenyatta National Hospital, Nairobi, Kenya.**
Subjects: **Fifty two patients who presented at Kenyatta National Hospital over the ten year period with histologically proven transitional cell carcinoma of the urinary bladder. There were 41 males and 11 females aged 27 to 84 years. The mean age was 57 years.**
Results: **The peak incidence was in the 60-69 years age group. The male to female ratio was 4:1. The regional (provincial) distribution revealed Central and Eastern had 77%, Rift valley had 6%, Nairobi, North Eastern, Western and Coast provinces had 2% each. In the ethnic distribution; Kikuyus, Kambas and Merus were 77% while others were 17.3%. Transitional cell carcinoma was found in 67% of the patients, 60% had advanced disease. Twenty nine percent were smokers while 25% consumed alcohol. The main occupation was farming in 65%. The most Common clinical presentations were haematuria 98% and lower abdominal pains in 71%. A total of 99,028 patients were admitted to the surgical wards,transitional cell carcinoma patients represented only 0.6%.**
Conclusion: **Transitional cell carcinoma is a rare disease. At Kenyatta National Hospital it only represented 0.6% of all surgical admissions during the study period. It accounted for 67% of all bladder tumours an increase in incidence compared to previous studies. It is common in males more than females, with a peak in the seventh decade. Majority of the patients were from central Kenya. Alcohol, smoking and farming were the most important risk factors. Haematuria was the most important presenting clinical feature. Poor record keeping may have contributed to the low number of patients enrolled into the study. There is need for a thorough prospective study to find out the actual prevalence of bladder tumours.**

INTRODUCTION

Urinary bladder cancer represents a significant proportion of urologist's caseload because of its ubiquity and in the superficial disease long natural history. It is more common in men than women (2.3: 1). In men it is the fourth most common cancer after prostate, lung and colorectal tumours(1).

Carcinoma arising from the bladder may be of three cell types; transitional, squamous and adenocarcinoma. Bladder cancer is the most common cancer of the urinary tract and transitional cell carcinoma accounts for more than 90% of bladder tumours in western countries(2). In areas where *Schistosoma haematobium* is endemic the proportions are different. Ndaguatha in a review of urinary bladder cancers in Kenyatta National Hospital found 53.3% were transitional cell, 17.3% were anaplastic, 13.3% were squamous cell carcinomas and others were 16.1%(3).

This tumour features the entire range of aggressiveness from low-grade superficial to high-grade invasive cancers. The incidences are higher in whites than blacks, ratio 2:1(4,5), however the increased risk in whites appears to be limited to patients with non-invasive tumours(6). The observation suggests that some superficial tumours in blacks may go undetected.

The tumour can occur at any age even in children but it is generally a disease of the elderly with the median age of diagnosis being approximately 67 to 70 years. The aetiology of urinary bladder cancer remains unknown, but there are several predisposing factors. These include chemicals, cigarette smoking, radiotherapy and chemotherapy, chronic cystitis and schistosomiasis and bowel interposition.

Increase in understanding of the genetics of the bladder cancer has provided insights into the basis of the clinical behaviour of the tumours(5). The first suspicion of a chemical cause of bladder tumours was

raised by Rehn in 1894 when he recorded a series of tumours in workers in aniline dye factories(7). Aniline dyes were introduced in the mid-1800s to colour fabrics. Other such chemicals (e.g. 1-naphthylamine, xenylanine and benzidine) have since been identified(8).

There is a strong correlation between incidence of bladder cancer and cigarette smoking, with a four fold higher incidence of the disease in smokers(9-11). The risk correlates with the number of cigarettes smoked, the duration of smoking and the degree of inhalation of the smoke. This risk has been observed in both sexes. Ex-cigarette smokers have a reduced incidence of bladder cancer compared with smokers(l2). Other forms of tobacco are associated with only a slight higher risk for bladder cancer(9,13). An estimated one third of bladder cancer patients may be related to cigarette smoking(14).

The specific chemical carcinogen has not been identified but nitrosamines as well as 2- naphthylamine are known to be present. Increased urinary tryptophan metabolites also have been demonstrated in cigarette smokers(15). A significantly higher incidence of bladder cancer has been seen in-patients previously treated with pelvic irradiation or the chemotherapeutic drug cyclophosphamide(5).

Chronic cystitis due to infections and bladder calculi have been associated with increased incidence of urinary bladder cancer. In African patients, schistosomiasis appears to be related to a high incidence of not only squamous cell carcinoma but also other histological types. In a recent study by Groeneveld *et al.* schistosomiasis of the bladder was found in 85% of patients with squamous cell carcinomas, 50% of those with undifferentiated tumours and adenocarcinoma, in 17% of those with mixed tumours or sarcomas and in 10% of the patients with transitional cell carcinoma(16).

The resurgence in the use of bowel in bladder augumentation, and orthotopic replacement of the bladder has led to an increase of reports of patients with bladder cancer arising in the interposed bowel. All patients with interposed bowel in the urogenital system need life long follow-up because of the potentially greater risk of neoplasia caused by increased formation of nitrites and nitroso compounds in the bladder hence the need for regular check cystoscopies.

Molecular genetics have a role to play. It is thought that tumour development and progression is driven by accumulation of multiple genetic alteration by the normal cell. Many phenotypic changes in tumour cell events that are secondary to primary genetic alterations and some of these may have been caused by changes in the environment. The genetics of the bladder carcinogenesis is thought to be multifactorial, involving the action of proto-oncogenes through mutation of gene amplification. Several proto-oncogenes are over-expressed in bladder cancers, these include HRAS (ERBBI), EGFR (ERBB2), MYC and SRC. Their precise role is yet to be defined.

It is still unclear, however, how these alterations and deletions may be integrated in the development of bladder cancer(17). Pathologically, bladder cancer appears to progress from carcinoma *in situ* to a fixed mass (T4b) with worsening of prognosis in successive stage of the disease.

Further more carcinoma *in situ* may represent a parallel rather than a continuous form of the disease.

MATERIALS AND METHODS

The study was carried out at Kenyatta National Hospital. This was a retrospective study covering a period of ten years from January 1990 to December 1999. Only those patients with histologically confirmed diagnosis of transitional cell carcinoma of the urinary bladder treated at KNH during the study period were included. The sample size was determined by the study period. The relevant records of the patients with TCC were reviewed after approval of the study proposal by the KNH Research Committee. Data were collected using tally sheets and analysed using statistical computer programme (SPSS).

RESULTS

During the period of 1990 to 1999, 92,028 patients were admitted to all surgical units of Kenyatta National Hospital. Of these 224 patients were clinically diagnosed to have urinary bladder cancer. Of these 127 (57%) files were traceable from which 79 had histologically proven bladder cancer. Fifty two, patients of these were transitional cell carcinoma and were enrolled into the study.

The patients were from all parts of the country some seen primarily, others as referrals from provincial, district and mission hospitals. The number of patients recorded from 1990 to 1999 varied from one to ten each year with an average of five patients per anum. The highest number of patients were seen and recorded in the period 1996 to 1998 constituting 69.2% of all the patients. The 1990 to 1994 figures were low and accounted for 21.1 %.

Age/sex: The 52 patients of transitional cell carcinomas were analysed according to the age at presentation. Incidence increased with age. The youngest recorded age was 27 years and the oldest was 84 years. The mean age at presentation was 57.19 years and the median age was 60 years. The range was 57 years. The peak age group was 60 to 69 years accounting for 16 (30.8%) of the recorded patients. The other age groups had the following distribution, 20 to 29 years two patients (3.8%), 30 to 39 years; four patients (7.7%), 40 to 49 years; 11 patients (21.2%), 50 to 59 years; eight patients (15.4%), 70 to 79 years; seven patients (13.5%), 80 years and above had four patients (7.7%) (Table 1). Gender distribution revealed 78.8% were males and 21.2% were females. The male: female ratio was 3.7:1.

Table 1

Patients characteristics

Characteristic	No	%	Cumulative %
Yearly characteristics in number of patients seen			
1990	3	5.8	5.8
1991	2	3.8	9.6
1992	4	7.7	17.3
1993	1	1.9	19.2
1994	1	1.9	21.1
1995	7	13.5	34.6
1996	10	19.2	53.8
1997	9	17.3	71.1
1998	10	19.2	90.3
1999	5	9.6	100
Age characteristics (mean age 57.19 years: Range years 27-84)			
20-29	2	3.8	3.8
30-39	4	7.7	11.5
40-49	11	21.2	32.7
50-59	8	15.4	48.1
60-69	16	30.8	78.9
70-79	7	13.5	92.9
80 and Above	4	7.7	100
Gender characteristics			
Sex			
Male	41	78.8	78.8
Female	11	21.1	100

Table 2

Regional and ethnic characteristics

Characteristic	No.	%
Region		
Nairobi	1	1.9
Central	24	46.2
Eastern	16	30.8
Nyanza	5	9.6
North Eastern	1	1.9
Rift Valley	3	5.8
Western	1	1.9
Coast	1	1.9
Ethnic distribution		
Kikuyu	27	51.9
Kamba	9	17.3
Meru	4	7.7
Luo	3	5.8
Other tribes	9	17.3
Total	52	100

Table 3

Occupation and risk factors characteristics

Characteristic	No.	%
Occupation		
Farmers	34	65.4
Self employed	7	13.5
Salaried employment	5	9.6
Unemployed	1	1.9
Missing data	5	9.6
Total	52	100
Smoking		
Non-smokers	31	59.6
Smokers	15	28.8
Tobacco Snuff	1	1.9
Missing Data	5	9.6
Total	52	100
Alcohol		
Alcohol use	13	25.0
No alcohol	34	65.4
Missing data	5	9.6
Total	52	100

Table 4

Tumour characteristics and clinical features

Characteristic	No.	%
Signs/Symptoms		
Haematuria	51	98.1
Lower abdominal pain	37	71.2
Pelvic mass	19	36.5
Dysuria	17	31.7
Histological types		
Transitional cell	52	67
Squamous cell	12	15
Adenocarcinoma	6	8
Anaplastic	5	6
Rhadomyosarcoma	3	4
Total	78	100

Regional and ethnic distribution: The provincial distribution was central province, 24 patients (46.2%), Eastern province, 16 patients (30.8%), Nyanza, five patients (9.6%), Rift Valley three patients (5.8%), Nairobi, North Eastern, Western and Coast had one patient each (1.9%). (Table 2). The ethnic distribution was as follows Kikuyu, 27 (51.9%), Kamba, nine (17.3%), Meru, four (7.7%), Luo three (5.8%) and other tribes nine (17.3%) (Table 2).

Risk factors: Smoking was found in 28.8% of the patients. One patient was using tobacco snuff. There were 13 patients (25%) who consumed alcohol, information of five patients was missing from the records (Table 3). The amount consumed and durations were not recorded in most of the files.

Clinical presentation: Patients presented with various signs and symptoms, namely haematuria; 51 patients (98.1%), low abdominal pains; 37 patients (71.2%), pelvic mass; 19 patients (36.5%), dysuria; 17 patients (32.7%). Haematuria was the most common presenting symptom (Table 4).

Histological diagnosis: There were a total of 78 patients seen in the hospital with histologically confirmed urinary bladder cancers for the ten year period. Fifty two (67%) of the patients had transitional cell carcinoma, 12 (15%) of the patients had squamous cell carcinomas, six (8%) had adenocarcinomas, five (6%) had anaplastic and three (4%) had rhabdomyosarcomas (Table 4). The commonest stage of TCC was muscle invasive in 22

patients (42.3%), superficial in 20 patients (38.5%), metastatic in nine patients (17.3%) and carcinoma *in situ* one patient (1.9%). Overall majority of the patients had invasive disease (59.6%) as compared to superficial (40.4%). Carcinoma *in situ* was only recorded at the peak age of 60 to 69 years. Metastatic disease was more common in the age group 30 to 59 years than in older patients.

DISCUSSION

Transitional cell carcinoma of the urinary bladder is a rare malignancy. In this study covering ten years only 52 patients of histologically proven transitional cell carcinoma patients were seen at Kenyatta National Hospital. This accounts for 67% of all bladder tumours. Over the same period of time total surgical admissions to the hospital were 99,028. Thus transitional cell carcinoma formed 0.06% of all surgical admissions in the hospital. The average annual incidence of this condition over the ten year period was 5.2 patients. These figures reveal that there is an increase in the incidence of transitional cell carcinoma from 53% to 67%(3).

The highest number of patients were seen and recorded in the period 1995 to 1998 constituting 69.2% of all the patients. The 1990 to 1993 period figures were low. This may be explained by the poor social economic situation prevailing in the country in this period, where most patients could not afford medical services and opted to stay away or seek medical advice from alternative sources. In the period of 1993 to 1994 there was a national doctors and university lectures strike and this affected the provision of medical services.

In 1995 to 1998, introduction of cystoscopy as a routine diagnostic tool and transient improvement of the country's economy explains the increase in the number of patients at this time. In the year 1999 the number of patients reduced due to falling social-economic status (Table 1). It is possible that there was better record keeping in the year l996 to 1998.

Peak age incidence of transitional cell carcinoma occurs between 67 to 70 years. In this study, overall peak incidence occurred between 60 to 69 year age group accounting for 16 patients (30.8%). This compares with the peak incidence of 67 to 70 in the existing literature. The youngest patient was 27 years and the oldest was 84 years with a mean of 57.19 and a median of 60 years. The majority of the patients were between 40 and 69 years (67.4%).

In this study 78.8% of the patients were males and 21.1% were females giving a male to female ratio of 3.7:1 compared to 2.3:1, reported elsewhere(4,5). There was a variation in provincial representation with 46.2% of patients coming from central province, 30.8% from Eastern province, 9.6% from Nyanza, 5.8% from Rift Valley while Nairobi, North Eastern, Western and Coast provinces had 1.9% each. The possible reason for this pattern is that KNH is in close proximity to patients from Central province and therefore easily accessible on logistic grounds. The other possible reason is because Central, Nyanza and Eastern provinces are areas where rice is grown and schistosomiasis is endemic (note that schistosomiasis is responsible for 10% of TCC)(16). In this study the ethnic distribution were Kikuyu 51.9%, Kamba 17.3%, Meru 7.7%, Luo 5.8% and other tribes 17.3%. The reason for this distribution is most likely as stated in the regional distribution.

About 28.8% were smokers, this account for about a third of all patients with transitional cell carcinoma and is similar to existing literature(14). One of the patients was using tobacco snuff and this is a known risk factor(9,13). None of the patients had a past history of surgery (ureterosigmoidostomy or bladder substitution), chemotherapy or abdominal irradiation which are known risk factors in developing TCC(5).

Farmers constituted 65.4 % of all the patients. It was not specified in the records the type of farming they were engaged in, but it is known that rice farming where schistosomiasis is endemic increases the risk of TCC(16). Haematuria was found in 51 patients (98.1%), lower abdominal pain in 37 patients (71.2%), pelvic mass in 19 patients (36.5%) and dysuria in 17 patients (32.7%). Pelvic mass was a sign of advanced disease.

Presentation of transitional cell carcinoma depend on the clinical stage of the disease, presence or absence of metastases, haematuria being the most common presentation(31). Transitional cell carcinoma was the most common urinary bladder malignancy accounting for 67% of the patients followed by squamous cell 15%, adenocarcinoma 8%, anaplastic 6% and rhabdomyosarcoma 8%. This revealed an increase in transition cell carcinoma incident compared with figures from other studies(3).

Of the various stages of transitional cell carcinoma, muscle invasive was the most common accounting for 22 patients (42.3%) followed by superficial in 20 patients (38.5%) metastatic in nine patients (17.3%) and carcinoma *in situ* in one patient (1.9%). Many early stage tumours could be missed and many patients presented late(6). Muscle invasive histological stage account for the majority of patients of transitional cell carcinoma across the age spectrum.

In conclusion, transitional cell carcinoma is a rare disease in Kenyatta National Hospital. It accounts for 67% of all bladder tumours, an increase in incidence compared to previous studies. It is common in males more than females, with a peak incidence in the seventh decade. Majority of the patients were from central Kenya. Alcohol, smoking and farming were the most important risk factors. Haematuria was the most important presenting clinical feature. Poor record keeping may have contributed to the low number of patients enrolled into the study. There is need for a thorough prospective study to find out the actual prevalence of bladder tumours.

Transitional cell carcinoma is a rare disease at Kenyatta National Hospital, common in males than in females, and it is a disease of the elderly. Majority of the patients were from central Kenya. Alcohol, smoking and farming were important risk factors. Haematuria was the most important presenting clinical feature. Poor record keeping may have contributed to the low number of patients enrolled into the study.

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