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International Journal of Current Research
Vol. 7, Issue, 06, pp.17426-17428, June, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

STONE - ASSOCIATED SQUAMOUS CELL CARCINOMA OF THE URINARY BLADDER IN MAIDUGURI NORTH EASTERN NIGERIA

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ARTICLE INFO

Article History:
Received 08th March, 2015
Received in revised form
16th April, 2015
Accepted 10th May, 2015
Published online 30th June, 2015

Key words:

Stone – associated,
Squamous cell carcinoma,
Urinary bladder,
Management outcome.

ABSTRACT

Background: Stone – associated squamous cell carcinoma is rare unlike other urothelial tumours, and it is a disease of neglect seen in the elderly harboring stone for a long time. It is usually aggressive with fatal outcome.

Patients and Methods: The study reviewed all patients with stone – associated squamous cell carcinoma of the urinary bladder managed in the University of Maiduguri Teaching Hospital, State Specialist Hospital Maiduguri, and Specialist Hospital Damaturu between January 2005 and December 2014. Emergency presentations were resuscitated with analgesics, antibiotics, intravenous fluids, blood transfusion, and hemodialysis where necessary. Operable patients had surgery under general anesthesia.

Results: A total of 13 patients were studied age ranged from 33 – 88 years, with a mean of 69.08 years, and male to female ratio of 3.33: 1. Duration of symptoms ranged from 2 – 27 years. Complications at presentations were UTI in 92.31%, anemia in 84.62%, impaired renal function in 61.54%, and vesico- cutaneous fistula in 15.38%. The clinical stages (Marshall's) at presentation were stage 2 in 15.38%, stage 3 in 53.8, and stage 4 in 23.08%. Histology revealed squamous cell carcinoma in all patients, 38.46% were moderately differentiated, and 30.77% poorly differentiated. The postoperative complications were acute renal failure in 23.08%, and metabolic acidosis in 30.77%. There were 23.08% mortalities. The one year survival rate was 46.15%.

Conclusion: Stone – associated SCC occur in patients with long - standing bladder stone that had no access to healthcare or neglected.

***Citation*:** Ibrahim, A. G., Aliyu, S., Tahir M. B. and Zarami, A. B. 2015. "Stone - Associated Squamous cell carcinoma of the urinary bladder in Maiduguri North Eastern Nigeria", *International Journal of Current Research*, 7, (6), 17426-17428.

INTRODUCTION

Non- bilharzias squamous cell carcinoma of the bladder is a rare malignancy that represents <5% of bladder tumours diagnosed in the western World (Rundle *et al*., 1982; Serretta *et al*., 2000). It is usually associated with chronic irritation of the bladder from urinary stasis due to bladder outlet obstruction, recurrent urinary tract infections, stones or indwelling catheters (Ibrahim *et al*., 2013; Ayush *et al*., 2015; Navon *et al*., 1997). Bladder cancer is associated with upper and lower urinary tract stones (Michaud, 2007). A 2 – fold increase in bladder cancer risk was observed with a history of bladder stones in a case – controlled study (Kantor *et al*., 1984). Several studies also showed positive association between kidney or ureteral stones and the risk of bladder cancer (Kjaer *et al*., 1989; Gonzalez *et al*., 1991). Long – standing bladder stones have been implicated as a cause of squamous cell bladder cancer via chronic mucosal injury with resulting inflammation and disruption of the protective glycosaminoglycan layer (Hadad and Chinichian, 1991). The majority of patients with non bilharzial SCC typically present with a poorly differentiated, muscle – invasive tumour with no previous history of urothelial carcinoma (Steffen *et al*., 2012).

Less than 10% of patients present with distant metastasis (Swanson *et al*., 1990). Even in the absence of distant metastasis, the prognosis of patients with non – bilharzial SCC of the bladder remains dismal because patients usually die after locoregional recurrence, in contrast to TCC in which distant metastasis accounts for the great majority of recurrences (Wishnow and Dmochowski, 1988). The response to chemotherapy and radiotherapy of non – bilharzial advanced SCC is not encouraging; therefore surgery remained the treatment of choice in operable cases. The study reviewed our experience in the management of non – bilharzial SCC resulting from bladder stone.

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PATIENTS AND METHODS

The study reviewed all patients with stone – associated squamous cell carcinoma of the urinary bladder managed in the University of Maiduguri Teaching Hospital, State Specialist Hospital Maiduguri, and Specialist Hospital Damaturu between January 2005 and December 2014. The permission for the study was granted by the Hospital Ethics and Research committee. Written informed consent was obtained from all patients. All patients with squamous cell carcinoma coexisting with schistosomiasis, history of exposure to radiation, smoking, and exposure or working in the dye industry were excluded from the study. Inclusion criteria were long standing vesical stone of at least one year duration. Information was extracted from the clinical and laboratory notes and data analyzed using SPSS version 16. Emergency presentations were resuscitated with analgesics, antibiotics, intravenous fluids, blood transfusion, and hemodialysis where necessary. The investigations done were urinalysis, urine cytology, full blood count, blood chemistry, abdominopelvic ultrasound scan, and chest x-ray. Others were cystoscopy and biopsy, ECG, and urine culture. Operable patients had surgery under general anesthesia with prophylactic antibiotics (ceftriaxone and metronidazole). Patients that could afford chemo- radiotherapy were referred.

RESULTS

A total of 13 patients were studied age ranged from 33 – 88 years Table 1, with a mean of 69.08 years, and male to female ratio of 3.33: 1.

Table 1. Patients demography

S/N	Age(yrs)	Sex	Stone duration(yrs)
1	88	M	15
2	87	M	6
3	83	M	13
4	80	F	5
5	76	M	11
6	75	F	12
7	72	M	3
8	65	F	2
9	62	M	27
10	60	M	9
11	60	M	3
12	57	M	4
13	33	M	21

The duration of symptoms ranged from 2 – 27 years with a mean of 10.08 years. Complications at presentations were UTI in 12(92.31%), anemia in 11(84.62%), impaired renal function in 8(61.54%), and vesico- cutaneous fistula in 2(15.38%). Associated bladder outlet obstructions were BPH in 5(38.46%), urethral stricture in 2(15.38%), and bladder neck stenosis in 1 (7.69%). The clinical stage (Marshall's) at presentation were stage 2 in 2(15.38%), stage 3 in 7(53.85%), and stage 4 in 3(23.08%), no patient with stage 1 disease. The 3 patients in stage 4, 2 had pulmonary metastases, 1 had frozen pelvis and carcinomatosis peritonii. The procedures done were biopsy only in 1(7.69%), partial cystectomy in 1(7.69%), radical cystectomy with ureterosigmoidostomy in 5(38.46%), radical cystectomy with ileal conduit in 3(23.08%), and radical cystectomy with cutaneous continent catheterizable diversion in 1(7.69%). Two (15.38%) had cutaneous ureterostomy with tumour insitu (non resectable tumour). The histology revealed squamous cell carcinoma in all patients where 4(30.77%) were well differentiated, 5(38.46%) were moderately differentiated, and 4(30.77%) poorly differentiated. Associated findings were squamous metaplasia, dysplasia, and atypia. Deep muscle invasion was seen in 11(84.62%). The postoperative complications were acute renal failure in 3(23.08%), metabolic acidosis in 4(30.77%), and urosepsis in 2(15.38%). There were 3(23.08%) mortalities. One patient died of tumour burden, 1 as a result of deep vein thrombosis and pulmonary embolisms while the 3rd from acute renal failure with uremic encephalopathy. At one year of follow up only 6(46.15%) were alive. Four that died 3 were from local recurrence, and 1 from pulmonary metastases as terminal events.

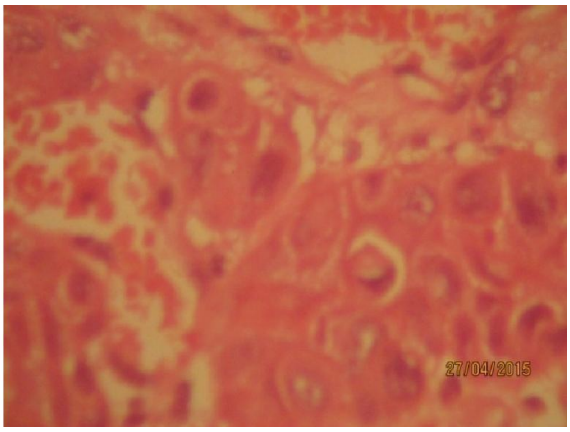

Figure 1. Squamous cell metaplasia with squamous cell carcinoma

Figure 2. Long standing (27years) giant vesical stone (1.51kg) that caused squamous cell carcinoma

DISCUSSION

The study found the mean age, male to female ratio, and duration of stone in stone - associated SCC were 69.08 years,

3.33: 1, and 2 – 27 years respectively. These when compared to bilharzial SCC with mean age of 46.8 years, and male to female ratio of 3.56, and a mean duration of exposure to schistosomiasis of 25 years (Ibrahim *et al*., 2015). Though similar male to female ratio, and both have long standing exposure to the agent of carcinogenesis, i.e. childhood schistosomiasis in all patients with bilharzial SCC (25years being the mean duration from first exposure to schistosomiasis to development of SCC), and 2 – 27 years as duration of stone burden (mean of 10 years). In this series late presentation was the norm associated with complication such as anemia, impaired renal function, and fistulae (vesicocutaneous fistula). Similar studies found vesicointestinal, visicovaginal fistulas, and carcinomatosis peritonii (Chun-Hsing *et al*., 2009; Rudresh and Aravind, 2014; Himisha *et al*., 2010). Bladder outlet obstruction such BPH, Stricture, and bladder neck stenosis are known to predispose to bladder stone formation this study found similar trends. Non bilharzial SCC is known to be aggressive and at presentation majority are muscles – invasive with high grade and high tendency to remain locoregional (Shokeir, 2004; Sigmund *et al*., 1984). The current study found similar trend. Surgery is the main stay for locoregional control in operable patients. Radical cystectomy and urinary diversion was done with acceptable complication. The mortality was 23.08% was rather high due to the aggressive tumour biology and late presentation. The 1 year survival rate of 46.15% buttresses the aggressiveness of the tumour. Anderson MD cancer centre, one of the best centres in the World has the 2 year, and 5 year overall survival rates of 47.6% and 10.6% respectively (Kassouf *et al*., 2007). Majority of death occurred due to locoregional recurrence and rarely distant metastases as terminal events. In conclusion stone associated squamous cell carcinoma of the bladder is very rare, it develop usually in patients harboring stone for a long time. It is a locally aggressive tumour with distant metastasis as terminal event. Radical cystectomy and urinary diversion offers the best locoregional control.

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