Original Article

Treatment Outcomes of Non- Adenocarcinoma Prostate in a Developing Country

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ABSTRACT

Objective: To assess the oncological outcomes of non-adenocarcinoma prostate cancers in a specialized cancer hospital in a developing country.

Study Design: Retrospective study.

Place and Duration of Study: This study was conducted at the Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore from January 2002 to July 2017.

Materials and Methods: All the patients with prostate cancer were studied retrospectively. The patients with ages more than 18 years and having histologically proven non-adenocarcinoma prostate cancers were selected for this study.

Results: A total of 7 patients of non-adeno prostate cancer were identified. The most common presenting complaint was acute urinary retention (57.1%) followed by hematuria (14.3%). As per TNM staging, most of the patients belonged to T4 (57.1%), N1 (57.1%) and M1 (57.1%). Radical chemotherapy and radiotherapy were given to 4 (71.4%) patients. Local recurrence was found in 1 (14.3%) and metastasis were reported in 4 of the patients andthe mortality rate was 71.4%.

Conclusion: Chemotherapy, radiotherapy and surgery were the main treatment modalities. Low recurrence and high mortality rates were observed.

Key Words: Prostate cancer, Ewing sarcoma, Chemotherapy, Radiotherapy, Adenocarcinoma

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INTRODUCTION

Prostate cancer is identified as one of the main reasons for morbidity and mortality among men. Its prevalence is increasing worldwide due to an increase in life expectancy, especially in developing countries[1]. Prostate cancer is considered as the fourth commonest cancer of the male gender. According to GLOBOCAN, in 2012 approximately 1.1 million cases of prostate cancer were reported globally and nearly 307,000 died due to this disease[2]. Ferly et al predicted that with increasing life expectancy worldwide, the incidence of prostate cancer will be increased to 1.7 million patients and mortality up to 499,000 in 2030 [3].

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Delay in prostate cancer diagnosis leads to disease metastasis resulting in higher mortality[4]. Adenocarcinoma accounts for 90% of the prostate tumors. Other less common histological diagnoses includes small cell cancer, urothelial cancer, Ewing sarcoma, Carcinosarcoma, and adenoidcystic cancer. The rarity of these histological diagnoses leads to the term non-adenocarcinoma of prostate cancers and constitute to about 10% of all cases.

Prostatic Small Cell Carcinoma (SCC) constitutes 0.5–2% of prostate cancers. However, autopsy studies of patients with castrate resistant cancers revealed SCC histology in up to 10–20% of patients. [5,6,7] Morphology of SCC of prostate was found to be similar to SCC involving other organs.[8,9,10] However, some differences have been reported including slightly more chromatin and minor nucleoli in about 30–40% of cases.[11] Prostatic urothelial cancer is a rare solid tumour of prostate that arise from transitional epithelium of intraprostatic peri urethral ducts.[8] Patient mostly present with obstructive voiding and hematuria. It should be differentiated from urothelial cancer of bladder with urethral or secondary prostate involvement.[9] Radical surgery (prostatectomy and cyst prostatectomy) provides optimum results in localized disease and external beam radiotherapy has promising results for short term local control. However, combination

chemotherapy provides good results in metastatic disease.

Ewing sarcoma(ES) is frequently mentioned as part of ES family tumors (ESFT).[10] Based on molecular studies Ewing's sarcoma (ES) and primitive neuroectodermal tumor (PNET) are considered as a single entity. These are the rare prostatic cancers.[11]

Carcinosarcoma is another rare type of prostate cancer, comprising of acombination of a epithelial component (carcinoma) and mesenchymal ormesenchymal-like (Sarcomatoid) component.[12] Due to its local growth in to urinary bladder it may present with lower urinary tract symptoms.[13] Carcinosarcoma has a poor prognosis and around 25% of patients have metastasis upon presentation.[14] Rodrigues et al. reported 3patients of Sarcomatoid carcinoma having a TMPRSS2-ERG gene, which is associated with adenocarcinoma, therefore suggesting that carcinosarcomas may arise from epithelial cells.[15]

Adenoidcystic cancer (ACC) constitutes 0.01% of prostate malignancies. ACC of prostate arises from basal cells and acini of the prostate.[16]

MATERIALS AND METHODS

This retrospective study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan. All the patients with prostate cancer presenting to the department of Uro-oncology, from January 2002 to July 2017 were included in the study. Patients above 18 years of age and those having histologically proven non-adenomatous prostate cancers were selected for this study. The clinical information of patients including demographics, medical comorbidities, presenting complaints, pre-operative and post-operative tumor characteristics and treatment in the form of surgery, radiotherapy or chemotherapy were extracted from the hospital information system. Records of included patients were followed for a minimum period of six months and a maximum of one year. Those patients who were unable to complete the proposed follow up were excluded from the study.

IBM SPSS Version 20.0 was used for Statistical analysis. Continuous variables were stated as mean ± standard deviation and categorical variables were computed as frequencies and percentages. Ethical approval was taken from the Institutional Review Board (IRB) of Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore before starting data collection.

RESULTS

A total of 7 patients of non-adenomatous prostate cancer were included in our study. Mean age of the patients was 64 ±10 years. Most common (57 %) comorbidity was hypertension, while 28.6% had no comorbid conditions. The main presenting complaint was acute urinary retention(57.1%).Currently 2 patients are alive and on follow up. The main cause of death was disease progression with development of metastasis. Patient characteristics are shown in (Table 1).

Table No.1: Baseline patient's characteristics

Variables	Categories	Total = N* (%)
Age (years)	Mean ± standard	64 ± 10.36
Comorbidity	None	2 (28.6%)
	Hypertension	4 (57.1%)
	Multiple	1 (14.3%)
Present complains	Hematuria	1 (14.3%)
	LUTS*	2 (28.6%)
	AUR**	4 (57.1%)
Present status	On follow up	2 (28.6%)
	Death	5 (71.4%)
Cause of death	Alive	2 (2e8.6%)
	Tumor progression	5 (71.4%)

Table No.2: Clinicopathological tumor characteristics

Variables	Categories	Total = N* (%)
cT	T3	3 (42.9%)
	T4	4 (57.1%)
cN	N0	2 (28.6%)
	N1	4 (57.1%)
	N2	1 (14.3%)
cM	M0	3 (42.9%)
	M1	4 (57.1%)
Histology	Small cell carcinoma	3 (42.9%)
	Urothelial carcinoma	1 (14.3%)
	Ewing sarcoma	1 (14.3%)
	Carcinosarcoma	1 (14.3%)
	Adenoid cystic carcinoma	1 (14.3%)

Table 3: Disease management and treatment

Variables	**Categories**	**Total=N* (%)**
Recurrence	No	6 (85.7%)
	Yes	1 (14.3%)
Metastasis	No	3 (42.9%)
	Yes	4 (57.1%)
Site of metastasis	None	3 (42.9%)
	Bone	1 (14.3%)
	Multiple	3 (42.9%)
Treatment of Metastasis	None	3 (42.9%)
	Chemotherapy	1 (14.3%)
	Radiotherapy	2 (28.6%)
	Chemotherapy+	1 (14.3%)
	Radiotherapy	
Radiotherapy	None	1 (14.3%)
	Radical	3 (42.9%)
	Palliative	3 (42.9%)
Chemotherapy	None	2 (28.6%)
	Radical	2 (28.6%)
	Palliative	3 (42.9%)

According to TNM staging, most of the patients belonged to T4 (57.1%), N1(57.1%) and M1 (57.1%) stage. Most common histological diagnosis was SCC and was reported in 3 patients followed by one each patient in Ewing sarcoma, Urothelial, Adenoid cystic and Carcinosarcoma as shown in Table2.Patients were managed with chemotherapy, given with curative intent in 2 patients and with palliative intent in 3 patients. Radical and palliative radiotherapy was given to 3 patients respectively.

DISCUSSION

Prostate cancer is a common tumor of male gender. It constitutes 29% of all Male tumors and accounts for 9% of all male cancer deaths.[17] The most common histology of prostate cancer is adenocarcinoma. In literature, other rare histologies area categorized as non-adenocarcinoma of prostate.[18]

Palmgren et al. reviewed 107 studies of small cell carcinoma of prostate from 1983-2005, it was observed thatmost typical age of diagnosis is 61 to 70 years, with range from 24 to 90 years, and prevalent complain was voiding urinary symptoms in 72 patients. Hematuria and hematochezia were found only in 9 patients.[19] Chemotherapy regimens specific for small cell carcinoma have been employed with a reported response rate of (60%) and median survival of 9 to 10 months. However, one large retrospective univariate analysis showed primary surgery to be the only independent prognostic factor for prolonged survival.[20] The prognosis of small cell carcinoma of the prostate is poor. The median survival is measured in months and long-term survivors are rare. Improved survival appears to be achieved with concurrent external beam radiation therapy and chemotherapy. In patients with resectable localized disease, radical prostatectomy with adjuvant chemotherapy and possibly radiation therapy may result in improved survival.[21] Metastatic disease is treated with primary chemotherapy. The role of radiation should be palliative. [22]

Furthermore, three patients of small cell carcinoma of prostate were included in this study. First patient of 66 years diagnosed as metastatic small cell cancer of prostate (T4N1M1b). He received palliative chemotherapy, and after follow up of 16 months developed brain metastasis for which he received palliative radiotherapy. He died due to progression of disease with a total follow up of 18 months from the day of presentation. Second patient of 70 years presented with metastatic small cell cancer of prostate (Lungs and liver).He underwent palliative chemotherapy and after 8 months of follow up he was diagnosed with brain metastasis for which he received radiotherapy. Patient succumbed due to tumour progression after a total follow up of 18 months. Third patient of 73 years of age was presented with small cell prostate cancer at stage T3N1M0. Chemo radiotherapy was given to the patient as a primary treatment and patient is on regular follow for last 39 months.

Primary urothelial carcinoma of prostate is an extremely rare tumour accounts for 1 to 5 % of all prostate cancers.[23] Patients presented with mean age of 54yrs which is about 10 years younger than adenocarcinoma of prostate.[24] Zhou et al. presented the case history of a 55-year-old man with primary prostate urothelial carcinoma with presenting complaints of Lower urinary tract symptoms. Treated with radical cyst prostatectomy and adjuvant chemotherapy. After 6 months of follow-up local recurrence or metastatic was not found.[25] It is biologically aggressive in nature with high tendency of recurrence and progression resulting in poor survival. Most patients die within 2 years of diagnosis.[23] In the current study an elderly patient of age 75 years with a history of LUTS was diagnosed as metastatic prostatic urothelial cancer of prostate (T4N1M1b). Patient survived for 36 months with palliative treatment.

Ewing's sarcoma is a rare entity arising from mesenchymal component of prostate stroma with incidence of less than (0.1%) of primary prostate cancers.[26] A study of 7 patients with Ewing sarcoma of prostate revealed a median age of 27 years on diagnosis. Main presenting complaints were dysuria and pelvic pain. Majority of patients were treated with chemotherapy.[5] Four patients underwent radical surgery(cyst prostatectomy or radical prostatectomy). External radiotherapy was administered in 3 cases. Local as well as distant metastasis is reported on presentation, with common involvement of urinary bladder and seminal vesicle. Chemotherapy, radiotherapy, and surgery are the main treatment modalities. Multiple treatment strategies lead to improvement in survival of localized disease with a 5-year relapse free survival of (55%) while patients with metastatic disease have poor relapse free survival of <25%.[27,28] In current study, one patient with Ewing's Sarcoma of prostate presented with hematuria at the age of 45 year with no co morbidity with clinical stage of T4N1Mo.He received radical radiotherapy and chemotherapy. After follow up of 40 months he developed recto vesical fistula due to local recurrence, for which he underwent urinary and fecal diversion. He died of tumour progression after 48 months from the date of presentation.

Prostatic Carcinosarcoma (PCS) that was first described in 1967 by Hamlin and Lund,[25] with mean age at diagnosis is around 66, it is very rare entity and has a poor outcome with the survival of around seven months.[14,29] The origin is still controversial with some believing that both carcinoma and sarcoma developed simultaneously with in the prostate while others suggest that adenocarcinoma transforms in to sarcoma.[30] Niwa et al. presented the case study of a 77old man with the complaint of hematuria; TNM staging revealed

T3aNoMo disease. Due to rapid growth of tumour, patient underwent pelvic exentration with bilateral ureterostomies and colostomy. Local recurrence was again detected and the patient died within12 months of first visit.[31] Treatment strategies for prostatic urothelial carcinoma are multimodal, including surgery, adjuvant chemotherapy, and radiotherapy.[32] The most common site of metastasis of PCSs was the lung (43%).[18] Despite the multiple therapies used to treat PCS, the reported 5-year survival is (41%) and 7-year survival of (14%).[33] Our study include 59 year old patient presented with metastatic Carcinosarcoma of prostate (metastasis to pelvic lymph nodes and bones).He received palliative radiotherapy for bone pains and died after 11 months of diagnosis due to tumour progression. Adenoid cystic/basal cell carcinoma of the prostate (ACBCC), was described in1974[37]. It has been reported in patients between 28-72 years of age.[34] Iczkowski studied 19 cases with a having mean age of 66 years, the main presenting symptom was of urinary retention (15 patients). Radical prostatectomy was performed in 5 patients, 2 underwent pelvic exenteration, while one patient was treated with radiotherapy. The remaining patients had no further treatment after trans urethral resection of prostate. Metastases advanced in 4 (21%) patients: liver in two, lung in two, and bowel in one, and corpus cavernous involvement in one patient. In fifteen patients during follow-up (3months–11.8 years), only 2 deaths were reported.[35] We have one patient of adenoid cystic carcinoma of prostate in our study. He was diagnosed at the age of 60 year following TURP for urinary retention. He received radical radiotherapy for stage T3NoMo. Currently remains well on follow up for the last 60 months.

CONCLUSION

Non-adenocarcinoma prostate cancers are rare and generally aggressive tumours with a poor prognosis. They present at a relatively younger age and require aggressive therapy in the form of chemotherapy, radiotherapy and surgery.

Author's Contribution:

Concept & Design of Study:	Siddique Adnan
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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