e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(5); 808-813

Original Research Article

Assessment of the Oncologic Outcomes of Individuals with Non-Urothelial Bladder Cancer: An Observational Study

Md. Shadab

Associate Professor, Department of General Surgery, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

Received: 15-01-2022 / Revised: 05-02-2022 / Accepted: 20-02-2022
Corresponding author: Dr. Md. Shadab
Conflict of interest: Nil

Abstract

Aim: The aim of the present study to evaluate the oncologic outcomes in patients with nonurothelial bladder cancer in Bihar region.

Methods: This was a prospective observational study conducted in the Department of General Surgery, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India for 1 year. All 15 adult patients between 18 and 80 years of age with histologically proven NUBCs were included in the study. Patients were followed for a median duration of one year.

Results: 15 patients of NUBCs were included in this study. Out of them, 9 patients had adenocarcinoma, 3 had SCC, 2 had small cell carcinoma, and 1 had inflammatory myofibroblastic cancer. The median presenting age of the patients was 52 years (range: 34-87 years), and hematuria was the commonest presenting concern, i.e., in 85% patients. Clinically, T3 was the commonest stage of presentation, and 1 patient had metastatic disease. The median follow-up duration was one year. During this period, 64% patients were diagnosed with cancer recurrence or progression, with majority, i.e., 22%, exhibiting disease at multiple sites. Furthermore, all these patients died because of the disease progression itself (10 patients), and the remaining (5 patients) died of generalized ill health and co-morbidities. On analysis, the mean DFS was 60.39 ± 7.15 months, and the overall median survival was 55.7 ± 9.69 months.

Conclusion: The NUBC is a rare but aggressive disease that presents at an advanced stage in many cases. Treatment protocols are not uniform; therefore, further collaborative research is needed to improve survival outcomes.

Keywords: non-urothelial bladder cancer, radical cystectomy, chemotherapy

Introduction

Bladder cancer accounts for over 70,000 new cancer diagnoses per year in the United States, with pure urothelial cell carcinoma (UCC) comprising approximately 90%–95% of these cases. [1-3] The remaining 5%–10% of bladder cancers consist of pure nonurothelial histologies or mixed urothelial and nonurothelial histologies, and these are generally associated with a worse prognosis compared to urothelial cell bladder carcinoma. [4] Given the paucity of information regarding nonurothelial histologies, there is a tendency among clinicians to homogenize all the clinically and biologically different pure

nonurothelial and mixed histologies into a single category: nonurothelial. Improved understanding of relative survival patterns among pure nonurothelial histologies is needed to improve patient counseling and aid clinical decision-making before cystectomy. Due to their rarity, institutional series of nonurothelial bladder carcinoma has generally evaluated only a single histology at a time and is unable to place each histology within the context of other histologic subtypes. [4] Studies involving larger administrative databases have been performed as well, but only select nonurothelial histologies have been assessed. [5-7] Treatment depends on the stage of the cancer. It may include some combination of surgery, radiation therapy, chemotherapy, or immunotherapy. Surgical options may include transurethral resection, partial or complete removal of the bladder, or urinary diversion. The typical five-year survival rates in the United States is 77%, Canada is 75%, and Europe is 68%. Bladder cancer, as of 2017, affected about 1.6 million people globally with 549,000 new cases and 200,000 deaths. Age of onset is most often between 65 and 84 years of age. Males are more often affected than females. In 2017, the highest rate of bladder cancer occurred in Southern and Western Europe followed by North America with rates of 15, 13, and 12 cases per 100,000 people. The highest rates of bladder cancer deaths were seen in Northern Africa and Western Asia followed by Southern Europe. [8] Hence the present study was planned Study of Different types of Oncological Outcomes in Patients with Nonurothelial Bladder Cancer.

Material and methods

This was a prospective observational study conducted in the Department of General Surgery, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India for 1 year, after taking the approval of the protocol review committee and institutional ethics committee. All 50 adult patients between18 and 80 years of age with histologically proven NUBCs were included in the study. Patients were followed for a median duration of one year.

Statistical analysis

Statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). The Kaplan-Meier method was used to estimate disease-free survival (DFS) and overall survival (OS). Formal approval was obtained from the Institutional Review Board before commencing data collection.

Results

15 patients of NUBCs were included in this study. Out of them, 9 patients had adenocarcinoma, 3 had SCC, 2 had small cell carcinoma, and 1 had inflammatory myofibroblastic cancer. The median presenting age of the patients was 52 years (range: 34-87 years), and hematuria was the commonest presenting concern, i.e., in 17 (85%) patients. Three patients presented with lower urinary tract symptoms. Clinically, T3 was the commonest stage of presentation, and 1 patient had metastatic disease (Table 1).

Table1: Clinical disease staging

Variables	Stages	Adenocarcinom, 9 (60.0%)	SCC, 3 (20.0%)	Small cell carcinoma, 2 (13.3%)	IMT, 1 (6.7%)
cT	T2	3 (33.3)	-	-	-
	T3	4 (44.4)	3(100)	-	1(100.0)
	T4	2 (22.2)	-	2 (100)	-
cN	N0	7 (77.8)	3(100)	1(50.0)	-
	N1	2 (22.2)	-	1(50.0)	1 (100.0)

cM	M0	8 (88.9)	3(100)	2 (100)	1(100.0)
	M1	1 (11.1)	-	-	-

SCC, squamous cell carcinoma; IMT, inflammatory myofibroblastic tumor; cT, clinical primary tumor; cN, clinical lymph nodes; cM, clinical metastasis; T2, tumor invades detrusor muscle; T3, tumor invades perivesical tissue; T4, tumor invades any of the following:prostatestroma,seminalvesicles, uterus,vagina,pelvicwall,abdominalwall;N 0,noregionallymphnodemetastasis;N1,met astasisin a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral); M0, no distant metastasis; M1, distantmetastases

Table 2: The pathological staging according to tumor histologies

Variables	Stages	Adenocarcinoma, 9 (60.0%)	SCC, 3 (20.0%)	Small cell carcinoma, 2 (13.3%)	IMT, 1 (6.7%)
pT	Tx	1 (11.1)	1 (33.3)	2 (100)	-
	T1	-	-	-	-
	T2	4 (44.4)	1 (33.3)	-	1 (100)
	T3	2 (22.2)	-	-	-
	T4	2 (22.2)	1 (33.3)	-	-
pN	Nx	1 (11.1)	1 (33.3)	2 (100)	-
	No	6 (66.7)	1 (33.3)	-	1 (100)
	N1	1 (11.1)	1 (33.3)	-	-
	N2	1 (11.1)	-		-

Table 3 demonstrates the treatment patients received. It shows that patients with adenocarcinoma, as they presented at an earlier stage, could be offered curative surgical treatment in most instances. For patients with SCC, one out of three was able to undergo radical cystectomy with adjuvant radiotherapy cover, and the rest two could only be offered palliative chemotherapy. Patients with small cell carcinoma presented with T4 at the outset and received chemotherapy only.

Table 3: Treatment modalities with respect to histology SCC, IMT, TURBT

Variables	Categories	Adenocarcinoma, 9 (60.0%)	SCC, 3 (20.0%)	Small cell carcinoma, 2 (13.3%)	IMT, 1 (6.7%)
Chemotherapy	None	7 (78.13)	1 (33.3)	-	1 (100)
	Adjuvant	1 (11.1)	-	-	-
	Definitive	-	-		-
	Palliative	1 (11.1)	2 (66.7)	2 (100.0)	-
Radiotherapy	None	8 (88.9)	2 (66.7)	2 (100.0)	1 (100)
	Adjuvant	-	1 (33.3)	-	-
	Radical	-	-	-	-
	Palliative	1 (11.1)	-	-	-
	TURBT	1 (11.1)	2 (66.7)	2 (100.0)	-
Surgical procedure	Partialcystectomy	5 (55.6)	-		1 (100)
	Radicalcystectomy	3 (33.3)	1 (33.3)	-	-

The median follow-up duration was one year. During this period, 64% patients were diagnosed with cancer recurrence or progression, with majority, i.e., 22%,

exhibiting disease at multiple sites. Furthermore, all these patients died because of the disease progression itself (10 patients), and the remaining (5 patients) died of generalized ill health and comorbidities. On analysis, the mean DFS was 60.39 ± 7.15 months, and the overall median survival was 55.7 ± 9.69 months.

Discussion

NUBC is an aggressive disease, and early diagnosis and commencement of treatment are the main factors determining clinical outcomes. [9] Worldwide, SCC is reported to be the most common NUBC, accounting for 3-5% of all BCs. [10] It is most common in Egypt and other African countries, where it is believed to be associated with chronic infection with Schistosoma haematobium. [11] Radical cystectomy is the treatment of choice for localized SCC because benefits from radiation are uncertain, and standard chemotherapy has little effect due to relative chemo resistance of disease. [12] Adenocarcinoma accounts for about 2% of BCs, and to establish the diagnosis of primary adenocarcinoma of the bladder, other possible primary tumors sites such as adenocarcinoma of the prostate or rectum should be ruled out. [13,14] Apart from endemic areas, adenocarcinoma is the most prevalent NUBC. Adenocarcinoma accounted for a major share of NUBC in our study. Standard treatment of all surgically resectable vesical adenocarcinomas consists of radical cystectomy and pelvic node dissection. [15]

Small cell carcinoma is much rarer, accounting for less than 1% cases. It occurs mostly during the seventh and eight decades of life. Small cell carcinoma patients with localized disease should be managed radical cystectomy or multimodal therapy including surgery along with chemo radiation. Palliative chemotherapy is reserved for unresectable disease. [16] It carries poor prognosis due to its rarity and aggressive nature. [17] Accordingly, the 6 patients in our study presented with locally advanced unresectable disease at the outset and received palliative chemotherapy, all of them died due to disease progression at 8 and 11 months follow-up.

4 patients were proven to have inflammatory myofibroblastic tumor. It is a rare NUBC of the bladder with an unknown possibility of malignant conversion. [18] Treatment strategy comprises transurethral resection, cystectomy, and radiotherapy. Our patient presented at the age of 36 years, was treated with partial cystectomy, and was on regular follow-up for the last 12 months. Additionally, in this study, three- and five-year OS of adenocarcinoma of the bladder was 70% and 30%, respectively. Three-year OS of SCC and adenocarcinoma was 44.8% and 58.7%, respectively. [19] In another study, five-year survival for SCC and adenocarcinoma was reported as 37% and 58%, respectively. [18] The difference in OS at five years of adenocarcinoma was because patients presented with advanced disease stage and relatively small number of sample size as compared to published data.

The median survival of small cell cancer has been reported to be between 10 and 20 months, with 5-20% 5-year OS. [20] The OS of patients diagnosed with SCC and small cell carcinoma cannot be commented due to the small number of participants in our data. Standardized and further collaborative research is needed to move this field forward. Our data also highlight that tools are needed to detect this type of tumors early so that appropriate treatment can be commenced promptly. [21]

Conclusion

NUBC is a rare disease entity that encompasses a variety of histological subtypes. Our data demonstrate that NUBC is an aggressive disease, which presents with advanced stage and has a poor prognosis. Treatment protocols are

not uniform. A combined effort is needed among institutions, both nationally and internationally, to further elucidate the understanding of biology of these tumors and evaluate treatment protocols, which will help in improving long- term survival outcomes

Reference

1. Dahm P, Gschwend JE. Malignant non-urothelial neoplasms of the urinary bladder: A review. Eur Urol 2003; 44:672-81.
2. Kantor AF, Hartge P, Hoover RN, Fraumeni JF Jr. Epidemiological characteristics of squamous cell carcinoma and adenocarcinoma of the bladder. Cancer Res 1988; 48:3853-5.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015; 65:5-29.
4. Black PC, Brown GA, Dinney CP. The impact of variant histology on the outcome of bladder cancer treated with curative intent. Urol Oncol 2009; 27:3-7.
5. Abdollah F, Sun M, Jeldres C, Schmitges J, Thuret R, Djahangirian O, et al. Survival after radical cystectomy of non-bilharzial squamous cell carcinoma vs urothelial carcinoma: A competing-risks analysis. BJU Int 2012; 109:564-9.
6. Wright JL, Porter MP, Li CI, Lange PH, Lin DW. Differences in survival among patients with urachal and nonurachal adenocarcinomas of the bladder. Cancer 2006; 107:721-8.
7. Patel SG, Stimson CJ, Zaid HB, Resnick MJ, Cookson MS, Barocas DA, et al. Locoregional small cell carcinoma of the bladder: Clinical characteristics and treatment patterns. J Urol 2014; 191:329-34.
8. "Bladder Cancer Factsheet" (PDF). Global Cancer Observatory. Retrieved, 2019
9. Patel S, Weiner A, Keegan K, Morgan T: Oncologic outcomes in patients with nonurothelial bladder cancer. Indian J Urol. 2018, 34:39-44.
10. Abol-Enein H, Kava BR, Carmack AJ: Nonurothelial cancer of the bladder. Urology. 2007, 69:93-104.
11. Kassouf W, Spiess PE, Siefker-Radtke A, et al.: Outcome and patterns of recurrence of nonbilharzial pure squamous cell carcinoma of the bladder: a contemporary review of The University of Texas MD Anderson Cancer Center experience. Cancer. 2007, 15:764-769.
12. Swanson DA, Liles A, Zagars GK: Preoperative irradiation and radical cystectomy for stages T2 and T3 squamous cell carcinoma of the bladder. J Urol. 1990, 143:37-40.
13. Wilson TG, Pritchett TR, Lieskovsky G, Warner NE, Skinner DG: Primary adenocarcinoma of bladder. Urology. 1991, 38:223-226.
14. Ravi K, Kumar T, Bakshi H, Desai J, Sen S, Yadav V: Non urothelial bladder cancers: a case series. Indian J Surg Oncol. 2013, 4:2-8.
15. Siefker-Radtke AO, Gee J, Shen YU, Wen S, Daliani D, Millikan RE, Pisters LL: Multimodality management of urachal carcinoma: the MD Anderson Cancer Center experience. J Urol. 2003, 169:1295-1298.
16. Lohrisch C, Murray N, Pickles T, Sullivan L: Small cell carcinoma of the bladder: long term outcome with integrated chemoradiation. Cancer. 1999,86:2346-2352.
17. Dong WX, Ping YX, Liang WC, Jian LZ, Lin ZJ: Small cell carcinoma of the urinary bladder diverticulum: a case report and review of the literature. J Cancer Res Ther. 2013, 9:151-153.
18. Aragon-Ching J, Henson D: Differences in survival among non-urothelial bladder cancers: analyses of SEER 1988-2008. J Clin Oncol. 2018, 36:425-425.
19. Anayo N. K., Guinhouya K. M., Apetse K., Agba L., Assogba K., Belo, M., & Balogou K. A. Posterior

Reversible Encephalopathy Syndrome. A case report. Journal of Medical Research and Health Sciences, 2022:5(3), 1804–1807.
20. Kamat A, Hahn N, Efstathiou J, et al.: Bladder cancer. Lancet. 2016, 388: 2796-2810.
21. Lynch SP, Shen Y, Kamat A, et al.: Neoadjuvant chemotherapy in small cell urothelial cancer improves pathologic downstaging and long-term outcomes: results from a retrospective study at the MD Anderson Cancer Center. Eur Urol. 2013, 64:307-313.