Original Article

A Retrospective Analysis of Carcinoma Penis Patients Treated at a Cancer Center in Nepal in a Period of Five Years

Umesh Nepal[1], Aditya Jalan[1], Binod Babu Gharti[1], Greta Pandey[2], Nirmal Lamichhane[1]

[1]*Urology Unit, Department of Surgical Oncology, B.P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal*

[2]*Department of Pathology, B.P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal*

ABSTRACT

Introduction: Carcinoma Penis is not an uncommon condition in a developing country like Nepal and comprises 1-10% of all the malignancies in males. In this study we analyzed the demographic and clinico-pathological profile of penile cancer patients who visited our cancer center during specified period.

Methods: This is a descriptive cross-sectional study, that altogether included 218 patients from January 2012 to December 2016 with penile cancer conducted at B P Koirala Memorial Cancer Hospital, Nepal. All the demographic and clinico-pathological data were collected and analyzed using SPSS 16.0 software. Tumor staging was standardized according to the American Joint Committee on Cancer system. Quantitative data were represented as mean and standard deviation whereas categorical variables were expressed as frequencies and percentages of an appropriate denominator.

Results: Among 218 patients, the mean ± SD age was 53.94 ± 13.69 years. Most were married (88.07%), smokers (67.88%), had poor personal hygiene (70.64%) and had not completed primary school (71.64%). The predominant profession was agriculture (81.65%). Most of the patients (56.88%) were diagnosed in clinical stage III b (T1-3, N2). Management was circumcision alone in 5.5%, Wide local excision in 6.88%, partial penectomy in 66.97 % patients, total penectomy with perineal urethrostomy in 11% of patients and 9.63% patients were sent for chemotherapy after initial biopsy for fixed and fungating inguinal nodes. Bilateral inguinal lymph node dissection was performed in 87.15% patients. Most of our patients were uncircumcised (90.82%) Squamous cell carcinoma was the commonest histopathology (98.6 %).

Conclusion: Penile cancer is more common among farmer with low socioeconomic status. The disease is already locally advanced and at the time of diagnosis. Surgery is the main modality of treatment.

Keywords: Penile cancer, Inguinal lymph node, Penectomy.

Introduction

Penile cancer (PC) is a rare cancer in the Western World like USA and Europe with incidence of <1.0/100 000 males[1]. However, in countries like India, Brazil and Angola, the incidence of PC varies from 2.3 to 8.3 cases/100000 men.[2] Nepal being a developing country, penile cancer is not an uncommon disease. However, we do not have many studies on penile cancer patients treated in Nepal. This study aims to retrospectively analyze the demographic and clinico-pathological profile of these patients who visited Urology clinics at B P Koirala Memorial Cancer Hospital (BPKMCH), Bharatpur, Nepal during the specified period.

Methods

This is a descriptive cross-sectional study conducted at B P Koirala Memorial Cancer hospital (BPKMCH), Bharatpur, Nepal from January 2012 to December 2016. The demographic and clinico-pathological profile of all patients who were diagnosed as penile cancer and visited Urology clinics at BPKMCH during the specified period were evaluated. Here, whole sampling method was applied. However, patients who were operated at other centers were

Correspondence
Dr Umesh Nepal, *Consultant, Urology Unit, Department of Surgical Oncology, B.P. Koirala Memorial Cancer Hospital, Bharatpur, Chitwan, Nepal, e-mail: uroumesh@gmail.com.*

excluded from the study. Ethical approval was taken from BPKMCH. Variables including patient characteristics such as year of diagnosis, age, marital status, education status, profession, personal hygiene and smoking status were analyzed. Pre-operative evaluation was conducted routinely and consisted of the following: chief complaint, medical history, physical examination routine blood test and presence of nodal enlargement. Disease characteristics included pathological stage and grade, clinical and pathological nodal stage, and receipt of inguinal and pelvic lymph node dissection. Tumor staging and nodal stage was standardized according to the American Joint Committee on Cancer (AJCC) system. Tumor histological grade was evaluated according to the criteria described by Velazquez et al.[3] Quantitative data were represented as mean and standard deviation whereas categorical variables were expressed as frequencies and percentages of an appropriate denominator. All continuous variables were converted into categorical variables. The data were analyzed with the SPSS software (SPSS Inc., Chicago, IL, USA), version 16.0.

Results

Altogether there were 245 patients who were suspected of having carcinoma penis from January 2012 to December 2016. However, only 218 patients who were histologically proven were included in this study (Table 1). The mean ± SD age was 53.94 ± 13.69 years with median age of 55 years. Most were married (88.07%, n=192), smokers (67.88%, n=148), had poor personal hygiene (70.64%, n=154) and had not completed primary school (71.64%, n=156). The predominant profession was agriculture (81.65%, n=178). Most common presentation was ulcer or growth (95.41%, n=207) followed by bleeding (55.04%, n=120) and associated secondary phimosis was seen in 48.62% (n= 106) of patients. At presentation, inguinal lymph nodes were palpable in 79.3%(n=173) of patients, out of which in 9.63% (n=21) of patients the lymph nodes were fixed and ulcerating. Fifty-seven (56.88%, n= 124) percent were diagnosed in clinical stage III b (T1-3, N2).

Table 1: The demographic profile of the penile cancer patients

Variables	Categories	n (%)
Age	Age ± SD	53.94 ± 13.69 years
	Median	55 years
Marital Status	Married	192 (88.07)
	Unmarried (separated, widow, Divorced)	26 (11.03)
Personal hygiene	Poor	154 (70.64)
	Good	49 (22.47)
	Unknown	15 (6.88)
Smokers	Smokers	148 (67.88)
	Non-smokers	47 (21.55)
	Unknown	23 (10.55)
Education level	Illiterate	156 (71.55)
	Primary level	39 (17.88)
	Secondary and above	17 (7.79)
	Unknown	6 (2.75)
Profession	Farmer	178 (81.65)
	Businessman	24 (11.00)
	Teacher	9 (4.13)
	Unknown	7 (3.21)

Management was circumcision alone in 5.5%, Wide local excision in 6.88%, partial penectomy in 66.97 % patients and total penectomy with perineal urethrostomy in 11% of patients. Those patients who had fixed and ulcerative lymph nodes (9.63%, n=21) were directly sent for Neo-adjuvant chemotherapy after initial biopsy. Bilateral Inguinal Lymph node dissection was performed in 87.15% (n= 190) patients. This was performed in the same sitting as penile surgery in 78.89% and as a delayed procedure in 8.25% cases. Squamous carcinoma was the commonest histopathology (98.6 %) followed by basal cell carcinoma (0.9%, n=2) and malignant melanoma (0.45%, n=1). Well-differentiated carcinoma was the most common histological grading (58.25%, n=127). Most common pathological tumor and positive nodal staging was T3 (35.77%, n=78/218) and N+ was 29.4% (n=56) respectively (Table 2).

Table 2: The clinico-pathological characteristics of penile cancer patients.

Characteristics	Categories	n (%)
Chief complaints	Ulcer/growth	207 (95.41)
	Bleeding	120 (55.04)
	Phimosis	106 (48.62)
Inguinal lymph nodes	Palpable	173 (79.3)
	Not Palpable	45 (20.7)
	Fixed/fungating	21 (9.63)
Clinical stage	Stage I/II	45 (20.64)
	Stage IIIa	21 (9.63)
	Stage IIIb	124 (56.88)
	Stage IV	28 (12.84)
Surgical procedure	Circumcision	12 (5.5)
	Wide local excision	15 (6.88)
	Partial penectomy	146 (66.97)
	Total penectomy	24 (11.0)
	Chemotherapy alone	21 (9.63)
	Bilateral Lymph node dissection	190 (87.15)
Histopathology	SCC	215 (98.5)
	Basal cell ca	2 (0.9)
	Melanoma	1) 0.45)
Grading	Well Differentiated	127) 58.25)
	Moderately differentiated	53) 24.3)
	Poorly/Anaplastic	13) 5.9)
	Unknown	25) 11.46)

Discussion

Penile cancer is the disease of older men causing significant physical and psychological stress to the patients. Coelho et al (mean age 59 years) and McIntyre et al. (57 years) found the disease to be more common among men above 50 years of age.[4, 5] However, it is not uncommon among younger men below 50 years (37.2%). Coelho et al. in the study conducted among 392 patients, found 19.7% of patients aged ≤40 years at diagnosis. In contrast, Chalya et al.[6] found 56.4% of patients are below 50 years of age.

In south Asian countries most of the men are already married by 50 years of age. In the present analysis, most of the patients (88%) were married. However, Chalya et al. mentioned the disease to be more common among divorced or unmarried men who either have multiple sexual partners or history of sexually transmitted diseases or do not use barrier contraceptives.[6-8]

Nicotine in tobacco in any form cigarettes, chewing tobacco or snuff is a known carcinogen. In context of penile cancer, a direct, dose-related association between penile cancer and smoking has been found. The association between smoking and penile cancer can be explained by the fact that nicotine usually become concentrated in smegma, making it carcinogenic, especially in men with phimosis. In our series, majority (67.88%) of patients were smokers that correlates with other studies.[6, 9, 10]

Many researchers have quoted that poor personal hygiene, low education levels and agricultural background are associated with penile cancer. Phimosis and inadequate hygiene of the preputial sac with consequent accumulation of smegma leads to a chronic local inflammatory process, contributing to the genesis of penile cancer.[9] Maintenance of poor personal hygiene and not cleaning genital after sexual contact increases the risk for penile cancer.[8] McIntyre et al. In their 10 year experience among 236 patients of ca penis found secondary phimosis in 62.3% of patients.[6] Favorito et al and Junior et al. found in 60% and 69% of patient respectively.[8, 11] In this study 70.64% of patients lacked personal hygiene and 48.62% of patients has secondary phimosis.

Dagher et al. mentioned circumcision is the simple means of prophylaxis to spare the organ at predictable risk of malignancy.[12] It appears to be vital when facilities for daily hygiene are lacking, however, it may not be as important in countries where good hygiene is practiced.[12, 13]

Agriculture is the main profession in Nepal and use of

agrochemicals for farming is prevalent like elsewhere. Junior et al. found the 69% of men were farmers in their study which is similar to the present study.[8]

Low education level, less awareness and knowledge about the disease has higher incidence of having advance T stage penile cancer.[14] Torband et al, in their population based study among 1676 patient found that people with low education seek medical advice when disease is at its advance stage.[7] In the present study, 71.55% didn't complete their primary education and presented when the disease was already in Stage III. Chalya et al. mentions study done in developing countries where most patients were from rural area and poor social background presented in advance stage III-IV[6]. This may be also due to social taboos and delay in seeking or receiving medical services. However, studies done in developed countries found that disease presented in earlier stages.[4, 15]

The commonest histological type identified in most of the studies is squamous cell carcinoma.[6, 14] Similarly in the present study 98% of the patients had SCC. Other histological types found in our study were basal cell carcinoma and melanoma are the rare findings.[14, 16] Moreover, well to moderately differentiated pathology is more common compared to poorly differentiated/ anaplastic disease.[17, 18]

The treatment modalities for penile cancer include surgery, chemotherapy and radiotherapy. Out of which surgery is considered to be the main stay of treatment.[19] In present study partial penectomy was done in most of cases followed by total penectomy with perineal urethrostomy. Most of the patients presented in advance stage with clinically palpable inguinal nodes (79%) and bilateral lymph node dissections 87% of cases. The study conducted by Altaf et al.20 among 230 patients found clinically palpable lymph node in 48%, they performed BLND in 62% of patients. The prognosis of the patient depends on the timing of lymph node dissection. Studies demonstrate improved survival outcomes without increased morbidity with inguinal lymph node dissection.[21, 22]. In our study we opted groin dissection in most of our patient. The reason behind this is (1) Patient seeks medical advice at late stage (2) Disease need inguinal lymph node assesment every 2-3 months and (3) Even in clinically non-palpable lymph nodes, the risk of inguinal lymph node metastasis is 25% [23] and (4) In our part of world where most of patients are from rural areas, patients compliance for follow-up is poor.

Chemotherapy has been utilized in the treatment of penile cancer either alone or in combination of surgery or radiotherapy. In the present study, 9.63% of the patients were sent for palliative chemotherapy as a primary treatment for nothing surgical can be offered. This observation correlates with the study conducted by Kirrand et al.[24]

This study reflects the patients who were treated in the single institute which may not reflect the whole population. Further prospective studies with regard to survival analysis, recurrence and challenges in the management needs to be addressed.

Conclusion

Penile cancer is more common among farmers with low socioeconomic status. The disease is already locally advanced and at the time of diagnosis. However, surgery is the main modality of treatment.

References

1. Robinson R, Marconi L, MacPepple E, Hakenberg OW, Watkin N, Yuan Y, et al. Risks and Benefits of Adjuvant Radiotherapy After Inguinal Lymphadenectomy in Node-positive Penile Cancer: A Systematic Review by the European Association of Urology Penile Cancer Guidelines Panel. Eur Urol. 2018.
2. Zequi Sde C. Penile cancer: the importance of prevention. Int Braz J Urol. 2013;39(5):611-3.
3. Velazquez EF, Ayala G, Liu H, Chaux A, Zanotti M, Torres J, et al. Histologic grade and perineural invasion are more important than tumor thickness as predictor of nodal metastasis in penile squamous cell carcinoma invading 5 to 10 mm. Am J Surg Pathol. 2008;32(7):974-9.
4. Coelho RWP, Pinho JD, Moreno JS, Garbis D, do Nascimento AMT, Larges JS, et al. Penile cancer in Maranhao, Northeast Brazil: the highest incidence globally? BMC Urol. 2018;18(1):50.
5. McIntyre M, Weiss A, Wahlquist A, Keane T, Clarke H, Savage S. Penile cancer: an analysis of socioeconomic factors at a southeastern tertiary referral center. Can J Urol. 2011;18(1):5524-8.
6. Chalya PL, Rambau PF, Masalu N, Simbila S. Ten-year surgical experiences with penile cancer at a tertiary care hospital in northwestern Tanzania: a retrospective study of 236 patients. World J Surg Oncol. 2015;13:71.
7. Torbrand C, Wigertz A, Drevin L, Folkvaljon Y, Lambe M, Hakansson U, et al. Socioeconomic factors and penile cancer risk and mortality; a population-based study. BJU Int. 2017;119(2):254-60.

8. Junior PFM, Silva EHV, Moura KL, de Aquino YF, Weller M. Increased Risk of Penile Cancer among Men Working in Agriculture. Asian Pac J Cancer Prev. 2018;19(1):237-41.

9. Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, et al. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. Int J Cancer. 2005;116(4):606-16.

10. Hellberg D, Valentin J, Eklund T, Nilsson S. Penile cancer: is there an epidemiological role for smoking and sexual behaviour? Br Med J (Clin Res Ed). 1987;295(6609):1306-8.

11. Favorito LA, Nardi AC, Ronalsa M, Zequi SC, Sampaio FJ, Glina S. Epidemiologic study on penile cancer in Brazil. Int Braz J Urol. 2008;34(5):587-91; discussion 91-3.

12. Dagher R, Selzer ML, Lapides J. Carcinoma of the penis and the anti-circumcision crusade. J Urol. 1973;110(1):79-80.

13. Madsen BS, van den Brule AJ, Jensen HL, Wohlfahrt J, Frisch M. Risk factors for squamous cell carcinoma of the penis--population-based case-control study in Denmark. Cancer Epidemiol Biomarkers Prev. 2008;17(10):2683-91.

14. Attalla K, Paulucci DJ, Blum K, Anastos H, Moses KA, Badani KK, et al. Demographic and socioeconomic predictors of treatment delays, pathologic stage, and survival among patients with penile cancer: A report from the National Cancer Database. Urol Oncol. 2018;36(1):14 e7- e24.

15. Jayaratna IS, Mitra AP, Schwartz RL, Dorff TB, Schuckman AK. Clinicopathologic characteristics and outcomes of penile cancer treated at tertiary care centers in the Western United States. Clin Genitourin Cancer. 2014;12(2):138-42.

16. Arya M, Li R, Pegler K, Sangar V, Kelly JD, Minhas S, et al. Long-term trends in incidence, survival and mortality of primary penile cancer in England. Cancer Causes Control. 2013;24(12):2169-76.

17. Thuret R, Sun M, Abdollah F, Budaus L, Lughezzani G, Liberman D, et al. Tumor grade improves the prognostic ability of American Joint Committee on Cancer stage in patients with penile carcinoma. J Urol. 2011;185(2):501-7.

18. Nam JK, Lee DH, Park SW, Kam SC, Lee KS, Kim TH, et al. Clinicopathologic Characteristics and Treatment Outcomes of Penile Cancer. World J Mens Health. 2017;35(1):28-33.

19. Burt LM, Shrieve DC, Tward JD. Stage presentation, care patterns, and treatment outcomes for squamous cell carcinoma of the penis. Int J Radiat Oncol Biol Phys. 2014;88(1):94-100.

20. Althaf S, Narayanakar RP, Gangaiah DM, Dev K, Kurpad VP, Gurawalia J. Inguinal Lymph Nodes in Carcinoma Penis-Observation or Surgery? J Clin Diagn Res. 2016;10(1):XC01-XC4.

21. Mistry T, Jones RW, Dannatt E, Prasad KK, Stockdale AD. A 10-year retrospective audit of penile cancer management in the UK. BJU Int. 2007;100(6):1277-81.

22. Ornellas AA, Kinchin EW, Nobrega BL, Wisnescky A, Koifman N, Quirino R. Surgical treatment of invasive squamous cell carcinoma of the penis: Brazilian National Cancer Institute long-term experience. J Surg Oncol. 2008;97(6):487-95.

23. Chang SS. Re: EAU Guidelines on Penile Cancer: 2014 Update. J Urol. 2016;195(5):1475.

24. Kirrander P, Sherif A, Friedrich B, Lambe M, Hakansson U, Steering Committee of the Swedish National Penile Cancer R. Swedish National Penile Cancer Register: incidence, tumour characteristics, management and survival. BJU Int. 2016;117(2):287-92.