

Retrospective Audit of Surgically Treated Patients of Carcinoma Penis at a Tertiary Cancer Centre of Eastern India

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Abstract

Introduction: Carcinoma of the penis is a disease of developing world with incidence rate of around 10% of all malignancies. There has been lack of data pertaining to carcinoma penis from this part of country. We therefore present our experience of management of penile cancer.

Methods: A retrospective audit of all cases of penile cancer surgically treated between May 2017 and April 2021 in Department of Surgical Oncology, State Cancer Institute, Patna, Bihar was done. Comprehensive clinico-epidemiological data was recorded.

Results: 56 patients were found to be eligible for our study. The mean age of presentation was 52.43 years. Majority of the patients were of rural background and low economic class. 66% of tumors primarily involved glans and 91% presented with ulcer. 59 % of patients had partial penectomy and 35.7% had total penectomy. 62.2 % patients underwent bilateral inguinal lymph node dissection, and 37.8 % patients underwent bilateral ilioinguinal lymph node dissection. Most common complication was reported to be lymphorrhoea. Majority of tumor (44.6 %) were of grade I differentiation. 34 out of 56 (60.7%) patients had lymph node involvement. Majority of tumors with T2 and beyond stage had lymph nodal involvement. Similarly, most high-grade tumors were associated with lymph nodal metastasis.

Conclusion: Incidence of carcinoma penis rises with age. Surgery remains the mainstay of treatment. The type of surgery depends on various factors like size, grade, lymph nodal status etc. Patients may require adjuvant radiation therapy. In locally advanced cases neoadjuvant chemotherapy may help in down staging of tumor. Nodal metastasis is significantly associated with higher T stage and high-grade lesions (grade II & III). In view of poor outcomes of patients with regional or distant disease and the lack of a reliable tool in predicting risk of regional metastases, we strongly recommend aggressive surgical management of the inguinal lymph nodes.

Keywords: Carcinoma Penis, Developing countries, Partial Penectomy, Ilioinguinal lymph node dissection

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Introduction

Carcinoma of the penis is a disease of developing world mostly seen in countries of Asia, South America and Africa. The incidence in these countries is in the range of 10% of all malignancies. It is very uncommon in Western countries accounting for just 0.4% of all male cancers and 3.0% of all genitourinary cancers. [1]

In Indian population, the age standardized incidence rate (ASR) is 0.8-3.0 per 100,000 men [2]. The ASR is 8.3 per 100,000 men in Brazil. In Puerto Rico, Uganda and China penile carcinoma represents 10–22% of all male malignancies [2-3]. Comparatively in the US and Europe, the ASR is between 0.1 and 1.0 [4-6]

Although exact etiology remains unknown, various risk factors like balanitis, smegma, phimosis, poor genital hygiene, smoking, history of sexually transmitted infections (STIs), and human papilloma virus (HPV) are implicated. Ritual or therapeutic circumcision has been found to be an important protective factor [7-12]. The incidence of penile cancer is showing declining trend of late. This can be attributed to increased awareness regarding personal hygiene and improvement in socio economic condition in developing world [10]. There has been lack of data pertaining to carcinoma penis from this part of country. We therefore present our experience of penile cancer.

Materials and Methods

After the institutional review board approval, we retrospectively evaluated our experience in treating penile cancer between May 2017 and April 2021 in Department of Surgical Oncology, State Cancer Institute, Patna, Bihar. All biopsy proven cases of penile carcinoma with or

without regional lymphadenopathy were included in the study. Patients with recurrence, metastatic disease or medically inoperable patients were excluded from the study. A total of 56 biopsy proven cases of carcinoma penis were found eligible for our study.

The case records of patients were reviewed to extract the information on age, risk factors, presenting symptom, site of primary tumor, lymph nodal involvement, stage of the disease, type of surgery done and its complications, and final histopathological characteristics. All patients underwent surgery. For penile lesion, a partial penectomy was done when a stump of at least 2 cm was available after tumor free resection margin. Otherwise, a total penectomy with perineal urethrostomy was done. Inguinal disease was addressed by bilateral standard inguinal lymphadenectomy for cN0 disease. For node positive disease, complete bilateral ilioinguinal lymphadenectomy was done. For those with bulky and fixed nodes, neoadjuvant chemotherapy was given. Responders to chemotherapy underwent complete ilioinguinal lymphadenectomy. Non responders were excluded from study and received palliative therapy. Adjuvant radiation was given as per NCCN guidelines. Entire surgically resected specimen was sent for histopathological examination. Pathological findings with respect to histological type, size, and depth of the tumour, grade of differentiation, lymph vascular invasion and perineural invasion were recorded. Tumor staging done as per AJCC 8th edition. Data was presented as frequency (percentage, %) for categorical variables and mean \pm SD for numerical variables.

Results

Table.1 Clinicopathological profile of patients

Age Distribution (in years)	Number of patients (n=56)	Percentage (%)
30-39	10	17.8
40-49	11	19.6
50-59	16	28.6
60-69	17	30.5
70-79	2	3.5
Socioeconomic status		
Low-income group	39	69.6
Middle income group	15	26.8
High income group	2	3.6
Clinical Features		
Pain	8	14.3
Ulcer	51	91.0
Bleeding	4	7.1
Pus Discharge	8	14.3
Phimosis	2	3.6
Swelling in inguinal region	41	73.2
Site of penile lesion		
Prepuce	3	5.3
Glans	33	59.0
Shaft	20	35.7
T staging		
T1	13	23.2
T2	33	59.0
T3	9	16.0
T4	1	1.8
Nodal staging		
NX	3	5.4
N0	19	33.9
N1	9	16.1
N2	17	30.3
N3	8	14.3
Surgery Done for Penile Lesion		
Partial penectomy	33	59.0
Total penectomy	20	35.7
Circumcision	3	5.3
Surgery Done for Nodal Disease (n=53)		
Inguinal Lymph node dissection	33	62.2
Ilioinguinal Lymph node dissection	20	37.8
Complications related to groin dissection (n=53)		
Flap necrosis	3	5.7
Wound dehiscence	4	7.1
Lymphorrhoea	12	21.4
Lower limb edema	8	14.2
No complications	26	35.7

Table 2: Correlation of T Stage and nodal involvement

T stage	No. of patients	Lymph node involvement	Percentage
T1	13	0	0.0
T2	33	25	75.8
T3	9	8	88.9
T4	1	1	100.0

Higher T- stage was strongly associated with pathologically involved lymph nodes.

Table 3: Correlation of tumor grade and nodal involvement

Grade	No. of patients	Lymph node involvement	Percentage
Grade I	25	6	24.0
Grade II	21	18	85.7
Grade III	10	10	100.0

Grade II/ III disease was significantly associated with metastasis to nodal stations.

Discussion

Age Distribution

In our study, most of the patients belonged to 50 -69 years age group. Majority of patients were in the age group 60-69 years (30.5%). Mean age was 52.43 years. The mean age at diagnosis was 60.4 ± 16.51 years in study by Vieira et al from Brazil [12]. In retrospective analysis of SEER data from United States, Hernandez et al found similar age incidence [13]. Overall, the median age at diagnosis of penile SCC was 68 years.

Socioeconomic status

The sociodemographic profile of patients in this study were very similar to those of other studies from developing countries like Brazil and worldwide [13-18]. Majority of the patients were of rural background and belonged to low economic class. Most of them of them had either no schooling or studied only through primary school. Their overall concern for penile hygiene was very poor owing to illiteracy, ignorance and lack of basic amenities. Various studies like Maden et al, have found in their study that neonatal circumcision, which is practiced by religious and ethnic groups, virtually

eliminates the risk of penile carcinoma [10]. However, this benefit of circumcision has not been observed when circumcision is delayed till puberty or adulthood.

Tumor topography

Penile tumors most commonly occur on the glans (48%) and prepuce (21%) but can involve any part of the penis [19]. Even in our study 66% patients had lesion on the glans, 9.6% on prepuce and 23% lesions involved the shaft. This distribution of these lesions may be attributed to the fact that, there is chronic irritation of this area owing to constant exposure to irritants like smegma, HPV infection etc.

Clinical features

91% patients presented with ulcer. Nearly 14% of the patients had pus discharge and associated pain from the lesion. More than 70% patients presented with palpable inguinal lymph nodes.

Only 3.6 % patients had phimosis at the time of presentation. This was in sharp contrast to previous studies from developing world where Soria et al and had reported phimosis in 24.5% of patients of penile carcinoma [20]. Comparable rates of various presenting feature have been reported by various other with the highest being 69% by Hanash et al [21].

Operative procedure

The surgery for penile primary lesion in carcinoma of penis is either partial or total penectomy. In the present study 59 % of patients had partial penectomy and 35.7% of patients had total penectomy. 62.2 % patients underwent bilateral inguinal lymph node dissection, and 37.8 % patients underwent bilateral ilioinguinal lymph node dissection. Prophylactic inguinal lymph node was done when the enlarged lymph nodes were found to be negative for tumor involvement on cytology and imaging, keeping in mind doubt associated with patient compliance and regular follow up. Bhagat et al., also opined that as patients' compliance for regular follow up cannot be guaranteed and in cases of tumor invasion beyond 3 mm, prophylactic groin dissection should be strongly considered. [22].

Surgical Complications

Around 50% patients suffered from one or more complications. Most common complication in our study was reported to be lymphorrhoea found in 21.4% followed by lower limb lymphedema in 14.2%, wound dehiscence in 7.1 %, and flap necrosis in 5.7% each. No death was reported in our study. Ravi et al¹² and Ornella[13] et al in their studies also reported similar complication rate of lymphedema (23-50%), seroma formation (6-17%) and death (1.3%) [23,24].

Histology, grade and nodal involvement

All 56 patients had squamous cell carcinoma histologically. Grossman et al have shown that more than 95% of penile carcinomas are of squamous cell histology [26]. No squamous cell carcinomas consist of melanomas, lymphomas, and sarcomas.

Majority of tumors 25/56 (44.6 %) were of grade I differentiation. 21(37.5 %) patients had grade II lesion while only 10 (17.9%) patients had grade III lesion. Lymph vascular invasion was seen in 21 patients. Ficarra et al^{had} shown in their

study a strong correlation between presence of vascular invasion and inguinal lymph node metastasis in squamous penile cancer [27].

Nodal metastasis is very common in carcinoma of penis. Infact, lymph node metastasis has been conclusively proven to be most important prognostic factor in patients with carcinoma penis [28]. 34 out of 56 (60.7%) patients had lymph node involvement in final histopathology report. Hardner et al and Grabstald et al in their study had reported incidence rate of nodal metastasis between 35-60% [28-29]. Although majority of patients in our study had grade I and II disease, there was comparatively high rate of nodal involvement.

Majority (33) of patients had pT2 in which 75.8% of those with T2 disease had pathological lymph nodal involvement had inguinal metastasis while almost all patients with pT3 (8/9) pathological metastatic nodal metastasis. Anantkrishnan et al and Pizzacaro et al had found reported that strong correlation of pathological T stage with the nodal metastasis. The high percentage of lymph nodal involvement in our study is similar to other studies reported from developing countries [30-31].

Grade of tumor has also been reported to be important predictor of lymph nodal metastasis. Caso et al had reported incidence rates ranging between spread to inguinal nodes 0-29 % for grade I, 26-65% for grade II& 80-100% for grade III tumors respectively. In our study, incidence of nodal metastasis in grade I tumour was 24%, 85.7 % in grade II and 100 % in grade III tumours. This is similar to various studied done in past [32,33]

Conclusion

Incidence of carcinoma penis rises with age and peaks in the 6th decade of life. Surgery remains the mainstay of treatment. The type of surgery should be decided depending on the size of the lesion, grade

of the tumor, and the age of the patient. Patients may require adjuvant radiation therapy. In locally advanced cases neoadjuvant chemotherapy may help in downstaging of tumor. Nodal metastasis is significantly associated with higher T stage and high-grade lesions (grade II & III). Metastatic nodes should be treated with ilioinguinal groin dissection. In view of poor outcomes of patients with regional or distant disease and the lack of a reliable tool in predicting risk of regional metastases, we strongly recommend aggressive surgical management of the inguinal lymph nodes. Prophylactic node dissection with its 15-20% yield of positive nodes and its associated morbidity is quite acceptable in a developing country where follow up and patient compliance remains an issue to be addressed. The present study provides valuable insight to clinicians and pathologists about clinicopathological features of carcinoma penis from this part of eastern India which can further be used to chalk out future management strategies for these tumors.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Coelho, R. W. P. et al. Penile cancer in Maranhão, Northeast Brazil: the highest incidence globally? *BMC Urology*. 2018;18, 50.
2. Yeole BB, Jussawalla DJ. Descriptive epidemiology of the cancers of male genital organs in greater Bombay. *Indian J Cancer* 1997; 34:30–39.
3. Christodoulidou, M., Sahdev, V., Houssein, S. & Muneer, A. Epidemiology of penile cancer. *Curr Probl Cancer*.2015: 39, 126–136.
4. Narayana AS, Olney LE, Loening SA, Weimar GW, Culp DA: Carcinoma of the penis: Analysis of 219 cases. *Cancer* 1982; 49:2185–2191.
5. Altwein J, Jacobi GH: Peniskarzinom: in Hohenfellner R, Zingg EJ (eds): *Urologie in Klinik und Praxis*. Stuttgart, Thieme, 1982:1:628–636.
6. Kamat MR, Kulkarni JN, Tongaonkar HB: Carcinoma of the penis: the Indian experience. *J Surg Oncol* 1993; 52:50–55.
7. Parkin, D. M. et al. *Cancer Incidence in Five Continents, Vol. VI (IARC Press, Lyon, 1992)*.
8. Hellberg D, Valentin J, Eklund T, Nilsson S: Penile cancer: Is there an epidemiological role for smoking and sexual behaviour? *Br Med J* 1987; 295:1306–1308.
9. Barrasso, R., De Brux, J., Croissant, O. & Orth, G. High prevalence of papillomavirus-associated penile intraepithelial neoplasia in sexual partners of women with cervical intraepithelial neoplasia. *N Engl J Med*. 1987:317, 916–23.
10. Maden, C. et al. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. *J Natl Cancer Inst*. 1993:85, 19–24.
11. Albero, G. et al. Male circumcision and prevalence of genital human papillomavirus infection in men? A multinational study. *BMC Infect Dis*. 2013:13, 1–10.
12. Morris, B. J. et al. The strong protective effect of circumcision against cancer of the penis. *Adv Urol*. 2011, 812368.
13. Vieira, C.B., Feitoza, L., Pinho, J. et al. Profile of patients with penile cancer in the region with the highest worldwide incidence. *Sci Rep* 2020:10, 2965.
14. Hernandez BY, Barnholtz-Sloan J, German RR, et al. Burden of invasive squamous cell carcinoma of the penis

- in the United States, 1998–2003. *Cancer* 2008; 113:2883–2891
15. Koifman, L., Vides, A. J., Koifman, N., Carvalho, J. P. & Ornellas, A. A. Epidemiological aspects of penile cancer in Rio de Janeiro: evaluation of 230 cases. *Int Braz J Urol.* 2011;37, 231–240.
 16. Favorito, L. A. et al. Epidemiologic study on penile cancer in Brazil. *Int Braz J Urol.* 2008;34, 587–91.
 17. Brumini, R., Torloni, H., Henson, D. E., Gotieb, S. L. D. & Souza, J. M. P. Câncer no Brasil - Dados histopatológicos: 1976–80 (Ministério da Saúde, Rio de Janeiro, 1982).
 18. do Couto, T. C., Barbosa, A. R. M., do Couto, M. C. & Dubourcq, B. F. Epidemiological study of penile cancer in Pernambuco: experience of two reference centers. *Int. braz j urol.*2014; 40, 738–744.
 19. Sufrin G, Huben R, Gillen water, JY Editor. Benign and malignant lesions of the penis in adult and paediatric urology:2nd edition: Chicago yearbook 1991: p1997- 2042
 20. J C Soria et al. Squamous cell carcinoma of the penis: Multivariate analysis of prognostic factors and natural history in a mono centric study with a conservative policy. *Annals of Oncology* 8: 1089-1098, 1997.
 21. Hanash KA, Furlow WL, Utz DC et al. Carcinoma of the penis: A clinico pathologic study. *J Urol* 1970; 104: 291-7.
 22. Bhagat SK, Walter N, Gopalakrishnan G. Predicting inguinal metastases in cancer penis. *Indian J Urol* 2006; 22: 351-4
 23. Ravi R, Prophylactic lymphadenectomy vs observation vs inguinal biopsy in node negative patients with invasive carcinoma of the penis. *Jpn J Clin Oncol* 1993;23(1):53-58
 24. Ornellas AA, Seixas AL, Marata A et al: Surgical treatment of the invasive carcinoma of the penis; retrospective analysis of 350 cases. *J Urol* 1994;151(5):1244-49
 25. Grossman HB. Premalignant and early carcinomas of the penis and scrotum. *Urol Clin North Am* 1992; 19:221–226.
 26. Ficarra V, Zattoni F, Artibani W, et al and the G.U.O.N.E. Penile Cancer Project Members. Nomogram predictive of pathological inguinal lymph node involvement in patients with squamous cell carcinoma of thepenis. *J Urol* 2006; 175:1700–5.
 27. Horenblas S, van Tinteren H. Squamous cell carcinoma of the penis. IV. Prognostic factors of survival: analysis of tumor, nodes and metastasis classification system. *J Urol.* 1994; 151:1239– 1243.
 28. Pasha, T., Hossain, M. M., & Chowdhury, R. (2020). Nutritional status of pregnant women in selected hospitals in Dhaka city. *Journal of Medical Research and Health Sciences*, 3(12), 1114–1117.
 29. Hardner GJ, Bhanapah T, Murphy GP, Carcinoma of the penis; an analysis of therapy in 100 consecutive cases. *J Urol* 1972; 108:428
 30. Grabstald H, Controversies concerning lymph node dissection for cancer of the penis. *Urol Clin North Am* 1980; 7:793-99
 31. Anathakrishnan N. Diagnosing metastatic disease in inguinal nodes in penile cancer: Do we have a test and the evidence? *Indian J Urol* 2006; 22; 345-50.
 32. Pizzacaro G, Pival, Nicolai N, Treatment of lymphatic metastasis of squamous cell carcinoma of thepenis, experience at the National Tumor institute Of Milan, *Arch Ital Urol Androl* 1996;68:169-72.
 33. Caso JR, Rodriguez AR, Correa J, Spiess PE. Update in the management of penile cancer. *Int Braz J Urol.* 2009; 35:406–415.