CARCINOMA PENIS, CLINICAL STUDY OF VARIOUS MODALITY OF TREATMENT
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ABSTRACT: INTRODUCTION: Cancer of penis is a rare tumor in developed country and affects the elderly patient population. The aim of this paper was to analyze and study the characteristics of this tumor in our patient population. MATERIAL & METHODS: A total of 40 patients taken up for study from LLR & Associated Hospital and JK Cancer Institute out of which 21 cases formed the retrospective part and 19 cases formed the prospective part of study. RESULTS: Out of 40 cases diagnosed and treated the median age of presentation was 51.3 years, common in uncircumcised hindus and commonest presenting feature is penile growth followed by penile ulceration. Surgery alone for 27.5%, surgery and radiotherapy for 35%, Surgery and chemotherapy for 27.5% and chemotherapy for 7.5% and radiotherapy for 2.5%. 22.5% mortality and 12.5% left follow-up. CONCLUSION: Carcinoma of penis is a pathology which mostly affects elderly patients. In our series the highest incidence observed in uncircumcised patients in age group of 41-50 years. The most common histological type epidermoid carcinoma in its various forms of presentation.

INTRODUCTION: Penile cancer is a malignant tumor in which malignant cells develop on the tissues of the penis. It is rare in Europe and United States but not in developing countries or in their immigrants to Europe and United States.1 Around 4000 cases are diagnosed each ear comprising less than 0.5 percent of all cancers.2 The variation in the world geographical incidence is evident and may be due to differences in hygiene, social and religious practices.3 Penile cancer has the –peak incidence in men over 70 years of age around the 60% cases present in men over 65 years of age.4 The involvement of regional lymph nodes is the best indicator of long-term survival in patients with invasive penile carcinomas.5 In addition to lymph node metastasis, other pathological factors, including grade, histological type, lymphovascular embolization, and stage and perineural invasion, have been described to be prognostic value in penile carcinoma. However, none of them can effectively predict outcome.6,7,8 The aim of our study was to present our series during the last 2 years from September 2012 to September 2014 and to analyse the result.

MATERIAL AND METHODS: A total of 40 cases seen between Sept. 2012 to Sept. 2014 were included for study, out of which 21 cases formed the retrospective part and 19 formed the prospective part of the study.

The details of patients were obtained from medical record section and wards and on the basis of information collected, a questionnaire was prepared which included age, details of present and past history, risk factors, anatomical site, clinical staging, general investigation, histological type and grade, presence and site of metastasis, treatment modalities, treatment outcome, hospital stay, post-operative morbidity and mortality and follow up.

Patients were classified into four stages using “Jackson” classification.9
TREATMENT: Patients were treated according to their respective staging. Surgery alone, Radiotherapy or combined (Surg.+R. T.) modalities of treatment were used according to the need of individual patient, both for treatment of primaries as well as secondary.

In early stage cases (Stage I and Stage II) primary tumour was treated with surgery. Only in one case with Stage I primary was treated with Radiotherapy. Surgery to primary tumor was performed in form of partial or total penectomy. Partial penectomy was performed where disease was localised to glans or prepuce. This has got the privilege of voiding standing and retain the ability of sexual intercourse. Tumor which invaded the shaft, corpora cavernosa & spongiosum and/or urethra were treated by total penectomy. Inguinal regions were irradiated prophylactically in some cases and radiation dose of 5000 CGy in 5 weeks was given to both the inguinal fields. In one case primary tumor which was localised to glans was treated with radiotherapy and 6000 CGy were given in 5 weeks’ time. In late cases (Stage III and IV) primary tumor was treated by partial or total penectomy and radiotherapy was given to the patient 5000 CGy. in 5 weeks duration. In highly suspicious cases for pelvic lymph node metastasis, palliative radiotherapy was given to pelvic region from anterior and posterior side of pelvis 5000 CGy. In 5 weeks’ time.

RESULT: In the present series of 40 Cases of carcinoma penis the following conclusions were drawn.

Incidence of carcinoma penis relative to total male cancers was 2.0%. The disease is common among uncircumcised Hindus (100%) and very uncommon among Muslims. Penile cancer is a disease of persons belonging to low socioeconomic status (95%) and those having poor personal hygiene (90%). Phimosis is a predisposing factor and its incidence was 20%. Venereal diseases did not have any significant role as only 2.5% cases were having positive V.D.R.L. test with in this series. However its exact role is open for discussion. Age varied from 26-80 years with peak incidence in the age group of 41-50 years and median age of 51.3 years. Among the premalignant lesions, leukoplakia was found in 10% cases of this series. Other premalignant lesions were not noticed. Commonest presenting feature is a penile growth (65%) followed by ulceration on penis (30%). Most of the patients first consulted a doctor with in 1st 6 months of onset of symptoms (68%). About 80% of patients reported within one year.

Commonest initial site of involvement was glans (57.5%) followed by glans and shaft (22.5%). Inguinal lymphnodes enlargement was found in 92.5% cases. In most of cases (80%), it was found to be bilateral enlargement. Metastasis due to direct infiltration was noticed among 32.5% patients, involving urethra (10), perineum (1) and scrotum (2). Majority of the patients presented with clinical stage III disease (67.5%) followed by Stage II disease (17.5%), Stage I (5%) and Stage IV (10%). Proliferative type (65%) is commoner than the ulcerative one (30%). Well differentiated squamous cell carcinoma is the commonest histopathological type (55%) followed by moderately
differentiated type (32.5%). Incidence of verrucous carcinoma was 5%. Poorly differentiated squamous cell carcinoma accounted for 7.5% cases only. Early stage lesions were well differentiated (66%) and poorly differentiated lesions were common among the late stage disease. Surgery may be the treatment of choice but radiotherapy - may also be curative to carcinoma of penis patients.

| Initial Site of Involvement | No. of Cases | Percentage |
|----------------------------|--------------|------------|
| Glans and corona           | 23           | 57.5%      |
| Glans and shaft            | 9            | 22.5%      |
| Glans and prepuce          | 6            | 15         |
| Shaft penis                | 1            | 2          |
| All penis                  | 1            | 2          |

| Clinical Stages of Disease | No. of Cases | Percentage |
|----------------------------|--------------|------------|
| I                          | 2            | 5          |
| II                         | 7            | 17.5%      |
| III                        | 27           | 67.5%      |
| IV                         | 4            | 10         |

| Microscopic Features       | No. of Cases | Percentage |
|----------------------------|--------------|------------|
| Verrucous                  | 2            | 5          |
| Squamous cell carcinoma    | 38           | 95         |
| 1. Well differentiated     | 22           | 55         |
| 2. Moderately differentiated| 13           | 32.5%      |
| 3. Poorly differentiated   | 3            | 7.5%       |

Table 1

| Histological Grade                  | Stage | I | II | III | IV | Total |
|-------------------------------------|-------|---|----|-----|----|-------|
| Verrucous carcinoma (Highly diff. sq.ca) | I     | 0 | 0  | 2   | 0  | 2     |
|                                     | II    | 0 | 0  | 7.7%| 0  | 5%    |
| Well diff. Sq. Ca                   | I     | 2 | 6  | 13  | 1  | 22    |
|                                     | II    | 100|85.7%|50% |20% |55%   |
| Mod. Diff. Sq. Ca                   | I     | 0 | 1  | 10  | 2  | 13    |
|                                     | II    | 14.3|38.5%|40% |40% |32.5% |
| Poorly diff. Sq. Ca                 | I     | 1 | 1  | 34% | 2  | 3     |
|                                     | II    | 3.4%|40% |40% |40% |7.5%  |
| Total                               | I     | 2 | 7  | 26  | 5  | 40    |
|                                     | II    | 100|100%|100%|100%|100%  |

Table 2: Showing Clinical Stage and Histological Differentiation

Early stage (I & II) patients were treated mainly by surgery (66%) or radiotherapy while late stage (III & IV) patients were treated by the combination of surgery and radiotherapy (45%). Primary lesions are treated mainly by partial (65%) or total (20%) penectomy. Partial penectomy
should be preferred in patients where the lesions are small and localised to glans or prepuce so that patients can void standing and retain the ability of sexual intercourse. Those primary lesions which have extensively involved the shaft or directly infiltrated urethra or scrotum are treated by total amputation of penis with orchidectomy. Surgery is also preferred for inguinal lymphadenopathy where the lymphnodes are of doubtful consistency, a 4-6 weeks antibiotic course given prior to lymphadenectomy. Lymphnodes which seem to be clinically malignant or proved to be malignant on histopathological examination treated preferably by ilio-inguinal lymphnode dissection. Some of the non-operative patient may be made operative by chemotherapy.

| Treatment given                      | No. of cases | Percentage |
|--------------------------------------|--------------|------------|
| Early cases (Stage I & II)           | 9            | 100%       |
| Surgery                              | 6            | 66         |
| Surgery + Radiotherapy               | 2            | 22         |
| Radiotherapy                         | 1            | 12         |
| Late cases (Stage III & IV)          | 31           | 100%       |
| Surgery                              | 5            | 12.5       |
| Surgery + Radiotherapy               | 12           | 45         |
| Surgery + chemotherapy               | 11           | 33         |
| Chemotherapy                         | 3            | 9.5        |

Table 3: Showing Treatment Given in Carcinoma of Penis Patients

Post-operative radiotherapy prevent reoccurrence in the draining lymph nodes. Those lymph-nodes which were very small in size and of doubtful metastasis were treated by radiotherapy to both inguinal regions. In view of micrometastasis to draining lymphnodes, role of prophylactic radiotherapy was considered in 10% cases. In patients with metastatic lymphnodes and highly suspicious of pelvic node metastasis, post-operative palliative radiotherapy was given to inguinal and pelvic regions in 8% cases. Commonest complication after partial (15%) and total (25%) penectomy is stricture urethra. Survival is, maximum among the patients with verrucous carcinoma (100%) and worst among the patients with poorly differentiated squamous cell carcinoma (33%). Patients with early stage disease outlive the late stage patients. Thus prognosis is best among stage I patients (100%) and worst among stage IV patients (50%).

| Histopathology       | Total | Dead | Alive | Last Follow up |
|----------------------|-------|------|-------|----------------|
|                      |       |      | With Disease | Without Disease |
| Verrucous carcinoma  | 2     | 0    | 0     | 2              |
| Mod diff. Sq. Ca     | 22    | 4    | 4     | 12             |
| Mod. Diff. Sq.Ca     | 13    | 2    | 4     | 3              |
| Poorly diff. Sq. Cell| 3     | 2    | 1     | 0              |
| Total                | 40    | 8    | 9     | 17             |

Table 4: Showing Histopathological: Type and Survival after Treatment
DISCUSSION:

**Incidence:** In present study, the incidence of carcinoma of penis among total male cancers at our institute was found to be 2.0%.

Reported incidence rates vary from 2.8% to 10.0% of all male cancers. The incidence rate of 4.7% at Cuttack.\(^{10}\) The incidence of penile carcinoma at Bombay 2.8%.\(^{11}\)

The incidence of penile carcinoma has remained at a low level and exhibits a decline during the last 3 decades. He explained the decline as possibly due to improved economic and hygienic conditions.\(^{12}\)

**Racial Factors and Circumcision:** All the patients in present series were Hindus comprising 100% and none of the patient was circumcised in early infancy or childhood.

Penile neoplasms are rare among Jews, who practice circumcision in infancy (Usually within 7 days of birth) and uncommon among Muslims and others, who practice the ritual a little later in the childhood. In India Khanolkar reported the incidence among Muslims as 2.2%,\(^{13}\) Riveros and Lebron as 2.5%,\(^{14}\) Pandas & Nayak as 1.7%.\(^{10}\)

Total absence of Muslims in the present series might be due to the high percentage of Hindus in the population of areas, people of which attend our hospitals. Total absence of incidence in Parsees, Hindu Jews (Bene Isarelis) and Christians could well be explained by the fact that very few people of these religions reside in this area.

**Hygiene and Socio-economic Condition:** Majority of subjects (90%) had poor personal hygiene and socio-economic status of most of them was low (95%). Several studies have indicated that a large proportion of penile cancer patients are laborers or farmers (Reddy and Gursel).\(^{15}\) Panda & Nayak\(^{10}\) found poor hygiene to be associated with the incidence of carcinoma of penis in 85% of cases in their study and low socio-economic conditions to be in 72.1% cases. Our findings are much, similar to those of Panda & Nayak.\(^{10}\)

**Phimosis:** Incidence of phimosis is found to be 30% in present series. Thomas & Small (1968) reported phimosis in 41% cases of their series.\(^{16}\) Paymaster & Gangadharan (1967) observed phimosis in 26% cases.\(^{17}\) Murell & Williams (1965) reported the incidence of phimosis in 48.9% cases.\(^{18}\)

**Treatment:** Surgery was the main treatment modality for the primary tumor with partial penectomy in 65% of cases and total penectomy in 20% of cases. Radiation therapy was given 37.5% patients and chemotherapy was given to the 35% of patients. Radiation therapy has been proposed as a method of preserving the phallus. Although superficial lesions have been cured by various modes of radiation therapy, approximately 50 percent will be refractory or recur.\(^{19,20}\)

**CONCLUSION:** Penile cancer is a rare disease, which has been studied through relatively small case series from large academic centers. Penile carcinoma is pathology with low incidence in relation to other tumors and is diagnosed late probably due to ignorance of the disease by the patients. The over treatment many times carries on a lot of side effects. The drive for decrease morbidity continued cancer control has lead to penile preservation surgery, better staging modalities, and minimally invasive technique for exploration of the inguinal lymph node. It is hoped these techniques proved to have equivalent or better oncologic outcome in order to lessen the morbidity associated with the
surgical therapy of this disease. Therefore it is advisable to run campaign in the elderly male population recommending hygiene and early consultation in the case of any change in the penis.

REFERENCES:
1. G. Micali, M. R. Nasca, D. Innocenzi, and R. A. Schwartz, “Penile cancer,” Journal of the American Academy of Dermatology, vol. 54, no. 3, pp. 369–391, 2006.
2. M. Mosconi, F. Roila, G. Gatta, and C. Theodorec, “Cancer of the penis,” Critical Reviews in Oncology/Hematology, vol. 53, pp. 165–177, 2005.
3. S. Misra, A. Chaturvedi, and N. C. Misra, “Penile carcinoma: a challenge for the developing world,” The Lancet Oncology, vol. 5, no. 4, pp. 240–247, 2004.
4. ENCR (European Network of Cancer Registries), Eurocim Version 4.0 European Incidence Database V2.2 (1999), ENCR, Lyon, France, 2001.
5. Ornellas, A.A.; Kinchin, E.W.; Nóbrega, B.L.; 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, 487–495.
6. Calmon, M.F.; Tasso Mota, M.; Vassallo, J.; Rahal, P. Penile carcinoma: Risk factors and molecular alterations. Scientific World Journal 2011, 11, 269–282.
7. Ficarra, V.; Akduman, B.; Bouchot, O.; Palou, J.; Tobias-Machado, M. Prognostic factors in penile cancer. Urology 2010, 76, S66–S73.
8. Lopes, A.; Hidalgo, G.S.; Kowalski, L.P.; Torloni, H.; Rossi, B.M.; Fonseca, F.P. Prognostic factors in carcinoma of the penis: Multivariate analysis of 145 patients treated with amputation and lymphadenectomy. J. Urol 1996, 156, 1637–1642.
9. Jackson SM. The treatment of carcinoma of the penis. Br J Surg. 1966; 53: 33-35.
10. Panda, K. and Nayak, K.R.: Clinicopathological studies on cancer penis. 3 md. Med Ass. 16, 75(2): 25 – 8 July (1980).
11. Paymaster J.C.: Cancer and its distribution in India. Cancer 17: 1026 – 1034, (1964).
12. Kochen, M. and McCurdy S.: Circumcision and the risk of cancer of penis. Am J Dis Child Vol. 134(45), p. 484, 9 May (1980).
13. Khanolkar V.R.: Cancer in India in relation to race nutrition and customs, symposium and geographical pathology and dermography of cancer. W.H.O. (1950).
14. Riveros M, and Lebron, R.P.: Geographic pathology of cancer of penis. Cancer 16: 798 – 811 (1963).
15. Reddy G.R.R.M., Raghavaiah N.Y and Mouli, K.C. Prevalence of carcinoma of penis with special reference to India. International Surgery, 60(9): 474 – 476 (1975).
16. Thomas, J.A. and Small C.S, Carcinoma of the penis in Southern India. J. Urol. 100: 520 - 526 (1968).
17. Paymaster J C and Gangadharan P: Cancer of penis in India. 3 Urol. 97: 110 – 113 (1967).
18. Murell D. S. Williams J.L. Radiotherapy in the treatment pf carcinoma of the penis. Br J Urol 37: 211 – 222. (1965).
19. Hardner. G. J. et al: Carcinoma of the penis: analysis of therapy in 100 consecutive cases. J. Urol. 108:428-430, 1972.
20. Kelley, C. D. et al: Radiation therapy of penile cancer. Urology 4: 571-573, 1974.
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