

A case study of carcinoma of penis at tertiary care centre– Two years study

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Abstract

Objective: A Retrospective study for two years from January 2015 – December 2016 undertaken to determine the histopathological spectrum of Penile lesions. The objective of the study was to estimate the frequency of penile carcinoma at the Department of Pathology, Government Thiruvapur Medical College Hospital, Thiruvapur, a tertiary health care centre. **Materials and Methods:** The study included a total of 58 cases of Penis. Samples were received in 10% formalin, embedded in paraffin and stained by Hematoxylin and Eosin Stains. **Results:** A total of 58 cases were studied over a period of 2 years. 30 cases were neoplastic and 28 were non-neoplastic constituting 51.72% and 48.28 % respectively. The neoplastic cases were distributed as Benign - 02(6.67%), Squamous Cell Carcinoma insitu – 03(10%) and Malignant –25(83.33%) cases which included 24 cases of Invasive Squamous Cell Carcinoma and 1case of Verrucous Carcinoma. In this study, the most common location of SCC *in situ* or invasive, was the Glans penis 10 cases (35.71%), followed by the foreskin in 7 cases (25%) and both in 8 cases (28.57%), shaft of the penis in 3 cases (10.71%). Invasive SCC was characterized by ulcers and vegetation, usually measuring bigger than 2 cm. Among the malignant cases, 7 patients had their penis amputated. **Conclusion:** Squamous cell carcinoma of the Penis is rare and Invasive SCC predominated over SCC *in situ*. Our study, highlights the significance and implementation of protocols for diagnosis and preventive measures of patients with cancer of the penis which can certainly affect their quality of life.


Key Words: Penis, Squamous Cell Carcinoma, SCC *in situ*, Verrucous Carcinoma, Glans Penis.

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INTRODUCTION

Penile cancer is an uncommon disease affecting only about one in 1,00,000 men worldwide annually.¹ The incidence of squamous cell carcinoma of the penis ranges from 10% to 20% of male malignancies. Etiological factors associated with penile cancer are phimosis, chronic inflammatory conditions, especially lichen sclerosis, smoking, ultraviolet irradiation, history of warts, or condylomas and lack of circumcision. The risk for penile cancer is 3.2 times greater among men who were never circumcised than in men circumcised at

birth.^{3,4} The carcinoma of Penis is related to personal hygiene and the carcinogenic effect of smegma, factors that might be enhanced by failure to circumcise.²

MATERIALS AND METHODS

This was a cross-sectional study carried out at the Department of Pathology of Government Thiruvapur Medical College hospital, Thiruvapur, a tertiary health care centre, during the period from January 2015 – December 2016. During the study period of 2 years, a total of 58 Penile cases were reported. The samples were received in 10% formalin, processed by the standard procedure, embedded in paraffin and stained by the routine Hematoxylin and Eosin Stains.

RESULTS

A total of 58 cases were studied over a period of 2 years and most of the Penile lesions were observed in the 6th decade constituting 18 cases (31.03%) and 12 cases (20.68%) in 7th decade. 12 cases of malignant Penile lesions were seen in the 6th decade and 8 cases in 7th decade. 30 cases were neoplastic and 28 were non-neoplastic constituting 51.72% and 48.28 % respectively.

Further, neoplastic lesions presented as Benign 02 cases (6.67%), Carcinoma in situ – 03 cases (10%), malignant – 25 cases (83.33%) which included 24 cases of Invasive Squamous Cell Carcinoma[Figure 6,7,8] and 1case of Verrucous Carcinoma[Figure 9,10]. In this study, the most common location of SCC *in situ* or invasive, was the

glans Penis -10 cases (35.71%), followed by the foreskin in 7 cases (25%) and both in 8 cases (28.57%), shaft of the penis in 3 cases (10.71%). Invasive SCC was characterized by ulcers and vegetation, usually measuring bigger than 2 cm. Among the malignant cases, 7 patients had their Penis amputated.

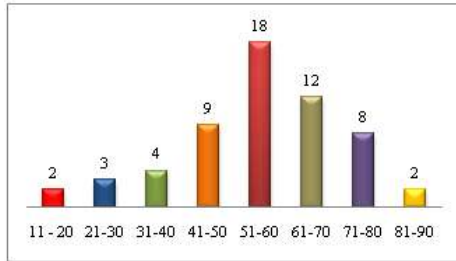


Figure 1

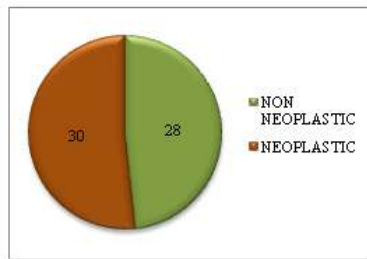


Figure 2

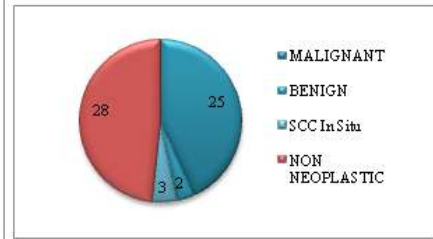


Figure 3



Figure 4



Figure 5



Figure 6



Figure 7



Figure 8



Figure 9



Figure 10



Figure 11

Legend

Figure 1: Age Distribution of Penile Lesions; **Figure 2:** Proportion of Neoplastic and Non Neoplastic Diseases; **Figure 3:** Spectrum of Penile Lesions; **Figure 4:** Ulcerating mass arising from the Penis; **Figure 5:** Cut surface shows a solid gray-tan growth arising from the Glans penis **Figure 6:** Well differentiated Squamous Cell Carcinoma showing keratin pearls; **Figure 7:** Cords and sheets of malignant squamous epithelial cells; **Figure 8:** Large squamous cells, abundant eosinophilic cytoplasm, vesicular nucleus, prominent nucleoli; **Figure 9:** Endophytic papillary growth, acanthotic, hyperkeratotic, and parakeratotic squamous mucosa; **Figure 10:** Bulbous expansions regular papillae, broad pushing base, and hyperkeratosis; **Figure 11:** Benign Squamous Papilloma- Finger like papillae with a central core of loose fibrovascular tissue covered by epithelium

DISCUSSION

Penile cancer, is more common in the elderly age group men, with a peak incidence at 70 years.¹ Risk factors for penile cancer include Human Papilloma Virus (HPV) infection, smoking, phimosis and poor genital hygiene, while neonatal circumcision has been depicted as protective. Penile cancer occurs almost exclusively in uncircumcised men, with a lifetime risk of one in 100,000 globally, compared to 0.1 in 100,000 in Israel, where the majority of men are circumcised.⁵ If circumcision is done shortly after birth, as is the Jewish custom, carcinoma of the penis develops very rarely. If the operation is delayed until the age of 10 years, as in some Moslem countries,

carcinoma is more likely to develop.⁶ Circumcision prevents conditions such as phimosis and decreases the risk of HPV infections. All the patients in our case series were uncircumcised and 44.8% of them had phimosis. The presence of phimosis allows the buildup of smegma, resulting in chronic irritation and inflammation of the glans penis and prepuce. Also phimosis could be a cause for the delayed diagnosis of penile cancer. Tobacco use, including cigarette smoking is also strongly associated with an increased risk of penile cancer. In our study, smoking history was elicited in 16 cases (64.00%) of the patients with invasive SCC and 2(66.66%)cases of SCC *in situ*. The Squamous cell carcinoma usually begins at

the glans penis or in the prepuce and gradually extends to involve the entire glans Penis, shaft and corpora. The lesion may take the form of an induration, a painless nodule, a wart-like growth, an ulceration, or an exophytic lesion. Subsequently, as the prepuce erodes, a foul odour and discharge from the lesion may occur. In this study, the principal location of tumor, irrespective of whether it was SCC *in situ* or invasive, was the glans penis in 10 cases (35.71%), followed by the foreskin in 7 cases (25%) and both in 8 cases (28.57%), shaft of the penis in 3 cases (10.71%). Our study showed a higher proportion of involvement of glans penis than that in the referred literature.^{7,8,9} In our series, most of the patients ignored the initial penile lesions and delayed seeking treatment until problems of ulcers, bloody discharge, obstructive urinary symptoms and symptomatic anemia occurred. The tumor presents as an ulcer; an indurated crater; a friable hemorrhagic mass, or an exophytic, fungating, papillary tumor. In the Spanish study cited, variable morphology of invasive SCC was observed: ulceration (53%), papule (33%), nodule (7%) and plaque (7%).¹⁰ With regards to the size of the lesions, invasive SCC lesions were larger than SCC *in situ*. Of the 22 invasive SCC, 77.2% measured more than 2 cm and 13.6% exceeded 5 cm; however, lesions smaller than 2 cm were observed in 22.7% of the cases. The gross appearance shows an irregular granular mass with a variably flat, exophytic, or even polypoid surface. Large lesions tend to be ulcerated. The cut surface shows a white to tan solid irregular tumor with either superficial or deep penetration into the various penile anatomic layers.

The microscopic appearance of Squamous cell carcinoma of the usual type shows infiltrating keratinizing type. The classification is based on a three tier system.^{11,12,13} Well-differentiated (grade 1) tumors are characterized by squamous cells with normal to slightly enlarged nuclei and abundant eosinophilic cytoplasm. Intercellular bridges are easily seen, and keratinization is prominent. Minimal pleomorphism, is seen near the basal layer. Moderately differentiated (grade 2) carcinomas show a more disorganized growth compared to grade 1 lesions, higher nuclear-to-cytoplasmic ratio, evident mitoses with less prominent keratinization. The majority of SCCs of usual type show a moderate degree of differentiation. Poorly differentiated (grade 3) neoplasms show foci of solid sheets or irregular small aggregates, cords, or nests of cells with little or no keratinization, high nuclear-to-cytoplasmic ratio, thick nuclear membranes, nuclear pleomorphism, clumped chromatin, prominent nucleoli, and numerous mitoses. Usually tumors are to be graded on the least differentiated element, even though it constitutes only a minor component of the neoplasm. Invasive tumors usually have a dense, chronic

inflammatory cell infiltrate in the dermis. Sometimes the adjacent epidermis shows dysplastic changes.¹³ The Squamous Cell Carcinoma. In Situ shows cytologic atypia of the keratinocytes of all layers of the epidermis, with parakeratosis or hyperkeratosis; papillomatosis with broad epidermal papillae; and thinning of the granular layer. By definition, the atypical keratinocytes do not invade the underlying dermis.

The regional inguinal lymph nodes are the common sites of lymphatic metastasis of penile carcinoma. The lymphatics from the prepuce join the lymphatics from the skin of the shaft and drain into the superficial inguinal nodes. The lymphatics of the glans penis join the lymphatics draining the corpus cavernosum and spongiosum, forming a collar of connecting channels at the base of the penis that also drains into the superficial inguinal nodes. The superficial nodes drain into the deep inguinal nodes, which then drain into the pelvic nodes. Penile carcinoma can metastasise to the lung, bone and liver. However, distant metastases occur late in the course of the disease, usually in patients with significant inguinal and pelvic lymphadenopathy.¹⁴ In our study, inguinal lymphadenopathy was associated in 30% of the cases of invasive SCC at diagnosis; Lymphadenectomy was performed in 5 patients, all the 5 cases showed reactive inflammatory changes and none revealed the evidence of metastases. We have also reported a case of Verrucous Carcinoma, which is commonly seen in middle-aged men, arising in the coronal sulcus, Behaves as a locally aggressive neoplasm; essentially no metastatic potential. Grossly it shows a large, fungating, warty tumor. Microscopy reveals a very well differentiated papillary neoplasm with acanthotic, hyperkeratotic, and parakeratotic squamous mucosa with minimal cytologic atypia and rare mitotic activity. Deep margin of the tumor shows a pushing, broad area of infiltration. This low-grade squamous cell carcinoma usually does not metastasize and surgical removal is curative. Verrucous carcinoma is considered not to be HPV-related. This is a slow growing tumour that may recur locally but metastasis does not occur in typical cases. Prognosis of the patients with penile cancer is correlated to the clinical stage and the histologic grade of the tumor. Poor prognosis is seen in poorly differentiated tumors, Vascular invasion and metastatic lymph node involvement.^{15,16} Treatment of SCC *in situ* of the penis depends upon the extent and location in the genitals, either by medication or surgery. But the Invasive SCC, is always treated surgically - Partial amputation or total amputation of the Penis; and if associated with lymphadenectomy, radiotherapy and chemotherapy.¹⁷ The European Association of Urology established in 2009

proposed the following recommendations for diagnosis and staging of penile cancer:

- a. Physical examination and Cytologic and/or Histopathological examination of the Primary tumor;
- b. Physical examination of the Inguinal regions:
 - i. Impalpable lymph nodes - sentinel lymphnode biopsy and in case the latter is not available, cytology of material aspirated with fine needle guided by ultrasound;
 - ii. Palpable lymph nodes - cytology of material aspirated with fine needle;
- c. Distant Metastasis: Pelvic CT and PET-CT scan; Abdominal CT; Chest radiography; Bone Scan.¹⁶

Specimens with poorly defined lesions and when different morphologies coexist, it is necessary to do more than one biopsy. In case of ulcerative lesions, the border of the lesion must be included. Biopsy of the suspected Verrucous Carcinoma cases, should be done such a way that includes the full thickness of the epidermis and dermis. The initiatives enhance the early diagnosis of carcinoma of penis, improve prognosis and reduces the health care costs and psychological damage to the patients.

CONCLUSION

Squamous Cell Carcinoma of the penis is rare and preventable disease. The incidence of Invasive SCC outweighed the SCC *in situ*. Invasive SCC was more common in patients over 60 years of age. Most of the invasive SCC cases have single large lesions measuring more than 2 cm, generally ulcerated or ulcero-vegetating. Pruritus with or without pain were the frequent symptoms. Cautious dermatological examination of the genital area helps in early diagnosis of penile cancer. It is suggested that circumcision results in maintaining better genital hygiene, which, also, decreases the exposure to carcinogens which are concentrated in smegma. Our study highlights the significance and implementation of protocols for the health education of the public creating awareness among them, regarding the maintenance of genital hygiene and to come forward to do the circumcision of the prepuce skin that certainly prevents the occurrence of Carcinoma of the Penis which positively affects their quality of life.

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