

CLINICO-PATHOLOGICAL STUDY OF CARCINOMA OF PENIS

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HOW TO CITE THIS ARTICLE:

Sarada Budamala, P. Venkataramana, N. V. Ramanaiah, B. Anuradha, B. Srihari Rao, C. Srikanth Reddy. "Clinico-Pathological Study of Carcinoma of Penis". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 19, May 11, 2015; Page: 2897-2905.

ABSTRACT: Carcinoma of penis is a tumor with devastating psycho sexual repercussions on the patient. It was reported from different parts of the world with wide variation in incidence. Several factors were considered as inducing agents for cancer of penis. A clinic- pathological study is undertaken to find the incidence, the probable causative factors and the possible treatment methods that can be adapted. Preputial hygiene seems to be an important factor in preventing carcinoma penis. All the cases were of squamous cell carcinoma. Patients are coming for treatment in advanced stage of disease due to lack of awareness about the condition, becoming ineligible for modern conservative surgeries.

KEYWORDS: Cancer of Penis, Factors, Pathology, Penile Hygiene, Penectomy.

INTRODUCTION: Carcinoma of the penis is an uncommon tumor that is often devastating for the patient.¹ Though it is of very low incidence in some western countries; it is not uncommon in India. Wide variation in frequency of carcinoma of penis was observed.² The disease appears more common in south Indian subcontinent.³

Smegma that collects in preputial sac is deemed the important causative factor and penile cancer is rare among neonatally circumcised individuals.^{4,5} Human papilloma virus infections,⁶ multiple sexual partners, venereal diseases, smoking,^{7,8} premalignant cutaneous lesions,⁹ penile trauma,¹⁰ and ultraviolet radiation are considered as etiological factors.

Early recognition has got a very good prognosis and patient can be given a cure. In 1884 Puzay for the first time introduced the real radical procedure of total amputation of penis and excision of inguinal lymph nodes. Better understanding of natural course of penile cancer has allowed evolution of various techniques of nodal assessment and sampling commencing with Cabana's sentinel node sampling in 1977.¹¹

Several procedures such as Mohs micrographic surgery,¹² with an aim to control disease with preservation of penis, which has better acceptance with patients and preserve sexual function to varying extent,¹³ have gained interest since then.

The present study is undertaken in S. V. R. R. Govt. General hospital, a tertiary hospital in Rayalaseema region of Andhra Pradesh to study the incidence of carcinoma of penis in our region, to identify the risk factors for carcinoma of penis, to study the various clinical presentations of carcinoma of penis, to study the pathological features of carcinoma of penis and to study the various modalities of treatment for carcinoma of penis.

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MATERIALS AND METHODS: Patients with penile cancer admitted in S. V. R. R. Govt. General Hospital, Tirupati between August 2008 and August 2010 are included, after due patient consent, in this clinical and pathological study of carcinoma of penis.

In addition the data of the cases of carcinoma of penis treated in S. V. R. R. G. G. Hospital from August 2005 is analyzed and included in this study.

Data comprising age, religion, occupation, socio economic status, whether circumcised or not, presence and duration of phimosis, smoker/alcoholic, penile hygiene, presenting symptoms and their duration, previous treatments taken, evidence of any preexisting venereal diseases or penile cutaneous disorders reviewed by dermato-venereologist, the clinical features, histopathological findings and treatment given are compiled and analyzed.

RESULTS AND ANALYSIS: Carcinoma of penis cases constituted 0.2% (52 out of 25206) of total surgical admissions and 0.3% (52 out of 15072) of male surgical admissions of S. V. R. R. G. G. Hospital during the study period. The percentage of ca. penis cases was 1.9% among all malignancies and 2.9% of malignancies affecting males.

The age of the patients ranged from 38 years to 65 years with peak incidence in the age group 51-60 years (Fig. 1).

All the 52 patients were of low socio economic status. Out of 46 cases for whom data regarding education is available, 40 of them had no formal education and 6 of them had discontinued primary education.

All the 52 patients were Hindus and all were uncircumcised except one who had undergone circumcision after the onset of ulcer on penis. 31% (16/52) patients had phimosis before the onset of the disease. Penile hygiene was poor in all the cases.

17% of ca. penis patients had past history of venereal disease. None of the patients had pre-existing penile pre-malignant cutaneous disease. 81% (42/52) were chronic smokers.

Low socioeconomic status, lack of penile hygiene and smoking were the major associated factors (Fig. 2).

81% of patients had the disease for more than 6 months and 19% had for more than one year. All the patients complained of an ulcer or ulcerated growth on penis. 73% of them had serous or serosanguineous discharge (Fig. 3). In most of the cases the lesion started on glans or prepuce. (Fig. 4).

All the 52 cases of cancer of penis in our study were of squamous cell carcinoma. 44% were of well differentiated and 42% were of moderately differentiated histology.

Palpable inguinal lymph nodes were present in 89% of cases at the time of presentation. Only 30 of these were found to have metastases by fine needle aspiration cytology.

Hypercalcemia was found in 27 cases and all of them had lymph node metastasis.

Partial amputation of penis was done for 16 cases. Total amputation of penis had to be done in 26 cases. Bilateral inguinal dissection was done for 18 cases and unilateral inguinal dissection for 2 patients. 10 patients required radiotherapy. Only six cases were available for follow up beyond one year and none of them had recurrence.

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DISCUSSION: Carcinoma of penis is rare in western countries but not so uncommon in India. Wide variation in frequency of carcinoma of penis within India was reported by Reddy C. R. et al (1975).²

In our study 52 cases of carcinoma of penis were treated during 2005- 2010 constituting 0.2% of all surgical admissions, 0.3% of all male surgical admissions and 2.9% of malignancies affecting males.

The age of the patients of carcinoma of penis in our study ranged from 38 to 65 years with a mean age of 53 years. 79% of the patients were above 50 years. The age of incidence is comparable with the studies by Heynes CF et al. (1997),¹⁴ Di Capua Sacoto et al (2009),¹⁵ and J. C. Soria et. al (1997).¹⁶

All the patients of carcinoma penis in our study were Hindus and none of them had circumcision. Most of the patients had no formal education and belonged to low socio economic status. Their concern for penile hygiene also was very poor. This poor penile hygiene was the probable cause for carcinogenesis.

It is universally acknowledged that neonatal circumcision prevents the carcinoma penis. Though the actual carcinogen is not yet identified smegma is widely implicated as inducing agent for carcinoma of penis. Within the uncircumcised population preputial hygiene may have much importance.¹⁷ Reddy CR et al., (1975),² (1984),¹⁸ also opined that lack of penile hygiene, poor sexual hygiene and lack of cleanliness with associated phimosis may account for variability in frequency and high incidence of carcinoma of penis in some areas.

Phimosis before the onset of disease was present in 31% of cases in our study. J.C. Soria et al., (1997),¹⁶ reported phimosis in 24.5% of patients of penile carcinoma and the other authors have reported comparable rates with the highest being 69% (Hanash KA et al, 1970,¹⁹ Fraley EE et al, 1985,²⁰ Solis WA et al, 1985).²¹

81% of the patients in our study were chronic smokers. Hellberg et al (1987),⁷ and Harish & Ravi (1997),⁸ have reported significant association between smoking and carcinoma of penis.

History of suffering with any venereal disease was present only in 17% of patients in our study. Though it is considered as one of the predisposing factors by some authors there is no conclusive evidence. In a study by J. C. Soria et al., only 6.8% of patients of penile cancer had history of venereal diseases.¹⁶

The presenting symptom in majority of the cases in our study was ulcerated growth on penis, often associated with serous or serosanguineous discharge. Similar observation was made by J. C. Soria et al.¹⁶

62% of the patients had the symptoms existing for more than 6 months and another 19% of patients did not attend the hospital for more than 1 year after they noticed the problem. This type of late presentation is reported by several authors especially from developing countries. This is due to ignorance, feeling of shame, embarrassment etc. Some of the patients mistook the discharge for seminal fluid. Most of the patients considered the growth/ulcer on penis as some sexually transmitted disease and were referred to surgery from dermato-venereology. Lack of primary health care was also another factor.

Glans and prepuce were the sites of commencement of disease in majority of the cases, extending to the shaft later. This is a common observation in several studies. Hence if the

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patients come at an early stage surgical cure without resorting to amputation of penis would be possible. 89% of the patients had palpable inguinal lymph nodes at the time of presentation. 58% of the cases were found to have metastasis in inguinal nodes by FNAC. DiCapuaSacoto et al found palpable lymph nodes in 34% cases at the time of presentation.¹⁵ Presence of palpable lymph nodes, in higher number of patients, in studies in south India maybe due to the habit of walking barefoot (Rangabashyam. N et al,² Wapnick Set al).²²

All the cases of carcinoma penis in our study were of squamous cell carcinoma, 44% of them having well-differentiated histology and 42% showing moderately differentiated histology. All the cases with lymph node metastasis had poorly defined or moderately defined primary tumor histology. It indicates that higher the grade of the tumor worse the prognosis.

Hypercalcemia was found in 52% of cases and all of them had metastasis in lymph nodes. In a study by Di Capua Sacoto et al, hypercalcemia was a common finding when patients of penile cancer had lymph node involvement.¹⁵

The treatment adopted in our hospital for the primary tumor of cancer of penis is either partial or total penectomy, as most of the patients came at advanced stage of the disease. In the present study 31% of patients had partial penectomy and 50% of patients had total penectomy.

These procedures give excellent cancer control with low recurrence rates. But these procedures are deemed rather radical. As many of the patients are still in sexually active age these procedures have very poor patient acceptance and often found to be significantly detrimental psychologically and psycho - sexually.

Further, the historic view that a minimum of 2 cm margin of clearance is needed to achieve adequate cancer control has been challenged. Current view is that a clearance of 1 cm or even a few millimeters is sufficient to achieve adequate cancer control (Minhas S et al, 2005).²³

With this view, partial or total penectomy seem to be an over treatment in most cases of localized diseases. Various penile preserving or sparing techniques including Moh's micrographic surgery, wide local excision, subtotal and total glanssectomy with glanuloplasty are being recently adopted aiming for adequate cancer control, at the same time achieving cosmetically acceptable results with preservation of as much penile length as possible and preservation of sexual function.

Gowardhan B et al., 2006 have opined that a penile preserving option is suitable for most patients with a primary tumor < 4 cm in size and a stage < T3 as first line treatment, with more radical procedures such as partial or total penectomy reserved for as a second line treatment.¹³

While distant dissemination is very rare, nodal metastasis is relatively common in carcinoma of penis (Ananthakrishnan N, 2006).²⁴ Lymph node metastasis is the most important prognostic factor in patients with carcinoma penis (Pandey D et al, 2006).²⁵ It has been said that the battle for control of squamous cell carcinoma of penis is either won or lost at the level of inguinal nodes. Hence dealing with nodal metastasis is very important in management of carcinoma penis.

In our hospital inguinal lymphadenectomy is done based on fine needle aspiration cytology of the palpable nodes. If it is positive for malignancy inguinal lymphadenectomy is done along with the surgery for primary tumor. If it is negative, after surgery for primary tumor patient is kept on antibiotics for four weeks and if the nodes still persist, lymphadenectomy is taken up.

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The inaccuracy of clinical examination in detecting nodal metastasis is well known (Ayyappan. K. et. al, 1994).²⁶ A false positivity of 43-70% (Edwards RH et al, 1968),²⁷ and a false negativity of 0-66% (McDougal WS et al, 1986),²⁸ of clinical examination were recorded.

In view of the inaccuracy of clinical examination attention was focused on prophylactic node dissection. Pizzocaro G et al., mention that an expectant policy can be dangerous and results of delayed Iymphadenectomy are poor. They recommended prophylactic Iymphadenectomy in all T2, T3, T4 patients and grade 2 or 3 T1 patients.²⁹

Mosconi et al. recommended prophylactic node dissection for patients with T2 or greater and for those with vascular invasion or those with high grade tumor. Ravi et al, Lubke et al & Ricos et al, also found better survival rates with prophylactic Iymphadenectomy than observational and therapeutic Iymphadenectomy.

In spite of clear advantage of prophylactic Iymphadenectomy in terms of survival it could not be the gold standard in management of carcinoma penis. 30-70% of groins dissected prophylactically had histological negative lymph nodes and hence considered as over treatment. In addition Iymphadenectomy for carcinoma penis was reported to be associated with 30- 50% incidence of major morbidity including wound breakdown, wound infection and lymph edema and 3% mortality rate (Beggs JH III, Cabanas).¹¹

FNA cytology of palpable inguinal lymph nodes in association with diagnostic biopsy of primary tumor in squamous cell carcinoma of penis has a high sensitivity and specificity for metastatic disease. FNAC is an innocuous minimally invasive excellent alternative to surgical staging for identifying nodal disease. It is accurate in detecting metastasis in palpable nodes. But, it is associated with problems of sampling when many nodes are palpable.

Where the inguinal nodes are not palpable several tests ranging from ultra sound guided FNAC, gallium citrate scanning, sentinel node biopsy, medial inguinal lymph node biopsy, DSLN, LNMRI, SCCAg, PCNA and DNA flow cytometry are being tried for reliable pre-operative lymphatic staging. The only test which currently holds promise is dynamic sentinel node mapping using radio isotope with or without intra operative color dye to identify the draining nodes for sampling (Ananthakrishnan N).²⁴

In the absence of reliable indicator of nodal metastasis, patients of carcinoma penis require an intensive and continued follow up. In developing countries where patients can't be relied upon for follow up and often present with fungating inguinal secondaries, a policy of early bilateral regional nodal clearance despite a level of morbidity is preferable (Ayyappan K et al).²⁶

Bhagat SK et al., (2006),³⁰ also opined that as patients' compliance for regular follow up cannot be guaranteed, any tumor invasion beyond 3 mm should be considered for prophylactic groin dissection.

In our study 90% of the people were lost for follow up and probably the prophylactic groin dissection is preferable in these circumstances.

The morbidity associated with inguinal dissection may be lowered if plane of raising flaps is just superficial to the membranous layer of superficial fascia of the thigh, thus preserving the arterial plexus in fatty layer (Jacobellis U 2003).³¹ Several other modifications of conventional block have been suggested to reduce the morbidity. In an attempt to reduce morbidity of groin

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dissection, utilizing various skin flaps incorporating plastic surgery principles should be considered.

G. Gopalakrishnan (2006) opined that waiting for clinical palpability and then offering lymphadenectomy is like 'shutting the barn door after the horse has fled'. Offering elective lymphadenectomy runs the risk of negative surgical exercises and an unacceptable complication. He has advised prophylactic inguinal dissection if the primary tumor is poorly defined or depth of the tumor >4 mm or if the patient is not motivated for surveillance.³²

CONCLUSION: Carcinoma of penis is not uncommon in our area.

All the cases of carcinoma penis in our study were of squamous cell carcinoma.

Lack of circumcision, illiteracy, low socio-economic status, associated with poor penile hygiene and smoking were uniform findings in all the cases and appear to be main predisposing factors for carcinoma of penis. Phimosis may be a factor increasing the risk.

Lack of awareness and lack of proper closed bathing facilities seem to be the cause for poor penile hygiene in these patients.

Fear, ignorance, feeling of shame, embarrassment and lack of basic health care may be the reasons for the patients of cancer of penis attending the hospital very late after the onset of the disease sometimes at a stage of inoperability.

The same factors hold good for the patients being lost for follow up. In such a situation of lack of motivation for follow up in patients, prophylactic inguinal lymph node dissection based on primary tumor pathology may be better than surveillance for inguinal metastasis.

Considerable numbers of patients of carcinoma of penis were in sexually active age. Hence, wherever possible penile preserving option and phalloplasty have to be considered.

A simple public health campaign highlighting the significance of penile hygiene, about retracting the prepuce and cleaning the glans, may go a long way in prevention of carcinoma of penis. An awareness campaign about carcinoma of penis and its complete curability by simple surgery without affecting sexual function, with an advice on self-examination of penis for any abnormality, may make the people attend the hospital very early in disease course.

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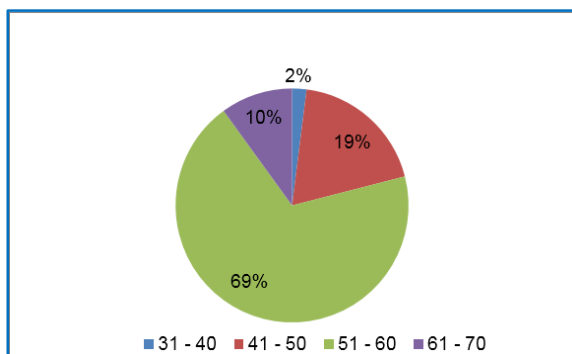


Fig. 1: Age Distribution of Carcinoma Penis

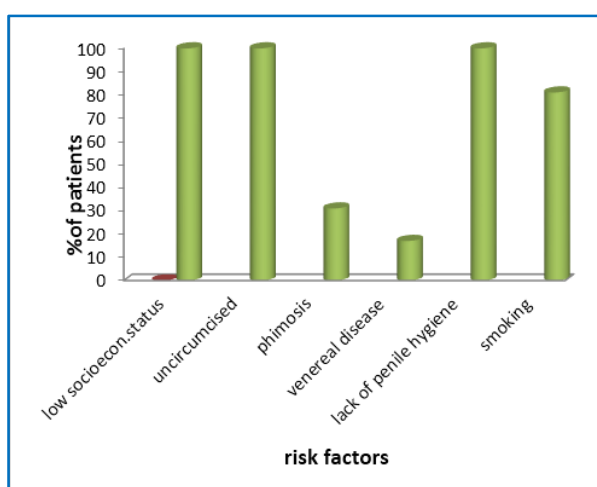


Fig. 2: Associated Risk Factors for Carcinoma of Penis

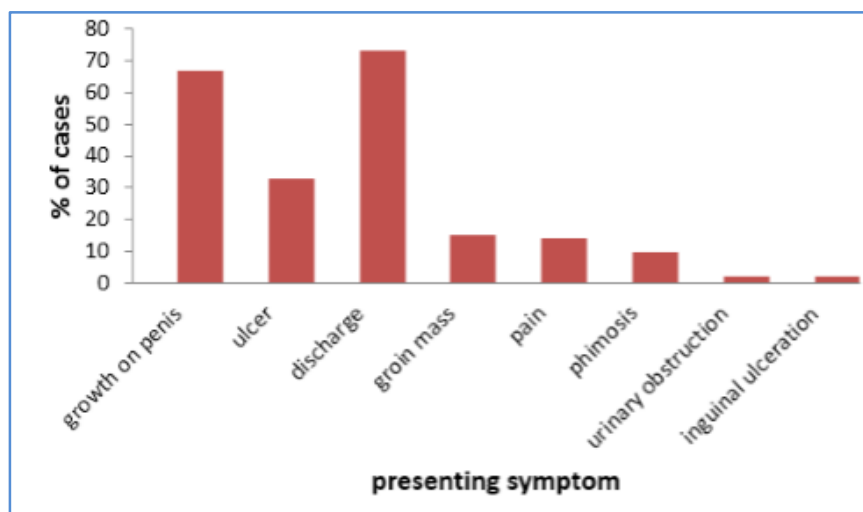


Fig. 3: Presenting Complaints of Carcinoma Penis

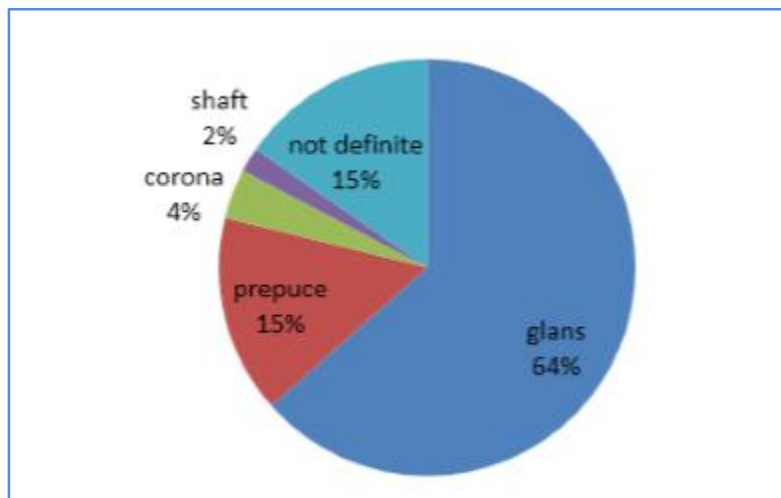


Fig. 4: Site of Commencement of Carcinoma of Penis

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Date of Submission: 21/02/2015.
Date of Peer Review: 22/02/2015.
Date of Acceptance: 03/03/2015.
Date of Publishing: 11/05/2015.