

JUSTIFICATION OF INGUINAL LYMPHADENECTOMY IN MANAGEMENT OF CARCINOMA PENIS

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ABSTRACT

BACKGROUND

Diagnosing penile cancer and grading the same with available diagnostic tools is not difficult, but the problem lies in the management and more so in groin node dissection. Lymphadenectomy is the treatment of choice in patients presenting with positive node at the time of diagnosis, but problem arises in deciding node negative patients. Our aim was to evaluate role of prophylactic inguinal lymphadenectomy in carcinoma of penis.

METHODS

This was a prospective study carried out at MKCG Medical College and Hospital from 2012 to 2017. The clinical, diagnostic and follow-up data were collected from patient records.

RESULTS

A total 30 cases of penile carcinoma were included in the present study. Youngest patient was 29 years of age and oldest was of 78 years. 18 patients showed inguinal lymphadenopathy at the time of diagnosis. FNAC showed node positivity in 10 cases. 2 out of 8 cytologically negative lymph nodes for metastatic deposits came out to be positive after biopsy. Histologically majority diagnosed as moderately differentiated squamous cell carcinoma and were in stage 2. 2 patients diagnosed as verrucous carcinoma. Radical inguinal lymphadenectomy was done in all patients with cytologically proven metastatic deposits, modified radical dissection done in cytologically negative lymphadenopathy cases. In remaining patients of carcinoma penis, without inguinal node involvement, an individualistic approach was undertaken.

CONCLUSIONS

In node positive cases, inguinal node dissection should be carried out, but in node negative cases decision should be more individualistic. It is better to go for a modified radical dissection even with negative node, as it is commonly seen in our set up that patients are lost to follow up. But it should be carried out in a judicious way with an individualistic approach as groin dissection is a mutilating surgery with many complications and decision making is a complex issue though we have many available clinical and pathological criteria.

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BACKGROUND

Penile cancer is a relatively rare malignancy of men and shows significant geographic variation across the globe. In Europe and united states, accounting for 0.4-0.6% of all malignancies.^{1,2} In India incidence ranges from 0.7-3 per 100000 males³ Though exact causes is not known, phimosis, chronic inflammatory conditions, HPV DNA are probable risk factors.⁴ The common histologic type is squamous cell carcinoma, and tends to arise from epithelium of inner prepuce and glans.⁵ Natural history suggests, the spread occurs to ilioinguinal nodes in quite predictable manner.^{6,7} Incidence of significant size palpable groin nodes during initial presentation is around 30-60%. More than 50% are

positive for metastasis but rest enlarged nodes are due to reactive hyperplasia.^{8,9} Though inguinal resection involves complex surgical procedure with associated morbidity, withholding prophylactic inguinal lymphadenectomy may affect the long-term complication. The aim of our present study is to justify inguinal lymphadenectomy in cancer penis patients.

METHODS

This was a prospective study carried out at tertiary care teaching institute from October 2012 to December 2017. 30 clinically diagnosed cases of carcinoma penis were included in the study group. From all cases detail clinical, investigational, cytological and histopathological data were kept.

RESULTS

In our study, peak incidence was in the age group of 60 years and above. Only 2 cases were in the 3rd decade. The youngest patient was 29 years old and the oldest 78 years. All the patients were from low socioeconomic status and there was a history of tobacco addiction in 90% cases. Usual presentation was a growth, and 80% cases came with

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associated discharge, pain and non-retractable fore skin. Period of illness before seeking medical advice was ranging from 1 month to 15 months. Maximum patients seek medical advice after 6 months of gross appearance of lesion. Only 2 patients seek advice within 1 month. Grossly, more than 90% show proliferative growth, rest ulcer infiltrative growth.

Among 30 diagnosed cases of carcinoma penis, 20 patients presented with clinically significant inguinal lymphadenopathy. Small, subcentimeter size lymph nodes were ignored, as it is common to find small nodes in this location due to reactive hyperplasia. 18 patients had unilateral inguinal nodes and 2 had bilateral inguinal lymphadenopathy at the time of presentation. FNAC from penile lesion shows positivity for malignancy in all clinically diagnosed cases except 2 which was given as suspicious for malignancy that later after biopsy came out to be verrucous carcinoma. But FNAC of lymph node shows positive for unilateral inguinal metastasis in 10 cases and 2 showing bilateral inguinal metastasis out of 20 cases. Rest 8 cases showed reactive hyperplasia of lymph node in FNAC. We did radical inguinal dissection with simultaneous partial /total penectomy in all 10 cases presented with positive inguinal nodes. In the remaining 8 cases with inguinal lymphadenopathy but negative for metastasis in FNAC, we opt for modified inguinal block dissection with primary penile surgery. Biopsy came out to be positive in 2 out of 8 FNAC node negative cases.

In the remaining 10 cases without inguinal lymphadenopathy, we took individualistic approach keeping in view of the associated morbidity of groin dissection with disease free survival of the patient. In 2 cases with moderate differentiated squamous cell carcinoma with tumour extending up to shaft of penis, we opt for modified radical groin dissection. Our decision was for modified inguinal lymphadenectomy as our patients show low compliance and do not come for follow up. So, in spite of a chance of increased morbidity we choose for modified inguinal dissection that will be of benefit to patient in terms of long-term disease progression and avoid recurrence. In 2 cases of verrucous carcinoma no groin dissection required. 6 cases with well differentiated squamous cell carcinoma and tumour confining to glans penis we, undertake penile surgery without groin dissection. But in rest 2 patients who were in 6th decade and above with associated comorbid conditions of diabetes with hypertension and COPD we prefer to avoid groin dissection though tumour was moderately differentiated squamous cell carcinoma and of grade T2. Common complication we encountered was lymphedema, wound margin necrosis and wound infection.

So, in the present study we included 30 carcinoma penis cases, out of which 20 have clinical inguinal lymphadenopathy (66%) but FNAC was positive only in 12(60%) cases. We did radical groin dissection in all 12 FNAC proven node positive cases and modified radical dissection in all remaining 8 cases. In 2 cases, lymph node histopathology came out to be positive for metastasis, while cytology report was negative for metastasis. So, false negative was 10%.

Biopsy was done from penile lesion and inguinal lymph nodes in all cases postoperatively. Histologically 2 cases revealed verrucous carcinoma and rest squamous cell carcinoma. Grading was done basing on cellular differentiation. -8 cases show well differentiated tumour, -18-moderately differentiated. Only 2 cases show poorly differentiated squamous cell carcinoma. In all cases TNM staging of the cases under study was done. Maximum patients turned up in stage II. No patient was in stage 4.

Grade of The Primary Tumour	Number of Patients (n=30)
Verrucous carcinoma	2
SCC grade I	8
SCC grade II	18
SCC grade III	2

Table 1. Histopathological Grade of Primary Tumour

DISCUSSION

The penile cancer is an uncommon malignancy with significant geographic variation across the globe. It is not uncommon in Indian population with incidence ranging from 2 to 6% of all cancers. In urban and rural India, it is 0.7-2.3 per 1 lakh male and 3 per 1 lakh male respectively.⁵ The disease itself and its treatment both has significant morbidity, both physical and psychological. Many risk factors are attributed like-phimosis, HPV infection, multiple sexual partners, local inflammatory lesion. The glans (penis is the most common site of origin followed by prepuce, coronal sulcus and shaft.¹⁰ most patients present with localised diseases a mass, ulcer or inflammatory lesion.¹¹ The presence and extent of inguinal lymph node metastasis are the important prognostic factors. As the spread of the disease is mainly by lymphatics, inguinal node management is the major crux in the outcome.

Majority of penile cancers are squamous cell carcinoma, but other malignancy observed are melanoma, sarcoma and basal cell carcinoma. According to WHO, penile squamous cell carcinoma classified as usual verrucous, papillary, warty, sarcomatous, adenosquamous and mixed.¹² Verrucous warty and papillary type associated with low grade and superficial invasion with better survival compared to other type.¹³

Site of Penile Cancer	Number of Patients	Histological Type
Prepuce	2	Verrucous carcinoma
Glans and prepuce	20	Squamous cell carcinoma
Shaft involvement	8	Squamous cell carcinoma

Table 2. Anatomical Site of Penile Involvement

Incidence of inguinal node involvement in cancer penis is around 30-60% at the initial presentation.¹⁴ FNAC is employed to achieve diagnosis with a positive value of 70-

80%.¹⁵ More than 50% are positive for a metastatic disease but rest of the enlarged nodes are because of reactive hyperplasia.^{8,9,13} 60% patients with inguinal lymphadenopathy showed lymph node metastasis by FNAC. After inguinal node dissection, 2 patients came out to be node positive after biopsy, out of the FNAC negative cases. This suggest there may be substantial false negative result. As the involvement of groin node occurs in a sequential and predictable manner, histopathology study is always confirmatory.

Palpable Nodes	Nonpalpable Nodes	FNAC Positive	FNAC Negative	Biopsy Positive
20	10	12	8	14

Table 3. Patients with Clinically Palpable Nodes with FNAC and Biopsy Correlation

As proper management of carcinoma penis depend upon precise diagnosis with staging of the tumour, important prognosis factor is status of inguinal node. The role of imaging is also important in staging the regional nodes. USG is useful to asses non-palpable lymph nodes in obese persons, in patients with prior inguinal surgery, and to know the status of pelvic nodes and distant metastasis. Newer imaging technology like MRI and PET scan, has more sensitivity and specificity in supplementing difficult inguinal region cases, however it is not definitive like cytology or biopsy. In our institution only USG and CT scan is available.

In the present study we included 30 carcinoma penis cases, out of which 20 have clinical inguinal lymphadenopathy (66%) but FNAC was positive only in 12(60%) cases. We did radical groin dissection in all 12 FNAC proven node positive cases and modified radical dissection in all remaining 8 cases. In 2 cases, lymph node histopathology came out to be positive for metastasis, while cytology report was negative for metastasis. So, false negative was 10%.

Biopsy was done from penile lesion and inguinal lymph nodes in all cases postoperatively. Histologically 2 cases revealed verrucous carcinoma and rest squamous cell carcinoma. Grading was done basing on cellular differentiation. -8 cases show well differentiated tumour, - 18-moderately differentiated. Only 2 cases show poorly differentiated squamous cell carcinoma in all cases.

TNM staging of the cases under study was done. Maximum patients turned up in stage 2(70%). No patient was in stage 4.

Risk stratification were done with node positivity and grade of tumour. In node positive cases, radical groin dissection was done. Previously, in node negative and in non-palpable groin node cases, no groin dissection undertaken, especially when the tumour is of low grade and no lymph vascular invasion in the primary tumour, and the patient was kept in regular follow up. Strong predictor of inguinal micro metastasis are tumour grade and presence of lymphovascular invasion, so controversy lie in managing clinically negative groin nodes. But we observed, prophylactic node dissection using modified procedure

shows better result in terms of disease-free survival and recurrence. It can be curative in 20-60% of histologically node positive cases.^{15,16} The five year recurrence free survival is 75-95%.¹⁷ As patient compliance is not good and difficult to follow up regularly, we prefer prophylactic superficial node dissection in node negative and nonpalpable inguinal cases with improved survival outcome and without increased morbidity. Non-invasive tumours are amenable to local measures like 5FU, laser or local excision. A partial and glans sparing appendectomy provides psychosocial benefits, preserves sexual function for a T1 tumour.¹⁸ A 2 cm margin has been advocated, although now some suggesting a 5-10 mm margin to be sufficient¹⁹ total penectomy preferred for >_T2 tumours, but some are amenable to partial resection depending upon the location, that is Mohs surgery if located on the glans and margins more than 3 mm can be attained. Despite the caveats of retrospective analysis, many data suggest the favourable impact of node dissections. Both EAU and NCCN guidelines suggest adapting the extent of lymph node dissection to clinical stage.^{20,21} for low risk patients, pTis/pTa and pT1G1 without palpable lymph nodes, surveillance was recommended. For all other patients, without palpable lymph node modified bilateral lymphadenectomy or sentinel node dissection was recommended. For biopsy proven lymph node metastasis, radical inguinal lymphadenectomy was recommended. In addition, pelvic LN dissection recommended in patients with multiple inguinal nodes, extranodal extension or node of Cloquet involvement. So, although early lymphadenectomy improves the survival in patients, yet the challenge remains to identify who are truly lymph node negative to avoid morbidity of traditional lymphadenectomy.

So, the presence and extent of inguinal lymph node metastasis are the most important factors of prognosis. Squamous cell carcinoma exhibits a prolonged loco regional phase before metastasizing and therefore regional lymphadenectomy advocated.²²

External beam radiation therapy indicated in high risk cases like bilateral metastasis, more than 4 positive nodes, or positive pelvic nodes. The recurrence risk in patients with or without radiation therapy is reported as 11 and 60% respectively. In present study 2 cases treated with EBRT. Neo Adjuvant chemotherapy (NACT) is used in patients with poor prognostic features including multiple, fixed and large (>4 cm) inguinal nodes, distant metastasis. Patients received NACT, to down stage the tumour and later underwent inguinal dissection.

The incidence of distant metastasis at the time of diagnosis is 1.9 to 7%.⁹ Survival is poor with palliative therapy.

CONCLUSIONS

Penile cancer is not uncommon and if detected early, better outcome is predicted. But our patients report late due to lack of awareness and associated psychological fear. As it is difficult to predict patients' compliance during follow up, and as inguinal dissection is the major crux in the management of node positive cases, inguinal dissection is the treatment

of choice, outweighing the associated morbidity. Also, there is always a chance of inaccuracy in clinical exam and FNAC evaluation, non-availability of modern non-invasive imaging technologies. So prophylactic lymphadenectomy has definite advantage though a risk of morbidity is there in node negative cases.

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