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Original Research Article

Clinical study of nodal involvement in carcinoma penis: role of perineural and perivascular invasion in lymph node metastasis

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ABSTRACT

Background: Penile malignancies constitute a major health problem in the developing countries especially the Afro Asian countries. It constitutes about 10% of all malignancy. The incidence of the penile malignancy is in decreasing trend in many parts of the world due to improved awareness about the personal hygiene. In this study special effort was made to analyze the histopathological correlation in predicting the lymph node involvement particularly the perivascular and perineural invasion of a tumor on his to pathology and its influence on the lymph node metastasis.
Methods: After getting prior ethical committee clearance 42 cases of histopathologically proven cases are included in the study. Those patients included are explained about the nature of the study, investigations that are done. They have also discussed the various treatment options available in Thanjavur medical college. Proper consent in patients own language is obtained before including in the study.
Results: The most common histological type found in present study was squalors type. More than 90% (93%) shows squamous variety. Verrucous carcinoma was found in two patients. One patient present with the mixed presentation.
Conclusions: Tumour with high grade, high stage, and perineural and per vascular invasion is associated with more nodal metastasis. It is highly recommended to carry out nodal dissection in such types of a tumor. Screening for the early stage of the disease and addressing for the inguinal nodes for the high-risk group will significantly reduce the morbidity and mortality of carcinoma penis.

Keywords: Nodal metastasis, Penis carcinoma, Squamous cell carcinoma, Verrucous carcinoma

INTRODUCTION

Penile malignancies constitute a major health problem in the developing countries especially the Afro Asian countries. It constitutes about 10% of all malignancy. The incidence of the penile malignancy is in decreasing trend in many parts of the world due to improved awareness about the personal hygiene.[1] The average age of presentation is usually the sixth decade but can also present even 2 to 3 decades earlier. In spite of overall improvement of health status in, India, the morbidity and mortality associated with the penile malignancy were still high. Most patients present very late to the medical attention.[2] In spite of very distressing presentation, most of the penile malignancy if present early is potentially curable due to the various modality of treatment options available.[3] The most important factors in determining the prognosis are the grade of a tumor, staging and the lymph node involvement. Lymph node management is always a challenging area.57% of a clinically positive node do not harbor metastasis and primarily due to secondary infection.[4] But 30% of clinically node-negative harbor metastasis. Since lymph node dissection is associated with higher rates of wound infection, lymphoma, lymphoedema, prophylactic lymph node dissection always remain controversial. In this study special effort

was made to analyze the histopathological correlation in predicting the lymph node involvement particularly the perivascular and perineural invasion of a tumor on histopathology and its influence on the lymph node metastasis. Since lymph node clearance cures the patient in about 80% of the cases proper assessment and timely intervention will save most of the patient.[5]

METHODS

This study is an observational study conducted on the proven cases of carcinoma penis admitted to Thanjavur medical college. This is a prospective study conducted between September 2012 and September 2014. This was conducted on 42 proven cases of carcinoma penis.Cases were selected from the general population of this locality around Thanjavur medical college, those who came for outpatient department. This represents a better interpretation of the result and the interventional strategies can be extrapolated to the general population. The case is defined as the histopathologically proven either by incision or excision biopsy on those patients who attend the outpatient department with clinical suspicious of carcinoma penis.

Inclusion Criteria

- All proven primary cases of carcinoma penis by histopathology.
- Patients with recurrence either at the primary site or nodal site.

Exclusion Criteria

- Other benign conditions of the penis.
- Those patients not willing to take part in the study are excluded.
- Those patients who left the follow up during the period are excluded.
- Those patients who deny the treatment option are excluded.
- Those patients who succumb to disease are excluded.

After getting prior ethical committee clearance 42 cases of histopathologically proven cases are included in the study. Those patients included are explained about the nature of the study, investigations that are done. They have also discussed the various treatment options available in Thanjavur medical college. Proper consent in patients own language is obtained before including in the study. After obtaining through history about the present condition and relevant past history also documented. And detailed clinical examination is made after proper consent and nodal involvement is also documented. Then the patients are subjected to basic investigations such as urine routine, complete blood count, bleeding time, clotting time. Random blood sugar, renal function tests, chest x-ray, and electrocardiogram are obtained. Ultrasound abdomen, computed tomography abdomen and pelvis and MRI penis in selected cases are made. A tumor is then staged clinically by both Jacksons and TNM staging. The patients are then subjected to incision biopsy of the lesion to confirm the diagnosis. Those patients with clinical node positivity were subjected to FNAC of the nodes. In the histopathology, the tumor histological type is studied. A tumor histological grading is made based on Broder's classification. Special interest is shown to corpora invasion. And the detailed study is made on the perineural and perivascular invasion of a tumor. Patients proceed with surgery based on the level of lesion. Patients are subjected to circumcision, partial or total penectomy. The patients with the clinically positive node are followed with 6 weeks of antibiotics. The pathological node at presentation and those nodes that are not regressed after 6 weeks are preceded by block dissection. Either unilateral or bilateral block dissection was carried out depending on the presentation. Patient with margin positivity is subjected to revision surgery. Patients with inoperable nodes are referred for radiation therapy.

RESULTS

Among the 19 cases of well-differentiated carcinoma, only 3 patients showed nodal positivity. Among the 14 cases of moderately differentiated carcinoma, 4 patients showed pathological node positivity. Whereas nodal metastasis was present in all poorly differentiated and mixed variety carcinoma.

Table 1: Correlation between histological grade and nodal involvement.

Histological grade	Pathological node	Percentage
Well differentiated	3/19	16
Moderately differentiatec	4/14	29
Poorly differentiated	2/2	100
Others (mixed)	1/1	100

In present study the correlation was maximum that is 100% for poorly differentiated carcinoma and mixed variety. This was followed by moderately differentiated carcinoma that constitutes about 29% nodal disease. Lastly, well-differentiated carcinoma showed 16% node positivity. Perineural invasion alone was present in 2 cases, out of which one shows positive for the nodal disease. Per vascular invasion alone was present in 7 cases and among them 3 patients present with node metastasis. Both perineural and perivascular invasion was present in 13 patients. And 6 patients showed pathological positive node. Either of the invasions was not statistically significant for the presence of nodal metastasis in present study. But both perivascular and perineural invasion was found to have more chances for nodal metastasis. From the analysis of present study it is seen that higher the stage of the disease, higher is the chance for nodal disease. 38% of the stage III disease in Jackson's stage is associated with the nodal disease. Two cases of stage II disease show nodal positivity. One

harbors an occult metastasis that is revealed after 6 weeks. Another had a mixed type of histology and develops node positivity later.

Table: 2 Correlations between perineural and perivascular invasion and nodal disease.

Neurovascular invasion	Pathological node	Percentage
Perineural invasion	1/2	50
Perivascular invasion	3/7	42
Both	6/13	46

It is seen that the percentage does not show the statistical significance. The numerical value of the node positivity with this study group was very much significant. Stage I disease does not show any nodal involvement. In this stage o and I does not show any node positivity. One case of stage II disease showed positive for a pathological node in the follow-up. Stage IIIa is associated with more lymph node positivity (6 out of 18) than any other stage disease. And stage IIIa is associated with a maximum percentage (100%) of nodal positivity. All the stage IIIb disease show positive for the presence of nodal metastasis. Thus, from both the staging, the nodal involvement is correlated with the higher stage of the disease.

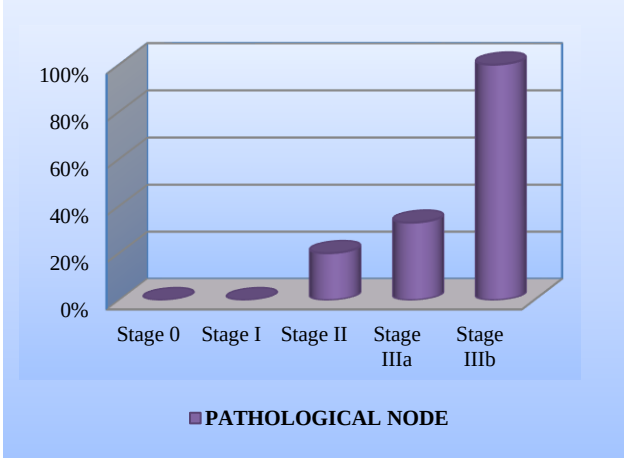

Figure 1: Correlation between stage and nodal disease.

DISCUSSION

Squamous cell carcinoma is the most common histological type seen in present study. It constitutes about more than 90% of the cases. Cubicle and their colleague in 2001 classified the histological variety of carcinoma penis showed squalors to be 59% then papillary is 15%. [6] This was followed by basaltic and warty both constitute 10% each. And finally, verrucous and sarcomatoid constitute 3% each. In present study apart from squalors, cell carcinoma verrucous carcinoma showed 5% incidence. [7] Well-differentiated carcinoma was the most common type of carcinoma in present study. It constitutes about 54% followed by moderately differentiated variety about 40%. According to match group study conducted in 1991 showed the grade 1 and grade 2 lesions were present in 70% to 80%. This incidence was similar to those seen in present study group. Where the both combined together showed slightly higher incidence around 90%.[8] Corpora cavernosa invasion is seen in 19% of the patients and urethral invasion alone is seen in 7% of the patients. In 2008 Beijing and colleague showed that urethral involvement alone is associated with better prognosis and better 5-year survival rate than corpora cavernosa invasion alone.[9] Nodal metastasis was present in all the poorly differentiated carcinoma seen in present study. And it was present in 29% of the moderately differentiated carcinoma. Nodal metastasis is present in only 16% of the well-differentiated carcinoma.[10] Thus the grade 3 a tumor is associated with a high chance of nodal disease. So, it is recommended to carry out block dissection in grade 3 or grade 4 lesion even if clinically palpable nodes are not present. Cuba al.et al. extensively studied the correlation between grade and prognosis depending on nodal metastasis. They found that poorly differentiated carcinoma was associated with more than 50% chance of nodal metastasis. Statistical correlation was obtained with Fischer's exact test for grade 1 and grade 2 a tumor compared with that of grade 3 and grade 4 tumors for nodal metastasis.[11] And the two-tailed P-value equals 0.0168. This was found to be statistically significant. In present study perineural invasion was present in 2 cases out of which one was positive for the nodal disease. Similarly, 3 out of 7 cases showed node positivity for perivascular invasion. And 6 persons out of 13 showed positive for nodal metastasis. Though the numbers are quite varying percentage wise all of them are around 50%.[12] With perineural invasion alone showing a greater chance for nodal metastasis. In his study, he concluded that perineural invasion is an independent prognostic marker for the nodal disease. In his study nodal metastasis was present in 69% of the cases with perineural invasion compared to 50% in present study.[13] Moreover, the study group was larger than the study group of ours. And so further analysis with large study groups on perineural invasion and nodal disease will be needed in future.[14, 15]

CONCLUSION

Health education about the natural course of the disease will have a significant impact on the incidence of the disease. Tumor with high grade, high stage, and perineural and perivascular invasion are associated with more nodal metastasis. It is highly recommended to carry out nodal dissection in such types of tumor. Screening for the early stage of the disease and addressing for the inguinal nodes for the high-risk group will significantly reduce the morbidity and mortality of carcinoma penis.

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