Penile Cancer – the Sentinel Lymph Node Controversy

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Abstract
The management of lymph nodes in penile cancer has always been a problem. Sentinel lymph node biopsy was supposed to solve this problem but has not been universally accepted due to conflicting results. We herein present a case of penile cancer with bilateral pathologically positive inguinal lymph nodes associated with concurrent negative sentinel lymph node biopsies. We discuss the possible reasons for this situation and suggest guidelines to study this issue.

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Introduction
One of the major problems in the treatment of penile cancer is the management of the inguinal lymph nodes [1]. This problem is compounded in developing countries where the incidence of penile cancer is much higher than in the USA, and a majority of the population walks barefoot, leading to non-specific inguinal lymphadenitis [2]. This chronic lymphadenitis usually does not subside after routine penectomy and 4- to 6-week courses of antibiotics. Hence, clinically detecting pathologically positive nodes in such a set-up is difficult.

10 years ago, Cabanas [3] postulated in his extensive work that the sentinel lymph node might be the first node involved in the spread of penile cancer. This work has not been substantiated by similar studies in the USA, primarily due to the small number of cases seen there yearly and hence has resulted in some reservations to the universal acceptance of sentinel lymph node biopsies.

We recently had a patient with penile cancer and bilateral inguinal nodal disease in whom sentinel lymph nodes were negative and this has made us re-evaluate the issue and suggest guidelines to solve the problem.

Case Report
A 45-year-old healthy man was initially seen in January 1986 with a 2-month history of an exophytic mass developing on the glans penis. There was no history of phimosis or venereal disease. Physical examination was unremarkable except for a $2 \times 3$ cm exophytic growth on the
glans penis with bilateral non-specific inguinal lymphadenitis. The largest node was 2.5 × 1 cm on the right side and was tender. Routine laboratory investigations were normal and metastatic work-up comprising of chest x-ray and ultrasound abdomen were negative. The patient underwent a partial penectomy after biopsy confirmation. The histology revealed a well-differentiated grade 2, non-invasive, epidermoid carcinoma confined to the glans penis, and the patient was asked to return after a 6-week course of antibiotics. He however returned in 4 weeks since the right inguinal nodes had increased in size and appeared malignant on clinical examination. A bilateral pelvic lymph node dissection was done through a midline incision and a right groin dissection through a separate elliptical incision. This was followed 3 weeks later by a left groin dissection. In both the groin dissection specimen, the sentinel lymph node was identified and labelled separately for the pathologist. The postoperative course was uneventful except for mild skin necrosis with delayed wound healing in the left groin wound. The final histology revealed negative pelvic nodes with metastasis in 5 out of 11 right inguinal nodes; metastasis in 1 out of 9 left inguinal nodes, and no metastasis in both sentinel nodes. In view of the bilateral involvement, the patient was given 3 courses of combination chemotherapy (methotrexate, bleomycin and cis-platinum) and is doing well 4 years post-operatively with no evidence of disease.

Discussion

The management of the primary penile lesion is non-controversial with partial and radical penectomy being carried out depending on the local tumour extent [4]. Occasionally, in highly selected cases, few centres advise local radiotherapy, instead of penectomy with favourable results [5].

The management of the inguinal nodes, however, has no universally accepted plan with centres advocating immediate (prophylactic) lymphadenectomy or delayed (therapeutic) lymphadenectomy or sentinel lymph node biopsy depending on their experience or preference [6–9].

The idea of sentinel lymph node biopsy, wherein a specific node is biopsied along with the initial penile surgery, is attractive, provided it correctly predicts inguinal lymphatic metastasis. The sentinel lymph node lies two finger breadths below and lateral to the pubic tubercle in the pre-saphenous region where the superficial epigastric vein joins the saphenous vein overlying the sapheno-femoral junction. Cabanas [3] stated that if the sentinel lymph node biopsy was negative, no further dissection need be done, and if the biopsy was positive, a groin dissection should be carried out on that side. In 15 patients with positive sentinel lymph node biopsy he found the groin nodes involved in only 3 cases thus suggesting that the sentinel node was the first and only node involved in the remaining 12 patients. Catalona [10] on the other hand has reported a case wherein the sentinel lymph node biopsy was negative but the patient subsequently developed inguinal lymph node metastasis. In our case the inguinal nodes were pathologically positive whilst the sentinel nodes were negative. However, from single case reports, no conclusions can be drawn. The possible reasons for problems in sentinel lymph node biopsy appear to be:
wrong node identified as the sentinel lymph node and biopsied. This should occur less frequently with more experience and a thorough anatomical knowledge of the surgical field. Improper sectioning of the lymph node thus overlooking microfoci of metastasis in the node – this can be overcome if there is a full discussion with the pathologist and the nodes are carefully step-sectionned.

A long-time lapse between initial sentinel node and groin dissection resulting in lymphatics permeating along alternate channels and metastasizing – a careful examination should be carried out after negative biopsies to detect such an occurrence early.

In our case, however, none of the above reasons can explain the negative sentinel node biopsy. It is possible that in some patients, especially in those with chronic lymphadenitis, secondary to walking barefoot, alternate lymphatic channels develop which bypass the sentinel node and drain directly from the penis to the inguinal nodes. This theory will have to be examined more carefully in a larger series.

Although public education regarding proper penile hygiene might go a long way in reducing the incidence of penile cancer, and improvements in the socio-economic programs might enable the population to afford footwear and thus avoid chronic lymphadenitis, the problem of lymph node management in a given case of penile cancer persists.

Sentinel lymph node biopsy has the potential to alter the management of penile cancer radically. We feel that a properly conducted prospective study is necessary, especially in countries with a large clinical base of penile cancer. At present, all our patients with clinically positive groin nodes are being subjected to a pelvic lymph node dissection with a groin dissection. During the groin dissection, the sentinel lymph node is identified and removed with the other nodes. The sentinel node is labelled separately, and the pathologist step-sections all the nodes carefully.

Thus, we are able to determine unequivocally the pathologic status of the sentinel lymph node, inguinal lymph nodes and pelvic nodes on both sides in every case. Although some operations may seem unnecessary, this sort of a study might be the initial step in resolving the sentinel lymph node controversy and benefit urologists dealing with this problem worldwide.

References