Selective lymphadenectomy for penile cancer

S. BUCHER, M. GUERRA, D. RIBUFFO*

Abstract. – Introduction: Lymph node treatment in patients with penile cancer has been longy debated in the last 15 years, with surgeons advocating therapeutic lymphadenectomy and others advocating selective lymphadenectomy (SLND).

Materials and Methods: We evaluated the outcome of clinically node negative penile cancer patients treated with SLND. Since March 2000, 35 node negative penile cancer patients were operated on mainly at the Division of Plastic Surgery, San Gallicano Institute, Rome (Italy), with SLND.

Results: A sentinel node was detected in 34 out of 35 patients (42 groins). With a minimum of five years follow up, metastases were noted in 5 out of 35 patients. Out of the remaining 30 patients, 2 developed node metastases in the operated inguinal region (6.6%).

Discussion: SLND for penile cancer compared to surveillance only greatly improves survival rate and disease-free rate (91% vs 79% after 3 years follow-up). Identification of more specific markers for SCC lymph node metastases will make the false negative-rate drop further.

Key Words:
Sentinel node, Penile cancer, Surgery, Selective lymphadenectomy.

Introduction

Cancer of the penis is a psychologically and physically devastating disease. The most frequent form is squamous cell carcinoma (SCC). Although it is rare in the western countries (0.5% of any tumour), penile carcinomas are particularly frequent in eastern countries (India: 6%), and in Africa they account for over 20% of any male tumours.

Regional lymph node metastases remain the most important determinants of outcome, with the frequency of inguinal metastases being 35-60%. Surgery remains the preferred treatment for regional lymph node disease (N1) that must be diagnosed after a 4 week antibiotic therapy, in order to reduce non specific lymphadenopathy. Nevertheless, its high morbidity in the form of flap necrosis, infection, seroma and limb edema makes it unsuitable as a routine procedure in N0-NX patients.

Clinical examination of inguinal nodes in penile carcinoma is notoriously inaccurate, and moreover metastases can be present in impalpable lymph nodes. Therefore, after unreliable attempts to detect early nodal metastases with non invasive methods such as ultrasonography, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), surgery has been playing an important role, with selective lymphadenectomy (SLN) being introduced by Cabanas in 1977, and possibly offering comparable results in terms of locating metastatic nodes if compared to radical inguinal lymphadenectomy (RIL). False negative rate still remains the most important problem with this technique, and might reach even 15% in non dedicated hospitals.

We report our caseload with 41 consecutive patients mostly operated within the Division of Plastic Surgery at the San Gallicano Institute, Rome (Italy), since 2000, and partially at the Section of Plastic Surgery at Cagliari University Hospital (Italy), followed up for at least five years after surgery.

Materials and Methods

Forty-one consecutive patients with a histologically proven SCC of the penis (Figure 1) and clinically node negative mostly operated at the Division of Plastic Surgery, San Gallicano Institute in Rome, were enrolled in this study. Jackson’s system of staging was used to categorize patients as:

Corresponding Author: Maristella Guerra, MD; e-mail: maristellaguerra@gmail.com
Lymphoscintigraphy was performed on the day of surgery. A dose of 60 MBq 99Tc nanocolloid in a volume of 0.4-0.6 ml is injected around the tumour. With the aid of a gamma camera, lymphatic flow is studied dynamically during the first 20 minutes. Subsequently, lateral and anterior static views are obtained for five minutes, and repeated 2 hours after injection (Figure 3). After marking the location of the sentinel node(s) on the skin, 1 ml of Patent Blue dye is injected intradermally around the tumour in a similar fashion. Approximately 20 minutes later, a small incision is made over the skin mark, and the sentinel node is searched both by tracing the blue stained lymphatic channels, and by using the gamma probe, searching for areas with at least twice the background activity. Once the sentinel (s) node is removed (Figure 4), the wound is scanned for possible remaining activity with the aid of the gamma probe.

Stage I, tumour confined to the glans and/or prepuce; Stage II: invasion of the corpora with no involvement of regional nodes; Stage III: tumour confined to the shaft, regional nodes involved but operable; Stage IV: involvement of adjacent tissues with inoperable local secondaries and distant metastases. After histological confirmation, the status of lymph nodes was examined. In case of suspect lymphadenopathy, Fine Needle Aspiration Citology (FNAC) was used to exclude macroscopic node positivity. Patients then underwent wide local excision, partial (Figure 2) or total penectomy as needed, according to the European Association of Urologists (EAU) 2009 guidelines. Patients with FNAC positive nodes, inoperable local disease or those with distant metastases (Stages III and IV) were excluded from the study. Mean age of patients was 61 years, clinical stage of the primary tumour was stage I in 21 patients and stage II in 20 patients. Differentiation grade of the tumour was grade I in 20 patients, grade II in 18 patients, and grade III in 3 patients.
Pathological examination of the sentinel node consists of hematoxylin and eosin staining, and immunohistochemical staining using antibodies against pankeratin and CAM 5.2. Standard inguinal node dissection is reserved for positive sentinel node patients.

All patients are seen at 2 months interval during the first 2 postoperative years, and every 6 months thereafter.

Results

Preoperative lymphoscintigraphy always indicated the sentinel node (s). A total of 69 sentinel nodes were detected in 51 lymph node basins. Intraoperative location of the sentinel node was successful in 40 patients. Mean exploration time was 40 minutes, range 10 min to 70.

Metastases were noted in 6 out of 41 patients, and in every such case patients underwent a radical inguinal lymphadenectomy, which took place one to two weeks postoperatively. When other metastases were noted in the inguinal dissection, iliac node dissection was carried out.

At follow-up, metastases in the operated groin were noted in 3 patients (false-negative rate: 8.57%).

Minor complications with uneventful definitive report such as infection, seroma and delayed healing were noted in 5 patients (12.1%).

Discussion

Penile carcinoma has a preferential trend to metastasize via a lymphatic route. More specifically, it has been shown that the prepuce and the shaft usually drain to the superficial inguinal nodes, whereas the glans and the corpora more frequently drain to the deep inguinal nodes.

Metastases to the regional node represent the most important determinant of outcome. Kroon and Horenblas\cite{2} have shown that an early resection of inguinal lymph node metastases is highly desirable, and greatly improves survival (84% vs 35%).

Nevertheless, prophylactic lymphadenectomy, which should be a bilateral procedure, has a very high morbidity, with possible flap necrosis, severe limb edema, seromas and infections, so that a non invasive method of locating node recurrence would be highly desirable.

However, clinical or instrumental examination alone is highly inaccurate in showing metastatic nodes, and this finding is peculiar to SCC of the penis and greatly differs, for example, from melanoma. In India, where this disease is particularly frequent, usual habit of barefoot walking for long distances produces reactive lymphadenopathy in almost 70% of patients\cite{7}.

Attempts to identify a subgroup of patients who are more likely to have nodal metastases have been made. Fine needle aspiration citology (FNAC) is an accurate method of identifying involved nodes, but, for example, in a patient with many small nodes all of them should be sampled before excluding recurrence, and false negative rates are high. Also, FNAC is obviously inapplicable when nodes are im palpable\cite{7}.

Cabanas\cite{3}, after a study of lymphangiograms and cadaveric dissections, concluded that the lymph node lying anteromedial to the junction of the saphenous vein and the superficial epigastric vein was the first site of lymphatic spread from carcinoma of the penis, and termed it the sentinel node. He suggested an en-block dissection of the inguinal basin only if that node was positive\cite{3}.

Although other Authors have investigated the role of the medial inguinal node (MIL)\cite{7}, were Morton et al\cite{8} who took the sentinel node concept a step further in 1992, using a vital dye together with a gamma probe locator for melanoma patients. Horenblas et al\cite{9} were the first to use this technique, which they called dynamic in contrast to Cabanas’ static procedure, for SCC of the penis only in 2000.

Therefore, surgical oncology research for carcinoma of the penis is pretty much recent and still ongoing, also because, in contrast with melanoma, most reported series are based on a low number of patients (hundreds compared to thousands). Solsona et al\cite{10} proposed three risk groups for occult lymph node metastases based on tumour stage and grade. However, a policy based only on risk stratification can still result in substantial false positive and false negative rates\cite{3}.

Currently, some important statement can be made, and these findings are similar compared with results on SLN for melanoma: (a) Perdonà et al\cite{4} have showed that SLN for cN0 penile cancer has the same rate of discovering occult metastases if compared to RIL (36.9% vs 36.4%), and then should obviously be preferred; (b) SLND compared to surveillance greatly improves survival rate and disease-free rate (91% vs
79% after 3 years)\textsuperscript{11}. This has been shown for melanoma only very recently, after big case series with long-term follow-up; (c) False negative rate still remains high (up to 15%), possibly due to non routine use of immunohistochemistry, or other markers, differently for melanoma\textsuperscript{5}, although Hughes et al\textsuperscript{12}, in the most extensive study on this topic, have shown that this rate can drop to 5%. The identification of more specific markers for SCC lymph node metastases certainly will make the false negative-rate drop further.

References


