Preoperative Lymphoscintigraphy and Dynamic Sentinel Node Biopsy for Staging Penile Cancer: Results With Pathological Correlation

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Purpose: We assessed the sensitivity of preoperative lymphoscintigraphy and dynamic sentinel node biopsy for staging the inguinal region of patients with penile cancer and no palpable inguinal adenopathy.

Materials and Methods: The records of 31 patients with invasive penile cancer and nonpalpable (29) or nonsuspicious (2) inguinal lymph nodes were reviewed. Preoperatively lymphoscintigraphy plus dynamic sentinel node biopsy with ^{99m}technetium labeled sulfur colloid and isosulfan blue dye was performed in 21 patients and dynamic sentinel node biopsy alone with blue dye only was done in 10. All patients underwent superficial lymph node dissection regardless of preoperative lymphoscintigraphy or dynamic sentinel node biopsy findings to establish pathological nodal status.

Results: Six of 32 groins that showed drainage on preoperative lymphoscintigraphy had inguinal node metastasis, as did 1 of 10 that was drainage negative. The sensitivity of preoperative lymphoscintigraphy drainage for cancer detection was 86%. Using dynamic sentinel node biopsy with blue dye plus radiotracer 5 sentinel lymph nodes were positive for cancer, although 2 false-negative results were obtained. Thus, the sensitivity of dynamic sentinel node biopsy per groin for cancer detection was 71%.

Conclusions: In our experience preoperative lymphoscintigraphy and dynamic sentinel node biopsy as currently performed remain insufficient for detecting occult inguinal disease. Superficial lymph node dissection remains the gold standard for detecting inguinal microscopic metastasis in select patients.

Key Words: penis, penile neoplasms, lymph nodes, radionuclide imaging, sentinel lymph node biopsy

In patients with SCC of the penis harboring microscopic metastases ILND is potentially curative.[2] Early ILND is efficacious as prior series have demonstrated 5-year survival rates of 57% to 100% vs 8% to 24% in patients who present later with clinically detected regional lymph node metastases.[1–3] Although the morbidity of prophylactic ILND has decreased in the last 2 decades with recently reported major and minor complication rates of 14% and 35%, respectively,[4] there remains some risk associated with the surgery, including leg edema, skin flap necrosis, infection or the need for wound reexploration.

To select higher risk candidates for ILND a number of prognostic factors for inguinal metastases have been identified, including tumor stage, grade, percent of poorly differentiated carcinoma and lymphovascular invasion.[3,5–7] Based on these data compliant patients with penile cancer who are candidates for careful surveillance of the inguinal region are those with clinical lymph node negative disease in whom the primary tumor shows carcinoma in situ or verrucous carcinoma alone, or stage T1 primary tumors that are well to moderately differentiated and lack lymphovascular invasion. Nevertheless, since many patients at high risk with node negative disease do not show inguinal metastases, accurate minimally invasive strategies are needed to decrease unnecessary ILND procedures and their associated morbidity.

The concept of a sentinel lymph node at the primary inguinal landing site in penile cancer was proposed almost 30 years ago by Cabanas.[8] However, reports of the diagnostic usefulness of sentinel lymph node biopsy at a designated inguinal area to identify regional lymph node metastasis have shown a significant rate of false-negative results and subsequent fatal outcomes in some cases.[9] The pioneering studies of Morton et al in melanoma and of researchers at NCI in penile cancer[10] stimulated a resurgence of interest in sentinel node biopsy via lymphatic mapping. Such techniques trace lymphatic drainage from the penis using blue dye alone or with radiotracer to a draining inguinal lymph node (DSNB).[11–13] Recent data from NCI showed that sentinel lymph node biopsy is feasible and associated with low morbidity, although the false-negative rate was approximately 18%.[11] We prospectively determined the sensitivity of preoperative ^{99m}Tc labeled sulfur-colloid POL and DSNB

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with ^{99m}Tc labeled sulfur colloid plus blue dye or with blue dye alone for identifying sentinel lymph node involvement of SCC of the penis.

METHODS

Study Design

A total of 31 patients with SCC of the penis and nonpalpable (29) or nonsuspicious, soft, less than 1 cm (2) lymph nodes were prospectively enrolled in 2 Institutional Review Board approved studies assessing DSNB with isosulfan blue dye only in 10, and POL plus DSNB with ^{99m}Tc labeled sulfur-colloid injected radiotracer and isosulfan blue dye in 21. Staging was accomplished by physical examination. Liver function tests and computerized tomography of the abdomen and pelvis were done as needed in patients who were obese or when physical examination of the inguinal region was believed to be unreliable. The 1997 TNM classification system was used for staging.[14]

All patients undergoing POL were injected with 0.2 cc (18.5 MBq) ^{99m}Tc labeled sulfur-colloid into the dermis adjacent to the penile lesion or into the dorsal dermal lymphatics if partial penectomy was performed previously. POL was performed within 7 days of scheduled ILND with subsequent γ imaging done to determine the pattern of lymphatic flow from the dermis to the inguinal/pelvic region (fig. 1). The morning of scheduled surgery patients received another dose of ^{99m}Tc labeled sulfur colloid and were subsequently taken to the operating room for DSNB. At surgery approximately 1.0 ml isosulfan blue dye was also injected into the dermis at the junction of the penile lesion and normal adjacent skin. If the patient previously underwent excisional biopsy or partial penectomy, the injection was placed into the dermal lymphatics adjacent to the scar. The sign of successful injection was a raised cutaneous bleb with evidence of blue dye in the dermal lymphatics coursing toward the inguinal region (fig. 2, *A*).

Approximately 30 to 60 minutes after preoperative injection of ^{99m}Tc labeled sulfur colloid and at least 10 minutes after isosulfan blue dye administration an inguinal incision was created for superficial dissection. Skin flaps were elevated at the level of Scarpa's fascia to expose the inguinal field and DSNB was performed. Using an open technique, which differs from that described by Horenblas et al,[13] we could actually trace lymph drainage from the base of the penis to the inguinal region. In an inguinal field a result was considered positive when blue dye was traced directly to a lymph node group, ie blue (fig. 2, *B*), or when γ detected counts obtained using a hand held γ probe were at least 5-fold higher than background counts, ie hot.

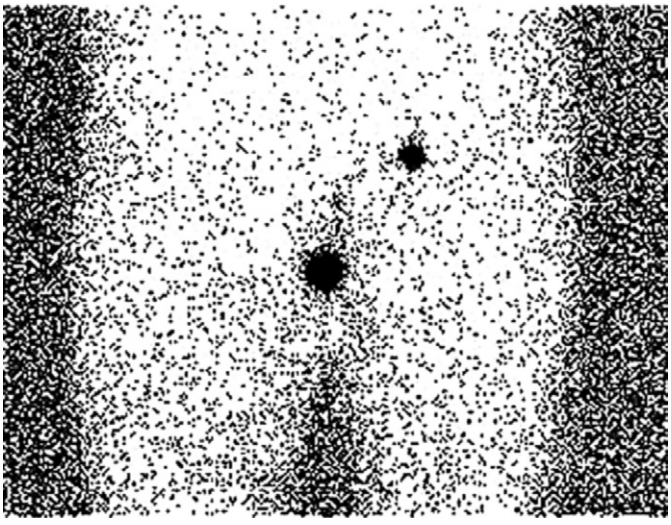

FIG. 1. Anteroposterior view in 67-year-old patient with T2N0M0 SCC of penis who previously underwent partial penectomy and had unilateral positive POL on left side.

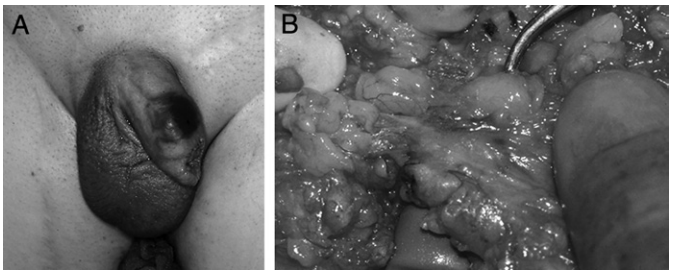

FIG. 2. Isosulfan blue dye injection during DSNB at site of surgical scar from previous partial penectomy (*A*) and subsequent staining of lymphatic channels and sentinel node with DSNB using isosulfan blue dye (*B*).

All lymph nodes that stained blue or in which γ tested counts were positive were marked with a silk suture. Inguinal lymph drainage from the penis was designated as unilateral or bilateral in the inguinal region. The location of lymph nodes in the superficial inguinal lymph node field was defined as medial or lateral with respect to the saphenofemoral junction.

Bilateral superficial ILND was performed in all patients regardless of POL or DSNB findings with immediate pathological assessment of nodal status done by frozen section analysis. All sentinel lymph nodes were serially sliced (bread loafed) perpendicular to the long axis of the lymph node at 2.0 to 3.0 mm intervals and submitted in their entirety for frozen section diagnosis. The nonsentinel lymph nodes obtained by superficial ILND were also submitted entirely for frozen section analysis. Deep ILND and ipsilateral pelvic lymph node dissection were performed if the patient had inguinal metastasis in the superficial ILND, as demonstrated on frozen section analysis. All ILND and pelvic lymph node dissections were performed by 1 surgeon (CAP). Patients were seen every 3 months for postoperative followup during years 1 and 2, and subsequently every 6 months thereafter.

Statistical Analysis

The range and median are reported for patient age at diagnosis, total number of sentinel lymph nodes detected, number of metastatic nodes detected and radioactivity counts on DSNB. The sensitivity of POL and DSNB for cancer detection was calculated as the number of positive test results divided by the number of positive and false-negative test results. All 31 patients were included in our analysis of DSS with a median DSS of 3.3 years. Of the patients 28 were alive at the time of analysis and 3 had died of penile cancer (1) and other causes (2). Median followup for our entire patient population from the date of initial treatment for penile cancer was 3.0 years (range 4.7 months to 12.3 years). Median followup in survivors was 4.1 years (range 5 months to 4.0 years). All statistical analyses were performed using