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Sentinel lymph node biopsy in penile carcinoma

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Sentinel lymph node (SLN) biopsy is a fairly new technique that is becoming the standard of care for regional lymph node staging of many solid tumors. This technique is based on the hypothesis of stepwise distribution of malignant cells in the lymphatic system. The absence of tumor cells in the first lymph node(s) in the lymphatic drainage of a tumor would indicate the absence of further spread in the regional lymph node basin(s). Therefore, this first lymph node is the guardian (sentinel) of the regional lymph node basin. To localize the sentinel node preoperatively, lymphoscintigraphy is usually performed after intradermal peritumoral injections of colloid particles labeled with technetium-99m. The tracer is transported through the lymphatic channels to the first draining nodes in the groins and is visible on the lymphoscintigram as hot spots. The main advantage of SLN biopsy in penile cancer is to decrease the treatment-related morbidity without compromising the survival benefit for the patient. Recent figures indicate a false-negative rate of 7%, with a complication rate of less than 5% for SLN biopsy. In conclusion, sentinel node biopsy of patients with penile cancer has evolved into a highly reliable procedure enabling the detection of lymph node invasion at the earliest possible time with minimal morbidity. With this technology at hand, which minimizes the treatment-related morbidity, there is hardly any place for standard lymphadenectomy in penile cancer patients.

Sentinel lymph node (SLN) biopsy is a fairly new technique in medical practice that is becoming the standard of care for regional lymph node staging of many solid tumors. This technique is based on the hypothesis of stepwise distribution of malignant cells in the lymphatic system. The absence of tumor cells in the first lymph node(s) in the lymphatic drainage of a tumor indicates the absence of further spread in the regional lymph node basin(s). This first lymph node is therefore the guardian (sentinel) of the regional lymph node basin. SLN biopsy is actually the preferred method of lymph node staging in breast cancer and melanoma.[1] This field is also rapidly extending to other tumors, including urologic malignancies. In 1977, the SLN concept was applied in penile cancer by Cabañas.[2] Since that time, several groups have reported the accuracy of SLN biopsy in penile cancer as an alternative to inguinal lymph node dissection. Moreover, this procedure has been included in the 2009 European Association of Urology guidelines on penile cancer.[3]

Lymph node staging in general is hampered by inaccuracy in detecting lymph node invasion at an early stage. Most patients with penile carcinoma present with clinically impalpable lymph nodes. Nevertheless, approximately 20% to 25% of these patients have occult regional lymph node metastasis that is undetectable by current imaging modalities. Removal of nodal metastases at the earliest possible time, preferably in patients with impalpable lymph nodes and only microscopic invasion, improves survival considerably compared with surgical removal at the time when metastases become clinically palpable.[4] Standard lymph node dissection in all penile cancer patients would circumvent all risks. However, regional lymph node dissection in penile cancer results in significant morbidity and is unnecessary in almost 75% to 80% of patients.[5] The main advan-

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tage of SLN biopsy in penile cancer is to decrease this morbidity without compromising the survival benefit of the patients.

History

The SLN concept was first described in parotid carcinomas by Gould and colleagues in 1960.[6] In 1977, Cabañas[2] investigated the SLN concept in 46 cases of penile carcinoma. They injected contrast medium into the dorsal lymphatics of the penis and found "evidence of the existence of a specific lymph center, the so-called 'sentinel lymph node,' in the lymphatic drainage of the penis." More importantly, biopsy of the sentinel node could indicate the tumor status of the entire nodal basin. Reports of SLN biopsy in patients with breast cancer emerged in the 1990s, along with the development of alternative methods for identification of the SLN.[7,8] These methods, including the use of radioactive tracers and patent blue dye, were further investigated in cervical cancer, endometrial cancer, melanoma, and penis cancer.[9-11] Modern sentinel node biopsy is based on pre- and peroperative imaging. Using a radioactive tracer, single photon emission computed tomography (SPECT)/computed tomography (CT) scanning, patent blue during the operation, and a handheld gamma camera, the node labeled as the sentinel node can be found with great accuracy.

Lymphatic drainage of the penis

The regional lymph nodes of the penis are located in the groin. Various authors have described the anatomy of these nodes.[12-14] It is customary to divide the inguinal nodes into two groups, superficial and deep. The superficial nodes are located beneath Scarpa's fascia and above the fascia lata covering the muscles of the thigh. Eight to 25 nodes are present. The deep inguinal nodes are situated around the fossa ovalis, the opening in the fascia lata where the saphenous vein drains into the femoral vein. Three to 5 nodes are present there. These nodes form the link to the second-line regional nodes (ie, the pelvic nodes). The deep inguinal nodes receive their afferents from the superficial nodes and directly from the deeper structures of the penis. From a clinical perspective, this anatomical distinction is useless because the superficial nodes cannot be distinguished from the deep nodes by physical examination.

The most constant and usually largest inguinal node is found medial to the femoral vein and just beneath the inguinal ligament, the so-called node of Cloquet or Rosenmüller. Traditionally, the inguinal region is divided into four sections by drawing a horizontal and vertical line through the point where the saphenous vein drains into the femoral vein. The nodes that are mainly involved in penile carcinoma are typically located in the craniomedial segment, although there is individual variation.[15] The penis drains bilaterally in most patients, as demonstrated by lymphoscintigraphy studies.[16,17] The pelvic nodes are located around the iliac vessels and in the obturator fossa. Approximately 12 to 20 pelvic nodes are present here. Inguinal lymphadenectomy consists of the removal of all regional nodes in the groin, and pelvic lymphadenectomy comprises the removal of all pelvic nodes.

Definition of sentinel node

Which node is defined as the sentinel node? The best definition is probably that of Morton, "the first lymph node that receives afferent drainage from a primary tumor."[18] Early experiences in finding the sentinel node were hampered by high false-negative findings resulting from the individual variations in the anatomy of lymphatic drainage. With the advent of radioactive tracers, preoperative individual mapping of the lymphatic drainage became a reality. Tracing the sentinel node is currently possible with great accuracy using preoperative lymphoscintigraphy and a handheld gamma detector during the operation to identify hot spots. Injecting patent blue just before surgery colors lymph channels and lymph nodes, helping the surgeon to identify the sentinel node and to distinguish second-echelon nodes from the sentinel node. A hot spot in the inguinal region on the scintigram is considered a sentinel node if an afferent lymphatic channel is visualized, if the hot spot is the only one in the basin, or if the hot spot is the first one seen in a sequential pattern. The location of the sentinel node is marked on the skin using real-time imaging and a ^{57}Co pen (Figure 1).

Lymphoscintigraphy

To localize the sentinel node preoperatively, lymphoscintigraphy is usually performed after intradermal peritumoral

Figure 1 Recurrent cancer after partial penectomy. Patient is scheduled for total amputation and sentinel node biopsy. Skin markings set during lymphoscintigraphy help to identify the sentinel node.