Sentinel Lymph Node Biopsy Performed With Local Anesthesia in Patients With Early-Stage Breast Carcinoma

Alberto Luini, MD; Giovanna Gatti, MD; Antonio Frasson, MD, PhD; Paola Naninato, MD; Cesare Magalotti, MD; Paolo Arnone, MD; Giuseppe Viale, MD; Giancarlo Pruneri, MD; Viviana Galimberti, MD; Concetta De Cicco, MD; Umberto Veronesi, MD, PhD

Hypothesis: Sentinel lymph node (SN) biopsy performed with local anesthesia has a positive effect on patients’ quality of life and on treatment management for early-stage breast carcinoma. This method represents an interesting development in breast-conserving surgery.

Design: We performed SN biopsy with local anesthesia in selected patients to test the feasibility of the technique and its impact on our organization and on patients’ quality of life.

Patients and Methods: From September 2000 to December 2001, we studied 115 patients with a palpable breast tumor (maximum diameter, 2.5 cm). The axilla was clinically negative for metastasis in all cases.

Results: Forty-eight patients (41.7%) had SNs that were positive for metastasis. In 20 cases (17.4%), the SN was macrometastatic and in 28 cases (24.3%), it was micrometastatic (diameter <2 mm). The SN was negative for metastasis in 66 cases (57.4%). In 1 case, the histologic examination revealed the presence of a non-Hodgkin B-cell lymphoma. The complete axillary dissection performed in the subgroup of patients with macrometastatic SNs showed that in 9 cases (45%), the SN was the only positive node. In another 9 cases (45%), patients had fewer than 4 positive axillary lymph nodes; more than 4 axillary nodes were metastatic in 2 cases (10%). Among the 28 patients with SN micrometastasis, 21 received complete axillary dissection: 15 patients (53.6%) had no other metastasis to the axillary nodes and 6 patients (21.4%) had cancer cells in other axillary nodes. In case of micrometastasis, we suggested that patients enter the International Breast Cancer Study Group 2301 trial (15 of them accepted and signed the informed consent), which compared completion of axillary dissection with no further surgical treatment of the axilla. Based on randomization, 7 patients (25%) in the group with micrometastasis to the SN received no axillary dissection. Patients’ tolerance to this kind of treatment was excellent.

Conclusion: Our experience indicates that SN biopsy performed with local anesthesia can be a suitable alternative to standard intraoperative evaluation with general anesthesia in patients with unifocal, early-stage breast carcinoma.

Arch Surg. 2002;137:1157-1160

The introduction of the sentinel lymph node (SN) biopsy has dramatically changed the surgical approach to early-stage breast cancer. The positive effect of this technique on patients’ quality of life and on treatment costs, without compromising oncologic information, allowed us to perform this procedure on a large population of patients. At the European Institute of Oncology in Milan, Italy, we recently performed SN biopsies using local anesthesia on a selected group of 115 patients to verify the feasibility of this procedure and its effectiveness on the therapeutic approach to early-stage breast carcinoma.

Surgical dissection of the axillary lymph nodes has been part of the standard surgical approach to breast cancer treatment for years. Its value is mainly informative, especially in limited-stage disease, to ensure the most accurate staging and then guide the adjuvant treatment decisions. Unfortunately, complete axillary dissection is not free of uncomfortable sequelae and often could be considered an unnecessary procedure.

In our experience, SN biopsy applied to early-stage breast tumors is a very good alternative option to predict axillary lymph node status while avoiding complete axillary dissection. In 1996, at the European Institute of Oncology, we performed a validation study of the SN biopsy with 3 main objectives: to successfully identify an SN using technetium Tc 99m, to surgically remove the SN, and to determine whether the SN accurately predicted the axillary lymph node status. Until March 1998, 376 patients were en-
rolled in the study. The SN was correctly identified in 371 patients (98.7%), and in 259 (96.8%), the SN accurately predicted the axillary lymph node status. Our experience with this validation study, together with the preliminary results of our randomized trial on SN biopsy, which is in the active phase of follow-up, gave us enough confidence to adopt SN biopsy as a standard surgical practice for the axilla in selected cases of early breast carcinoma. Sentinel node biopsy has usually been performed on patients receiving general anesthesia, with a significant prolongation of the time needed to complete surgery. The aims of this article are to report our experience with SN biopsy performed with local anesthesia and to demonstrate the feasibility of this procedure.

PATIENTS AND METHODS

From September 2000 through December 2001, 115 patients with invasive T1/T2-N0 breast cancer underwent SN biopsy while receiving local anesthesia at the European Institute of Oncology. We selected patients with a histologically proven, invasive, unifocal breast carcinoma with a maximum mammographic/ultrasonographic diameter of 2.5 cm. These patients had no clinical and ultrasonographic evidence of axillary node involvement. After being fully informed of the different steps of the procedure and signing the informed consent, they were injected with a mixture of colloidal human albumin particles labeled with technetium Tc 99m the day before surgery or the same day, a few hours prior to surgery in the nuclear medicine division. The SN was identified using a gamma probe and removed; it was then extensively examined histologically and immunohistochemically.

SURGICAL TECHNIQUE

The SN biopsy can easily be easily performed with local anesthesia in 1 day or a few hours after the injection of the radiocolloid substance and the localization of the corresponding skin projection of the SN by the gamma probe (Neoprobe; Ethicon Endosurgery, Cincinnati, Ohio). In principle, the surgical procedure can be started 1 hour after the radiocolloid injection. The patient, supine with the ipsilateral arm extended at a 90° position, receives continuous monitoring by electrocardiogram and pulsoxymetry. It is important to have peripheral venous access for infusion of fluids or drugs if necessary. The first step is to choose the best incision skin incision technique to be used. When making the surgical incision, the following should be kept in mind:

1. Selection of the skin fold closest to the SN skin marker to obtain a good cosmetic result after healing.
2. Careful consideration of the primary tumor site, especially if it is in the upper external quadrant. In this case, 2 separate incisions may give a less acceptable cosmetic result.
3. Selection of a skin incision that is surgically and cosmetically compatible with a possible subsequent axillary dissection.

Intradermic local anesthesia is administered by injection with 2 to 5 mL of carbocaine without adrenaline (2% mepivacaine, 4 mg/mL, maximum 400 mg; onset, 3–5 minutes; peak, 15–45 minutes; duration, 0.75–1.5 hours) and sodium bicarbonate (1:10). At the end of the injection, before the surgical incision, we administer 0.05 mg of intravenous fentanyl, which is repeated after 5 minutes in case of pain. In anxious patients, we administer 1 mg of midazolam.

After making cutaneous and subcutaneous incisions 3 to 4 cm long, the axillary fascia is opened to expose the axillary cavity. The SN is then detected by the gamma probe, which is slowly moved inside the surgical brech until the SN is clearly localized, after which the adipose tissue is dissected until the node is completely isolated and the radioactivity is measured to confirm the identification.

The highest accuracy is required when dissecting the SN to respect the surrounding anatomical structures and to protect the lymph node capsule (which is critical for the subsequent evaluation of the entity of nodal involvement) from possible damage caused by the electrocoagulation. During the surgical session, further infiltration of local anesthesia is usually needed. The SN could be localized strictly close to small vascular or nervous structures (sometimes also to thoracic-dorsal or intercostal-brachial nerves). The total amount of local anesthesia used in most patients is 10 to 20 mL. When surgery is prolonged for technical reasons, we repeat the administration of fentanyl and midazolam after 30 minutes.

The procedure is concluded by the coagulation of blood in the SN and the section of the lymphatic vessels. After the SN excision, the surgeon again checks the radioactivity of the removed lymph node and of the surgical brech in the axillary cavity to look for additional radioactive nodes.

At the completion of the operation, hemostasis is carefully controlled and the cutaneous and subcutaneous incisions are sutured with absorbable monofilament. Patients are dismissed after a short clinical observation in the breast surgery division.

HISTOPATHOLOGIC EXAMINATION

All of the SNs are received fresh in the pathology department and fixed uncet if they are less than 5 mm in thickness. If they are 5 to 10 mm thick, the lymph nodes are bisected along the major axis; if thicker than 1 cm, they are sliced at 3- to 4-mm intervals before being fixed in 10% neutral buffered formalin for 6 to 8 hours under vacuum at 37°C. All of the available tissue slices are then dehydrated, cleared, and embedded in paraffin. From the paraffin blocks, pairs of sections are cut at 30-µm intervals until the nodes are completely sectioned. One section of each pair is routinely stained with hematoxylin-eosin while the mirror sections are kept unstained for the possible immunohistochemical localization of low-molecular-weight cytokeratins, using the MNF116 monoclonal antibody (Dako, Glostrup, Denmark). Immunohistochemical analysis is only performed when deemed necessary to assess the nature of atypical cells suspicious for malignancy as seen in the corresponding hematoxylin-eosin preparations. The maximum size of the lymph node metastases along the 3 planes is recorded as previously reported and the metastatic loci whose greatest dimensions reached 2 mm are reported as micrometastases.

RESULTS

From September 2000 through December 2001, 115 patients in our center underwent SN biopsy while receiving local anesthesia. The mean age of the patients was 54 years (range, 27–77 years) and the mean number of SNs identified per patient was 1.56 (range, 1–4). A total of 180 lymph node were removed in this group of patients. Forty-eight patients (41.7%) had SNs that were positive for metastasis. In 20 cases (17.4%), the SN was macrometastatic and in 28 cases (24.3%), it was micrometastatic (diameter < 2 mm). The SN was negative for metastasis in 66 cases (57.4%). In one case, histologic analysis revealed the presence of a non-Hodgkin B-cell lymphoma.
The complete axillary dissection performed in the subgroup of patients with macrometastatic SNs showed that in 9 cases (45%), the SN was the only positive node. In another 9 cases (45%), patients had fewer than 4 positive axillary lymph nodes; more than 4 axillary nodes were metastatic in 2 cases (10%).

Among the 28 patients with SN micrometastasis, 21 received complete axillary dissection: 15 patients (53.6%) had no other metastasis to the axillary nodes, and 6 patients (21.4%) had cancer cells in other axillary nodes. In case of micrometastasis, we suggested that patients enter the International Breast Cancer Study Group 2301 trial (15 of them accepted and signed the informed consent), which compared completion of axillary dissection with no further surgical treatment of the axilla. Based on randomization, 7 patients (25%) in the group with micrometastasis to the SN received no axillary dissection.

The overall results of the histologic analyses for SNs in our group of patients are presented in Table 1. The mean primary tumor diameter was 1.44 cm (range 0.2-4.5 cm; median value 1.4 cm). In 79 patients, histologic analysis revealed the presence of an infiltrating ductal carcinoma; in 13 patients, an infiltrating lobular carcinoma was found; and in 20, we detected other types of breast neoplasm. Two patients had a noninfiltrating breast carcinoma (Table 2). One patient underwent an SN biopsy for a breast lesion and had a diagnosis of non-Hodgkin lymphoma.

Because of the greater confidence of the surgeons in performing the technique after the first patients, the mean time to complete the procedure was 20 minutes. No patients suffered immediate or late surgical complications. No cases of postoperative axillary hematoma or infection were observed in the days and weeks following SN biopsy. All patients underwent conservative surgery for the breast carcinoma 1 week later without any delay caused by the previous SN biopsy.

<table>
<thead>
<tr>
<th>Table 1. Histologic Characteristics of Sentinel and Axillary Nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total No. of cases</strong></td>
</tr>
<tr>
<td><strong>Average No. of nodes indentified and removed</strong></td>
</tr>
<tr>
<td><strong>Negative sentinel node</strong></td>
</tr>
<tr>
<td><strong>Positive sentinel node</strong></td>
</tr>
<tr>
<td><strong>Total micrometastases of the sentinel node</strong></td>
</tr>
<tr>
<td><strong>Macrometastasis of the sentinel node only</strong></td>
</tr>
<tr>
<td><strong>Macrometastasis of the sentinel node and other axillary metastases</strong></td>
</tr>
<tr>
<td><strong>Total micrometastases of the sentinel node</strong></td>
</tr>
<tr>
<td><strong>Micrometastasis of the sentinel node only</strong></td>
</tr>
<tr>
<td><strong>Micrometastasis of the sentinel node and other axillary metastases</strong></td>
</tr>
<tr>
<td><strong>Micrometastasis of the sentinel node, no axillary dissection</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2. Breast Histologic Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. (%)</strong></td>
</tr>
<tr>
<td><strong>Ductal infiltrating carcinoma</strong></td>
</tr>
<tr>
<td><strong>Lobular infiltrating carcinoma</strong></td>
</tr>
<tr>
<td><strong>Other types of breast malignancies</strong></td>
</tr>
<tr>
<td><strong>Noninfiltrating carcinoma</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

Comment

There are only occasional reports on the practice of performing the SN biopsy on patients with breast carcinoma who are receiving local anesthesia. Fenaroli et al showed that in 14 patients, SN sampling with local anestheisa is feasible and could in principle reduce surgical time. Moreover, a report from Barillari et al on 71 patients with clinical T1N0 breast carcinoma who underwent conservative breast surgery with SN biopsy while receiving local anesthesia rated this procedure “a satisfactory practice for the majority of patients.” Cattelani et al described the experience of their hospital in Parma (Italy) with 109 patients. They concluded that SN biopsy with local anesthesia is a good alternative to complete axillary dissection but before the technique becomes a routine procedure in breast cancer management, further confirmation by prospective clinical trials comparing the survival of patients staged by SN biopsy vs traditional axillary dissection is necessary.

There are several advantages to performing an SN biopsy with local anesthesia. First of all, the knowledge of the axillary status before breast surgery allows a more accurate planning of the therapeutic and diagnostic (staging) strategy. The gain in terms of time spared during breast surgery is evident, both in cases of negative and positive SNs: for negative SNs, the breast is treated with quadrantectomy as described by Veronesi et al with or without intraoperative radiotherapy, while for positive SNs, the patient undergoes quadrantectomy and complete axillary dissection with or without intraoperative radiation therapy. In both cases, there is no additional time spent waiting for the histopathologic diagnosis of the SN, and time is saved from the general anesthesia regimen as well.

In the surgical biopsy of the SN, the conventional intraoperative diagnosis after examination of 1 to 3 frozen sections stained with hematoxylin-eosin is not recommended because of the high risk of a false-negative result. In our experience, the incidence of false-negative results in these cases is as high as 20%. The intraoperative examination of the whole SN carries the advantage of a complete lymph node study, with the detection of even a small aggregate of tumor cells. The time needed to assess the SN status with this technique, however, may be 45 to 60 minutes, which is too long for some centers and represents a serious limitation for the wide use of the technique.

The formalin-fixed, paraffin-embedded tissue gives the surgeon a complete histologic picture of the SN on which to base a diagnosis and a plan for breast surgery in 48 to 72 hours. Breast carcinoma will then be treated with conservative surgery (quadrantectomy/wide excision) alone or in combination with complete axillary dissection. As already mentioned, in case of micrometastasis to the SN, the patients in our study were able to participate in the International Breast Cancer Study Group 2301 trial, which aims to identify the most appropriate
approach to patients with micrometastases to the SN (metastases with a diameter <2 mm).

One observation derived from our experience with SN biopsy using local anesthesia was the incidence of micrometastasis. In the current group of patients, the rate of micrometastasis was 24.3%, while in our patients receiving general anesthesia, it was 20% or less even though the histologic technique was the same for both groups.

Another advantage of performing this procedure with local anesthesia is that in the anticipation of tumor spread, before any therapy, preoperative chemotherapy can be offered without the risk of successive understaging of the disease. This aspect of the technique could be useful in cases where preoperative chemotherapy is required.

Our patients who received local anesthesia were comfortable with the procedure; moreover, the idea of undergoing surgery without hospitalization is well accepted by most patients. We did not observe any acute or late adverse effect from surgery.

One limit to our technique concerns the location of the breast primary tumor in the axillary tail. In this case, the intense uptake of radioactivity at the primary tumor level may create problems in the identification of the SN. In this limited group of patients, the surgical removal of the primary tumor and the SN, with local anesthesia in a unique session, could be an option; the decision on the axillary dissection could be delayed until the results of the histologic analysis of the SN become available.

In conclusion, our experience indicates that SN biopsy performed with local anesthesia can be a suitable alternative to standard intraoperative evaluation with general anesthesia in patients with unifocal, early-stage breast carcinoma.

We thank Marco Venturino, MD, Director of the Anesthesiology Division of the European Institute of Oncology, for his precious advice in our surgical practice and in the preparation of the manuscript.

Corresponding author and reprints: Alberto Luini, MD, Senology Division, European Institute of Oncology, via Ripamonti 435, 20141 Milan, Italy (e-mail: alberto.luini@ieo.it).

REFERENCES