LYMPHATIC MAPPING AND RADIOGUIDED SURGERY WITH SENTINEL LYMPH NODE BIOPSY: A NEW, MINIMALLY INVASIVE PROCEDURE FOR CANCER STAGING

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INTRODUCTION

Cancer surgery involves the science and art of excising primary tumors and possible metastatic sites, the most common of which is the regional lymph node basin. Examples of lymph node basins include the axilla for breast cancer and the groin for a cutaneous malignancy on the extremity. The information gained from removing the lymph nodes aids in the staging of the disease and in decision making for further treatment such as chemotherapy. In the past, patients diagnosed with malignant melanoma or breast cancer who were suspected of having cancer spread to the lymph nodes were subjected to a full dissection (complete removal of all the lymph nodes) of the suspected lymph node basin. This resulted in a high rate of complications, including infection, wound breakdown, seromas (abnormal fluid collections), and worst of all, lymphedema (swelling of the extremity).

Approximately forty percent of patients that have the radical node dissection develop lymphedema and in 5% the swelling is chronic and never goes away. Furthermore, so many lymph nodes (15-30) have to be removed during the dissection that the pathologist could not examine each lymph node in enough detail to identify micrometastases (very small collections of tumor cells). Therefore, a patient with no actual tumor in the lymph nodes could be subjected to an unnecessary full dissection and could develop lymphedema. On the other hand, cancer spread could be missed by the pathologist and the patient would not be offered additional necessary treatment that might improve their survival.

At Moffitt Cancer Center (MCC), we have helped develop a minimally invasive technique of identifying the lymph nodes at risk for disease and have applied a new technique — called RTPCR assay — that examines the genetic material of the lymph node to identify small numbers of tumor cells for accurate diagnosis and staging of patients with malignant melanoma and breast cancers. These methods have lower complication rates over the conventional total lymph node dissections.

BACKGROUND

The first node in a basin is identified as the sentinel lymph node (SLN) and has been proven to be the area where the cancer first spreads. As originally shown by Morton and colleagues, if there are no tumor cells seen in the SLN then there should be no further tumor cells found in the rest of the lymph node basin. This SLN can be located by injecting a radioactive substance or dye around the cancer. These substances have the right particle size so that they are taken up by the lymphatics and will color or make hot (identify by radioactive label) the first node or the SLN. If cancer cells are breaking off the primary tumor they will travel through the same lymphatics and be deposited in the same first node. This allows us to remove only those lymph nodes or SLN(s) that may harbor cancer cells.

This principal has not yet been universally accepted for breast cancer. However, at MCC, by using these lymphatic mapping techniques, we were one of the first to successfully show, at a high enough success rate, that breast cancer may spread to the lymph nodes in an orderly fashion. In our prospective study of 62 breast cancer patients, the technique was successful in finding the SLN in 57 (92%). In 12 (67%) of 18 patients with spread of disease, the SLN was the only site of disease.

THE LYMPHATIC MAPPING TECHNIQUES

Preoperative Lymphoscintigraphy

This technique involves obtaining a pre-operative lymphoscintigram to image the basins at risk for metastatic disease and provide a road map for the surgeon. Lymphoscintigraphy was introduced by Sherman and Ter-Pogossian in 1953 as a tool to define cutaneous lymphatic flow. Now this study is performed under the direction of a radiologist specializing in Nuclear Medicine.

The actual tumor or cancer site is injected with a special protein that is labeled with a minute amount of radioactivity. The radioactivity is small and is no more than what is produced by routine chest x-rays or mammograms. No adverse reactions have been reported to the injection of this radiolabeled colloid. The radioactive protein flows through the lymphatic channels toward the lymph node basins. This allows an image to be obtained of the basins into which tumor cells migrate. The image obtained is used by the surgeon to determine in which basin the SLN is located (Fig. 1).

At MCC, we compared the drainage patterns identified by lymphoscintigraphy to those predicted by anatomic guidelines and clinical experience, and found up to 62% of them did not match. The operative plan had to be changed in 47% of patients and hidden disease would have been missed in 17% of cases. We recommend that this study be performed on all patients with melanomas and some patients with breast cancer before their operation.

Intraoperative Lymphatic Mapping

Patients are then injected intraoperatively with a combination of vital blue dye and a radiolabeled sulfur colloid. Lymphazurin Blue is injected around the primary melanoma or breast cancer site. The dye is allowed to be taken up by the lymphatics. After the injection, the patient is prepped and draped, and attention is directed initially to the nodal basin and the location of the sentinel node by preoperative lymphoscintigraphy. A small incision is made for the sentinel node biopsy. Affected blue-staining lymphatics are identified and followed to the sentinel nodes, which stain a pale blue (Fig. 2). A hand-held gamma probe (Neoprobe Corporation, Dublin, Ohio) is also used to localize the SLN. The activity of the radionuclide (similar to that injected in nuclear medicine for the lymphoscintigraphy) within the SLN is measured with the Neoprobe (Fig. 3). "Hot" spots are identified through the skin with the Neoprobe so that the SLN can be harvested with outpatient surgery, 40% of the time under local anesthesia.

The SLN(s) is harvested and submitted to pathology as a separate specimen. All blue staining nodes, or "hot" nodes, are harvested and called sentinel nodes. "Hot" nodes are described.
Lymph Mapping... (cont.)

as nodes with counts three times the background count. The Neoprobe is again used to confirm that the activity remaining in the nodal bed has fallen to a background level. This ensures that all SLN(s) have been harvested. If there is still a large amount of activity in the nodal basin then additional sentinel nodes are present. These additional nodes are localized and removed until the activity in the basin returns to background.

Pathologic Examination

The SLN(s) are submitted to a pathologist for examination. Many sections are made of the SLN and it is placed in the block for imbedding. One or two sections are obtained from the approximate center of the node and then stained with conventional stains. Other slides are then submitted for special markers of melanoma such as S-100 protein. S-100 is a protein found only in tissues with melanoma and helps to identify melanoma cells in the node by staining them brown. The lymph node specimen from breast cancer patients are specifically tested for Keratin-19, or mucin, in the same way. In addition, a new technique called RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) is a specialized genetic test that allows us to locate single tumor cells in a background of millions of normal cells. This test increases the sensitivity two orders of magnitude, compared to regular examinations with the naked eye under the microscope.

PATIENT ELIGIBILITY

Currently all patients with newly diagnosed melanomas of thickness greater than .76mm and all newly diagnosed early stage invasive breast cancer patients are eligible for these lymphatic mapping procedures. Patients must have no clinical evidence of disease in the blood stream or in the lymph nodes. It is preferable that wide excision around melanoma and excisional biopsies of breast masses be performed after the lymphatic mapping. If possible, the breast cancer diagnosis should be made with a needle aspiration so that the tumor and the lymphatics are intact during the mapping procedure.

COMPARISON OF COMPLICATION RATES

At MCH, we have analyzed the outcomes of these lymphatic mapping procedures and compared them to the standard method of total lymphadenectomy for both melanoma patients and breast cancer patients. Patients were monitored carefully after surgery for wound infection, seroma, wound breakdown and lymphedema.

In melanoma patients, the complication rate of the sentinel node biopsy was consistently less than that of the complete procedure (Fig. 4). Of the 268 melanoma patients seen in 1995, only 50 had complications. Most of these complications were in patients treated with the more radical complete node dissection. No patients who had sentinel node biopsies had lymphedema or wound breakdown. Only 4% had wound infection and 6% had seromas in the SLN biopsy group, compared to 11% infections and 22% seromas in the total lymphadenectomy group.

For patients with breast cancer, 41 patients had SLN biopsy only and only two had complications (4.76%). Both patients had seromas aspirated. None of the breast cancer patients undergoing SLN biopsy developed lymphedema, wound infection or wound breakdown (Fig. 5, see page 6). No patients undergoing SLN biopsy required a drainage catheter after surgery.

DISCUSSION

The most serious complication of any procedure involving the lymph nodes is lymphedema. The treatment of lymphedema is limited. Once lymphedema develops, the patient is at increased risk for developing infection to that extremity. These patients get into a vicious circle: the lymphedema makes patients more prone to infection, and with each infection the lymphedema gets worse.

The best approach to lymphedema is its prevention. We presented a new combination of mapping techniques that will prevent the formation of lymphedema in patients with breast cancer and melanoma. No patient has developed lymphedema to date following this selective minimally invasive procedure. The advantage of a low complication rate makes it the best option for staging. If no tumor is found when the SLN is carefully examined by special stains, then there is no need to complete the dissection to remove more nodes. This significantly reduces the rate of lymphedema.

BIBLIOGRAPHY


FIGURE LEGENDS

Figure 1
This lymphoscintigraphy represents a melanoma of the back, with affluent lymphatics draining to the SLN in the left axilla.

Figure 2
SLN removed with visible blue dye.

Figure 3
A "hot" SLN on top of the Neoprobe.

Figure 4
Melanoma complications.

Figure 5
Breast Cancer Complications.

From the Comprehensive Breast Program and the Cutaneous Oncology Program at H. Lee Moffitt Cancer Center, University of South Florida, Tampa, FL.

Minimally Invasive Selective Lymphadenectomy and Sentinel Node Biopsy, a 2-day technical educational program on preoperative and intraoperative surgical techniques for treatment of melanoma and breast cancer is now being offered by Douglas S. Reintgen, MD, Professor of Surgery & Program Leader, Cutaneous Oncology Program at Moffitt Cancer Center (this is a CME course). General surgeons, nuclear medicine physicians, plastic surgeons, dermatosurgeons, pathologists and radiologists are invited to attend. Upcoming course dates in June, August, October and December. For information on upcoming courses: (813) 974-4295. Patients wishing to receive more information about procedures discussed in this article, call: (800) 456-7121.