

Sentinel Lymph Node Biopsy for Breast Cancer

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The regional lymph node status is the most powerful predictor of survival in women with invasive breast cancer.

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Key words: Breast cancer, sentinel
lymph node, histology.

Received: November 15, 2000.

Accepted: February 16, 2001.

CASE

The applicant is a 59-year-old female who had a core-needle biopsy of the right breast at a large medical center on February 5, 1998, because of a suspicious mammogram. Needle biopsy pathology report: invasive grade 4 (of 4), nuclear grade 2 (of 3) ductal adenocarcinoma (approximately 0.3 cm in the greatest dimension). Ductal carcinoma in situ, non-comedo type comprised 50% of the tumor. The neoplastic cells react with antibodies to estrogen and progesterone receptor proteins.

A modified radical mastectomy was then performed on February 16, 1998. A complete pathology report described the tissue from the right breast, a separately submitted lateral margin, a right sentinel lymph node, low axillary lymph nodes, and right mid-low axillary lymph nodes. The pathology diagnosis was residual carcinoma identified in the previous biopsy site involving an area of $1.5 \times 1 \times 1$ cm³. The tumor is mostly composed of grade 3 (of 3) intraductal carcinoma with a

microscopic focus of invasive carcinoma present. The margins of excision are negative, after the re-excision of the lateral margin.

Lymph nodes, right mid-low axillary dissection: a single (1 of 15) lymph node is involved by metastatic grade 3 (of 3) adenocarcinoma. The lymph node measures 2 cm in the greatest dimension.

Lymph node, sentinel, excision: fibroadipose tissue with foci of benign breast parenchyma.

Lymph nodes, right low axillary dissection: no lymph nodes identified.

The patient was put on tamoxifen. Follow-up studies have been negative.

HISTORY

The regional lymph node status remains the most powerful predictor of survival in women with invasive breast cancer. For breast cancer, the presence of regional metastases decreases 5-year survival by 28–40%.¹

The sentinel lymph node is defined as the

first node (occasionally 2 or 3 nodes) in the lymphatic basin that receives primary lymphatic flow.¹ Evaluation of this lymph node in cancer cases was first suggested over 20 years ago. Morton et al² pioneered the procedure for malignant melanoma in 1992. Several years later, this procedure was attempted for breast cancer for 2 express reasons: (1) doctors hoped to increase detection of micrometastases and (2) over 80% of women who undergo axillary dissection have at least 1 postoperative physical or emotional complication.²

If the sentinel lymph node biopsy is sufficiently informative and is negative for cancer, lymph node dissection may be eliminated. If the node is positive, a full regional lymph node dissection is still done.

TECHNIQUE

One of the 2 techniques, or a combination of both, is used to identify the sentinel lymph node. In one, a lymphangiogram dye (isosulfan blue) is injected intraoperatively into the tissue adjacent to the tumor site. The dye can be detected in the lymphatics within 5–10 minutes with the use of a limited skin incision. This blue stained lymphatic channel is traced from the breast tissue to a blue-stained lymph node. The other method of sentinel node localization utilizes a radiolabeled colloid, most commonly a colloid labeled with technetium 99m. The radioactive substance is injected 1–3 hours before the operation to allow time for the substance to reach the sentinel node. This procedure is particularly helpful to identify nonaxillary sites of lymphatic drainage, especially the internal mammary nodes with inner-quadrant breast cancers. A combination of the dye and the radiolabeled colloid techniques yields the most accurate localization of the sentinel node.¹

THE SENTINEL LYMPH NODE PROCEDURE: SERIAL SECTIONS, SPECIAL STAINS

This procedure needs serial sectioning and special stains to be advantageous.³ Serial sec-

tioning means multiple sections of the lymph node specimen, in contrast to the usual bivalving of the specimen, when only 1 or 2 sections are made. Thus, in an ordinary lymph node dissection, the largest part of each lymph node is not examined. In contrast, multiple sections allow a more thorough evaluation. Thirty percent of lymph node-negative patients with operable breast carcinoma experience disease recurrence within 10 years. Retrospective serial sectioning of axillary lymph nodes has revealed undetected metastases in 9–30% of these patients.⁴ Although serial sectioning is impractical for all axillary lymph nodes harvested from axillary dissection, it is mandatory when only the sentinel node is studied.

In addition, immunohistochemical stains for cytokeratin will identify micrometastases that would otherwise have been called negative on hematoxylin and eosin stains.⁵

A MULTICENTER VALIDATION STUDY

In October, 1998, David Krag and colleagues published a multicenter validation study of the sentinel node in breast cancer.² This study found that the accuracy of sentinel nodes was 97%. The other findings included:

- positive predictive value—100%;
- sensitivity—89% (surprisingly, all false negatives occurred when the primary tumor was in the lateral half of the breast);
- specificity—100%;
- sentinel nodes were located outside of level 1 of the axilla in 11% of cases (level 1 is the area most adjacent to the breast);
- three percent of positive sentinel nodes were in nonaxillary locations.

The authors concluded that the pathological examination of the sentinel nodes accurately predicts the status of the axillary nodes. They were particularly enthusiastic about the 3% of patients with positive nodes that would have been missed by conventional axillary lymphadenectomy. They admitted that the procedure can be technically challenging and that the success rate varies according to surgeon and patient characteris-

tics. (A recent validation study confirms these favorable statistics.⁶)

In an accompanying article, McMasters and colleagues responded that, at least at that time, sentinel lymph node biopsy for breast cancer was not yet the standard of care.⁷ In a very balanced evaluation, these authors suggested performing sentinel lymph node biopsy with a concurrent axillary dissection, stating that this improves the accuracy of nodal staging. Orr and colleagues have recommended that, to insure accurate staging of patients with breast cancer, all surgeons should, at first, perform full axillary lymph node dissection while learning sentinel node biopsy techniques.⁸

PROBLEMS

Not all patients with breast cancer are appropriate subjects for this procedure. Women with multifocal or extensive malignant disease, those with clinically involved axillary lymph nodes, and those with previous damage to lymphatic drainage are not good candidates.

In addition, recent studies have suggested that axillary dissection provides excellent local disease control. An 85% 10-year survival for stage 1 breast cancer patients who had axillary dissection compares to a 66% survival in a comparable group who did not have axillary dissection.⁹ This potential benefit should be considered before axillary dissection is abandoned.

Other problems include up to a 15% prevalence of "skip" metastases, defined as metastases to level 2 and 3 axillary nodes without the involvement of level 1 nodes.¹ This is illustrated by our case.

Failure of the sentinel lymph node to detect metastases has been attributed to medial lesions, extensive metastases, extranodal invasion, and surgeon inexperience.¹⁰

SUMMARY

We will continue to see increasing use of the sentinel lymph node biopsy for breast cancer. One would hope that the advantages outweigh the disadvantages for patients and also for medical directors.

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