Sentinel Lymph Node Biopsy in Breast Cancer

The Aarhus Experience

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Eighty patients, with newly diagnosed unifocal breast cancer and with no axillary metastases verified by ultrasonography, underwent sentinel lymph node (SLN) and subsequent axillary lymph node dissection. To identify the SLN, we used a combination of Tc-99m labelled colloid (Albures) and blue dye (Patent Blue V) injected peritumorally. Lymphoscintigraphy was not performed. The SLN was successfully identified in 78 out of 80 patients (97.5%); 43 patients (54%) were found to have metastatic disease. In 33 patients (77%) the SLN was the only node involved. No false-negative nodes were found, defined as SLNs that tested negative but with higher nodes that tested positive. If SLN biopsy is accepted as a routine procedure and when the exact indications are defined, the method described probably could be offered to the majority of breast cancer patients.

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It has been repeatedly demonstrated in recent literature that a sentinel node can be identified in the axilla in the majority of breast cancer cases (1). There is, however, no consensus yet about the applicability of the method in clinical practice. Before the method can be introduced to clinical practice, several questions have still to be discussed. Different centres make use of different detection techniques and both lymphoscintigraphy and lymphatic mapping with or without the use of blue dye seem useful. One crucial question concerns the false-negative rate. It is obvious that false-negative biopsies cannot be completely avoided but a decision has to be made on what is an acceptable level of false-negative sentinel nodes. Moreover, it is necessary to discuss which group of patients is likely to benefit from the method. Can patients with multifocal cancers be included?

This paper is a preliminary report on our experience with sentinel lymph node biopsy at Aarhus University Hospital.

MATERIAL AND METHODS (August 1998–February 2000)

During this period, 258 women with newly diagnosed invasive breast cancer underwent surgery. Only patients diagnosed by fine-needle aspiration biopsy (FNAB) or core biopsy and with surgery planned according to the Danish Breast Cancer Cooperative Group 89 Protocol (DBCG 89) were enrolled in the study. Those excluded included 27 patients with non-palpable tumours, 26 patients with multifocal tumours verified by mammography/ultrasonography, 36 patients with axillary lymph node metastases verified by ultrasonography and fine needle aspiration, 10 patients with advanced cancer and 27 patients scheduled for frozen sectioning. In all, 80 patients underwent sentinel lymph node biopsy and 140 patients were excluded according to the protocol. Fourteen patients declined to participate and 24 patients did not enter the investigation because of lack of capacity in the operating theatre.

For identifying the sentinel lymph node (SLN), we used a combination of radioactive tracer (Tc-99m Albures) and blue dye (Patent Blue V). The Tc-99m labelled colloid in a saline solution (1.0 cc/15 MBq) was injected around and close to the tumour 2 h preoperatively. No lymphoscintigraphy was performed. Ten to 15 min before surgery the blue dye (1.5 cc, 150 mg/cc) was injected around the tumour and the axillary, parasternal and periclavicular area were searched for 'hot spots' with a gamma detector (C-Track). Surgery began with sentinel lymph node biopsy. Incisions were made according to the planned

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procedure. For breast-conserving surgery, the incision in the axilla was made as close to the 'hot spot' as possible. When mastectomy was planned, the incision lines were demarcated and incisions for SLN biopsy were made through the lateral part of the demarcations. The sentinel nodes were localized by careful dissection, guided by the gamma detector, along the blue-stained lymph vessels. A SLN was defined as any blue and/or 'hot' lymph node. Following sentinel lymph node biopsy, the planned surgery, including axillary dissection, was carried out. All SLNs were immediately sent for pathological examination and divided in half, one half for frozen sectioning and subsequent paraffin embedding and the other half for paraffin preparation for later conventional examination. The frozen sections were stained with hematoxylin and eosin (H&E), and after serial sectioning with sampling from four levels, the paraffin-embedded specimens were stained with H&E and immunohistochemically for cytokeratin. If micrometastases were detected by the cytokeratin stain only, the pathologist re-examined the H&E-prepared specimens for confirmation of the diagnosis.

RESULTS

The SLN was successfully identified in 78 out of 80 patients, with a median of 2 SLN per patient and a median of 14 axillary lymph nodes per patient; 43 patients (54%) were found to have metastatic disease. In 13 patients the frozen sections showed no metastases, but the paraffin-prepared specimens revealed micrometastases. There were no false-negative SLNs, defined as SLNs without metastases but with nodes testing positive. In 33 out of 43 patients (77%) with metastatic disease, the SLN was the only node involved, and in 20 patients (47%) only micrometastases were found. In 4 patients a 'hot spot' outside the axilla was found preoperatively; in all 4 patients an attempt was made to find and remove the node. In one of the four patients two parasternal lymph nodes were removed, showing micrometastasis. In 6 out of 80 patients (8%) the SLN showed no uptake of blue dye and in 4 out of 80 patients (5%) the SNL would have been missed if the radioactive tracer only had been used.

In two patients, neither dye nor radioactivity was found outside the injection site. Neither patient had any metastatic involvement of the removed axillary lymph nodes. The median tumour size was 21 mm (9–45 mm).

DISCUSSION

No valid conclusions concerning the future applicability of SLN biopsy can be drawn from our results so far. We plan to include 150 patients before any statistical evaluation is made. We found the chosen method easy to use and without any discernible learning curve.

Only a third of the incident cases was included in the study. In cases with obvious metastatic disease in the axilla, sentinel node biopsy has no meaning. The diagnostic acuity of a clinical examination in this respect is low. Ultrasound, CT and MRI all show a fair specificity for metastatic disease (2–6) but not high enough to be used to exclude axillary dissection. Ultrasound is used routinely at our institution in the diagnostic work-up on all breast cancer patients. It takes little extra effort to examine the axilla and to perform FNAB on pathological lymph nodes. By applying this method, we have excluded 36 patients and the axillary tumour load of the node-positive cases included has therefore been low, reflected in the finding of 33 out of 43 node-positive cases, the sentinel nodes being the only positive lymph nodes.

In Denmark, 50% of breast cancer cases are found to have metastatic involvement of the axillary lymph nodes. Even though patients with ultrasound-positive glands were excluded, we found axillary involvement in 54% of cases. Whether this high percentage of patients with axillary metastases is due to random variation or is caused by the improved diagnostic methods offered by SLN biopsy is too early to decide, but the fact that more than one-third of the patients with axillary involvement had only micrometastasis could point in the latter direction.

Twenty-four patients were excluded for logistic reasons, caused by inability to perform more than one SLN biopsy a day. Obviously this obstacle will have to be overcome should the procedure become clinical routine. In conclusion, the described method using both blue dye and the gamma probe seems efficient in identifying the SLN. If SLN biopsy is accepted as a routine procedure and when the exact indications are defined, the combined method probably could be offered to the majority of breast cancer patients.

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