original paper

Value of sentinel node biopsy in the management of breast cancer

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Abstract

Aims To determine the rate of detection of the sentinel node using both blue dye and radioisotope, and the accuracy with which the sentinel node histology reflects the nodal status of the axilla in a series of patients with clinically node-negative breast cancer.

Patients and methods During a 32-month period from May 1998 to December 2000, 73 patients with clinically node-negative breast cancer underwent sentinel node biopsy immediately followed by formal axillary lymphadenectomy. The sentinel node(s) was identified using a combination of lymphoscintigraphy, blue dye and an intraoperative hand-held gamma probe.

Results The mean age of the 73 patients was 58 years (range 32-83 years). Twenty-six per cent (19/73) had previous surgical/excisional biopsy. Pre-operative lymphoscintigraphy was positive in 74% (54/73) of patients. Combination of blue dye and radioisotope was better than either method in isolation for identifying the sentinel node, yielding a success rate of 96% (70/73). A total of 32 cases proved to have positive nodal disease on histological examination. In 44% (14/32) of patients, the sentinel node was the only positive node. Forty-seven per cent (15/32) of patients in whom the sentinel node was positive also had positive nodes in the axillary nodal basin. There were 3/32 false negative cases, giving a false negative rate of 9.4%.

Conclusion Sentinel node biopsy will have a role in the management of breast cancer. However, widespread adaptation of this technique awaits the results of prospective, randomised trials.

Introduction

The histological status of the axillary lymph nodes is the strongest prognostic variable in patients with breast cancer.[1,2] Apart from representing an important staging procedure, axillary lymphadenectomy provides excellent regional tumour control. The axillary lymph node status plays a key role in designing post-operative treatment.

Breast cancer is detected at an earlier stage in increasing numbers of patients, and an increasing number have node-negative disease. Considering the morbidity of axillary dissections, the need for routine axillary clearance requires re-evaluation. Sentinel lymph node biopsy (SLNB) is a staging procedure in malignant melanoma and more recently has been used in breast cancer.[3-5]

The sentinel node is defined as the first lymph node in a regional basin that receives lymph flow from a primary tumour.[6,7] This node has the greatest chance of harbouring metastatic deposits. Numerous studies have shown that it is possible to identify the lymphatic drainage of breast cancer with lymphoscintigraphy and to trace the sentinel node intraoperatively with a gamma probe and blue dye and excise it for histological evaluation.[8-11] These studies suggest that the histologic status of the sentinel node accurately reflects the pathologic status of the remaining axillary lymph nodes in patients with clinically node-negative breast cancer.[8-11]

The aims of this study were to evaluate the detection rate of the sentinel node using both blue dye and radioisotope, and the accuracy with which the sentinel node histologic status reflects that of the rest of the axilla in a series of patients with clinically node-negative breast cancer.

Patients and methods

Over a 32-month period from May 1998 to December 2000, 73 patients with clinically node-negative breast cancer underwent SLNB immediately followed by formal axillary lymphadenectomy which is the current standard of care. These patients had clinical T_1–$T_3N_0M_0$ breast cancer. Informed consent was obtained from all patients before the procedure. All patients had histologically-proven invasive cancer (see Table 1). Patients with clinically node-positive disease were excluded from this study.

On the morning of surgery, 40MBq of Nanocoll was injected into the breast parenchyma around the tumour or around the biopsy cavity at four points (12, 3, 6 and 9 o'clock positions). Lymphoscintigraphy was performed 90 minutes later using a gamma camera. Scintigraphic images were recorded in anterior and oblique projections and the position of the sentinel node was marked on the skin.

Intraoperatively, prior to making the first skin incision, gamma counts were taken of the room background, the breast injection site and the 'hottest' spot in the axilla.

Isosulphan blue dye (4cm^3) was injected around the tumour or immediately adjacent to the excision cavity if biopsy had been performed previously, five minutes before the axillary incision was made and SLNB performed. The sentinel node(s) was identified using a combination of lymphoscintigraphy, blue dye and an intraoperative hand-held gamma probe (Neoprobe 2000). Counts were taken of the node(s) in situ and ex vivo, and then of the axillary background. The radioisotope localisation was deemed successful if the axillary background had counts of 25% or less compared with the sentinel node counts ex vivo.

All 73 patients went on to have complete level three axillary

dissections combined with either breast conserving surgery or mastectomy.

The specimens were stained with hematoxylin and eosin (H&E) and examined microscopically. Specimens that were negative for metastatic disease on H&E stain were examined with immunohistochemistry using CAM 5.2 for cytokeratin.

Table 1. Patient profile

	n	%
Breast affected		
Right	29	40
Left	44	60
At presentation		
Palpable mass	67	92
Non-palpable mass	6	8
Tumour site		
Upper outer quadrant	29	40
Lower outer quadrant	10	14
Upper inner quadrant	12	16
Lower inner quadrant	6	8
Central	16	22
Method of diagnosis		
Core biopsy	49	67
Surgical biopsy	18	25
Ultrasound-guided biopsy	3	4
Stereotactic core biopsy	2	3
Punch biopsy	1	1
Clinical size		
≤ 2cm	49	67
2cm < x ≤ 3cm	16	22
> 3cm	8	11

Results

The mean age of the 73 patients was 58 years (range 32-83 years) (see Table 1). Nineteen patients (26%) had previous surgical/excisional biopsy. Pre-operative lymphoscintigraphy was positive in 74% (54/73) of patients, in 64% (47/73) an axillary node was identified and in 10% (7/73) an internal mammary node was identified. In one case, the sentinel node was in a non-standard position in the axilla, the node being much lower in the axilla than usual (see Table 2).

The sentinel node was successfully identified by blue dye in 89% (65/73). The success rate with radioisotope was 90% (66/73), and the combination of blue dye and radioisotope yielded a success rate of 96% (70/73) (see Table 3). The mean number of sentinel nodes removed was 1.6 (range 1-4) and the mean number of nodes excised in the remainder of the axilla was 33 (range 5–48). The internal mammary node was identified on lymphoscintigraphy in seven cases. Biopsy of these was performed on five occasions and was histologically positive in only one.

A total of 33 of the 73 cases (45%) proved to have positive nodal disease on histological examination. All patients with palpable lesions or scars from previous excisional biopsies were included in the analysis. Five patients had impalpable lesions but had scars from a previous biopsy, these were included. One patient was excluded from the analysis. This woman was diagnosed on stereotactic core biopsy. Her cancer was impalpable and thus had a wire localisation. The isotope was injected around the localising wire but was noted to leak out along the wire tract. Hence, 32 patients

Table 2. Lymphoscintigraphy results

	n	%
Positive (total)	54	74
Axillary nodes	47	64
Internal mammary node	7	10
Negative	19	26

Table 3. Results of mapping techniques in identifying sentinel node

	Identification rate of sentinel node		Histologically positive sentinel node		False negative sentinel node bx	
	n	%	n	%	n	%
Blue dye	65/73	89	29/65	45	1/65	1.5
Isotope	66/73	90	27/66	40	2/66	3.0
Combination	70/73	96	30/70	43	0	0

with positive nodal disease met the inclusion criteria and were used in the analysis. In 44% (14/32) of patients, the sentinel node was the only positive node. Forty-seven per cent (15/32) of patients of whom the sentinel node was positive had further positive nodes in the axillary nodal basin. There were 3/32 false negative cases, giving a false negative rate of 9.4%.

Discussion

The combination of breast screening and patient awareness, amongst other factors, has led to earlier detection of breast cancer. In a small proportion of these patients, the axillary lymph nodes are histologically positive for metastases, which has prognostic implications. In an increasing number of patients in whom the axillary lymph nodes are histologically negative, complete axillary lymphadenectomy adds no further survival benefit but adds to the morbidity of surgery.

Sandrucci et al through an extensive international literature review from January 1993 to September 1999,[12] confirmed that SLNB is an accurate, feasible and reliable technique for staging the axillary lymph node basin in breast cancer. In this study, the combined use of blue dye and radioisotope yielded the highest rate of sentinel node identification (96%), compared with either method in isolation. These results compare favourably with other prominent studies where the identification rate using both techniques in combination was 93%.[6,7]

The sentinel node was localised and excised in 98% (54/55) of whom lymphoscintigraphy was positive. These results compare well with other studies, including those of Dunnwald et al (85%), Paganelli et al (97.6%) and Alazraki et al (94%).[13-15] A positive lymphoscintigram suggests a very high likelihood of successful localisation of a sentinel node at operation.

Alazraki et al suggested that the use of radionuclide imaging before surgery assisted in guiding surgical incision planning.[15] This was especially true for one of the patients in this study in

whom the sentinel node was located in an atypical position in the axilla; the node being much lower in the axilla than normally expected. The position of the surgical incision was altered as a result and facilitated successful localisation and excision of the sentinel node.

The false negative rate was 9.4% (3/32), which compares favourably with false negative rates quoted in other papers. Veronesi et al, with a sample size of 160 patients, reported a false negative rate of 4%.[11] Rodier et al studied 73 patients and reported a false negative rate of 9%.[16] Hill et al had a 10% false negative rate on a sample size of 500 patients.[7] Krag et al describes an 11% false negative rate, having studied 423 patients.[9] deKanter et al had a 16% false negative rate from 232 patients.[18] Most recently, Tafra et al,[17] with a sample size of 529 patients, published a false negative rate of 13%. This procedure is, therefore, most beneficial in patients who have a low risk of axillary lymph node involvement.

In conclusion, the histology of the sentinel node accurately reflects the nodal status of the axilla. Both blue dye and radioisotope should be used in combination to maximise the success rate of localisation. Sentinel node biopsy will have a role in the management of early breast cancer. However, widespread adaptation of this technique awaits the long-term results of prospective, randomised trials.

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