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Sentinel Node in Breast Cancer

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Abstract

Aims of the study: To investigate the sensitivity and negative predictive value of sentinel node biopsy in breast cancer in a Swedish hospital.

Materials and methods: Sixty-One patients with invasive breast cancer who were scheduled for breast conserving therapy or modified radical mastectomy in Orebro Medical Center, Sweden, were asked to participate and gave their informed concent. A peritumoral injection of 40 mBq of Tc-99-nanocolloid was given the day before operation or on the morning of the same day. A lymphoscintigraphy was performed to localise the sentinel node. At the operation, after general asesthesia, 1 milliliter of Patent Blue Dye® was injected subcutaneously just above the tumor. A handheld gamma probe was used to localise a hot spot in axilla, indicating the position of the sentinel node.

A small incision was made in the lower part of axilla in the area where sentinel node was found with the probe and blue coloured lymphatics were soughted for. If a blue node was found the probe was used to confirm that it also contained the isotope. And if the blue node could not be found, the probe was used to identify the hot spot. The sentinel nodes that could be identified were removed and separately sent for pathological examination. Thereafter the tumor was removed by partial mastectomy or total mastectomy followed by a dissection of the nodes in the axilla.

Results: The sentinel node could not be identified in 6 out of 61 patients. Two of these partients had positive axillary node involvement. Out of 55 identified, 18 were positive for metastasis. In 7 cases the sentinel nodes were the only positive nodes. Among the 37 negative sentinel node cases, 3 cases were found to have metastasis in other lymph nodes in the axilla. This gives a sensitivity of 85.7 per cent and a negative predictive value of 91.9 per cent.

Conclusion: The results of this pilot study concur with other reports in the literature. Probably the sensitivity and negative predictive value will improve as we go along the learning curve. A national multicenter study is underway in Sweden aiming at including 500 patients to confirm that the method can safely be used in all surgical hands.

The basic principle in treatment of breast cancer always includes axillary dissection with mastectomy. Careful axillary dissection is essential not only for staging the axillary node involvement for therapeutic consideration, but also for less axillary recurrences, and better overall survival.[1] Furthermore incomplete axillary dissection may lead to incorrect classification of axilla status. The patients then may receive inadequate treatment which leads to poorer prognosis. However, the morbidities associated with axillary dissection include seroma formation, lymphadema, and neuropathy of the arm with numbness, stiffness, im-

paired shoulder movement and pain.[2-4]

There is great need for developing minimally invasive techniques to diminish arm morbidity and equally as effective as the standard axillary dissection. Giuliano,[5,6] Albertini,[7] Veronesi[8,9] and other[10-12] are among the pioneers in identifying sentinel node in breast cancer. We try to do the sentinel node method in our hospital in the same way to find our experience, identify the sensitivity and negative predictive value.

Patients and Metyhods

From March 1998 to April 1999, all patients presenting with palpable invasive breast cancer (histologic proved) and clinical negative axilla in Orebro Medical Center, Sweden, were asked to participate and gave their informed consent. Women with previous incisional or excisional biopsy of the breast cancer, multifocal tumors, need pre-op treatment and pregnant women were excluded.

The day before operation or in the same day, the patients underwent preoperative lymphoscintigraphy by injected 40 MBq of Tc99 nanocolloid (˜olco nanocoll) peritumoral area with a fine needle to identify and localize the sentinel node. The isotope has a half-life of 6 hours. The scintigraphic images were taken 60, 120 and (if necessary) 180 min after injection. Anterior and lateral view are taken. A mark was placed on the skin over the site of the sentinel node.

At operation (4-23 hr after injection of Tc), after general anesthesia, 1 milliliter of Patent Blue Dye® (Guerbert, France) was injected subdermal above the tumor. Thereafter a handheld gamma probe (Navigator®), in a sterile plastic bag was used to localize the area of hot spot in the axilla by measuring gamma counts on the skin overlying and comparing the counts over the hot spot to the background and the injection site. An incision was made in lower part of axilla above the area of hot spot. The dissection started with trying to identify the blue lymphatic vessel and blue node. Before removing the sentinel node, the probe was used to confirm that node was containing isotope or not. If the blue node could not be identified, we used the probe to identify the hot (radioactive) node and called that sentinel node too. After removing the sentinel node, we used the probe to search for more active spot in the axilla, then the tumor was removed in the way of sector resection or total mastectomy according to the tumor size and location. And axillary dissection was completed after that including level I, level II and at least some level III nodes. Identified sentinel nodes were sent separately to pathologists.

Results

Sixty patients underwent lymphoscintigraphy and intraoperative lymphatic mapping (by gamma probe and dye), and sentinel lymphadenectomy before modified radical mastectomy or breast conservative surgery for treatment of their breast cancer. Median age of the patients was 62 years. One patient presented with synchronous bilateral breast cancers. So there were 61 surgical procedures as shown in Table 1.

Among sixty-one cancers, invasive breast cancer was diagnosed by FNA in 51 cases (83.6%); others were confirmed by true-cut needle after the report of FNA showed atypia. Most of the tumors were in upper quadrant in 28 cases (45%). Primary tumor was invasive ductal carcinoma in 53 cases (86.9%). The mean tumor size was 21 mm (range 5-53 mm.).

Staging of tumor revealed 23 cases (37.7%)in stage I, 35 cases (57.4%) stage II and 3 cases (4.9%) stage III. The patients were scheduled for conservative breast cancer surgery in 51 cases (83.6%) and modified radical mastectomy in 10 cases (16.4%).

Preoperative lymphoscintigraphy identified sentinel node in 42 cases (68.8%). Sentinel node were seen in 60 min in 33 cases (54%), 8 cases in 120 min and 1 case in 180 min.

Intraop-gamma probe detected sentinel node in 44 cases (72.1%) and the blue dye technique detected sentinel node in 48 cases (78.7%). Over all sentinel node could be detected in 56 cases (91.8%). But sentinel node could be removed surgically in 55 cases (90.2%) (Table 3). The mean number of sentinel nodes was 1.9. There were some cases that the localized node was identified by lymphoscintigraphy situated in medial part (Table 2). An attempt to resect internal mammary lymph node was made in few cases (especially in the case that received MRM), but the dissections were limited due to the danger to pleura. And we could find sentinel node in only one case.

In 61 cases, there were axillary nodes positive for metastasis in 21 case (34.4%). In 55 identified sentinel node cases, sentinel nodes were pathological positive

Table 1 Patient characteristics.

Total numbers of cases	**61**
Total numbers of patient	60
Median age	62 yr.
Age range	35-88 yr.
Operative procedure	
Breast conservative surgery	51 (83.6%)
Modified radical mastectomy	10 (16.4%)

Table 2 Lymphoscintigraphy.

	No.	**Per cent**
Seen SLN node	42	68.8
Axillary node only	34	55.7
Internal mammary node only	5	8.2
Axillary and internal mammary node	3	4.9
Not seen SLN node	19	31.2

Table 3 Identified sentinel node.

Mothod	**Number of cases (%)**
Lymphoscintigraphy	42 (68.8)
Gamma probe	44 (72.1)
Blue dye	48 (78.7)
Gamma probe and/or blue dye	55 (90.2)

Table 4 Compare sentinel node with total axillary nodes.

Sentinel node	**Axillary nodes**	**No. of cases**
Pos. for metastasis	Pos. for metastasis	18
Neg. for metastasis	Neg. for metastasis	34
neg. for metastasis	Pos. for metastasis	3
Total		**55**

for metastasis in 18 cases. And in 7 cases the sentinel nodes were the only positive nodes in the axilla. There were 3 cases in which the sentinel node was negative for metastasis when other axillary nodes were pathological positive (Table 4). These gave a false negative rate 14.3 per cent and negative predictive value was 91.9 per cent. Sensitivity was 85.7 per cent and specificity was 100 per cent (Table 5). Overall accuracy was 94.6 per cent.

Discussion

Lymphatic mapping and SLN biopsy using a combination of mapping techniques (lymphoscintigraphy, blue dye, gamma probe) is a new procedure that can provides nodal staging with minimal morbidity. Our results successfully identified sentinel node in 55 of 61 cases (90.2%) and had slightly high false negative rate (14.3%) when comparing with the large series of Veronesi[9] that had identification rate 98.7 per cent and false negative rate was 6.7 per cent.

The details of the 3 false negative cases were shown in the Table 6. In the first false negative case, the inaccuracy might be caused by inexperience with the procedure. The report from pathologist found that other positive node had minimal cancer metastasis (2 mm). But the last two cases, we found by pathology that these were multifocal tumors. In the last case, tumor was 40-mm by clinical examination and 30-mm by mammogram. Multifocal tumors may have extensive lymphatic network and are not suitable for sentinel node procedure.

We believed that this procedure is useful to stage axilla in early breast cancer especially if the tumor is 15 mm. or lesser.[8] The accuracy might reach 100 per cent[10] as in our results that there was no false negative

Table 5 Statistics of predictive values, sensitivity and specificity.

Negative predictive value	$\frac{\text{No. cases without axillary LN metastasis}}{\text{No. cases with negative SLN biopsy}}$	$\times 100$	$= 91.9\%$
False negative rate	$\frac{\text{No. cases with negative SLN biopsy}}{\text{No. cases with axillary LN metastasis}}$	$\times 100$	$= 14.3\%$
Sensitivity	$\frac{\text{No. cases with positive SLN biopsy}}{\text{No. cases with axillary LN metastasis}}$	$\times 100$	$= 85.7\%$
Specificity	$\frac{\text{No. cases with negative SLN biopsy}}{\text{No. cases with no axillary LN metastasis}}$	$\times 100$	$= 100\%$

Table 6 Details of the three false negative cases.

	Pt. No. 23	Pt. No. 26	Pt. No. 41
Tumor location	LOQ	LIQ	UOQ
Tumor size (patho)	17 mm	30 mm and 3 mm	17 mm (2 tumors)
Lymphoscintigraphy	SLN was seen at 60 min (axilla)	SLN was seen at 60 min (axilla)	SLN was seen at 120 min (axilla)
Other Identified	By probe	By probe	By probe and color
SLN count (ex vivo)	No. 1 = 338 No. 2 = 41	No. 1 = 3600 No. 2 = 21800	No. 1 = 140 No. 2 = 77
Specimen axilla count (ex vivo)	235	300	9
Residual axilla bed count	87	290	10
SNBR	4	75	14
Tumor type	Ductal	Ductal and tubular	Both ductal
Multifocality	No	yes	yes

Note: SNBR (sentinal node-to-background ratio) is the ex vivo sentineal node count/residual axillary bed count.

case if we considered only tumor size 15 mm and smaller.

The efficacy to identify the sentinel node by using blue dye alone is 78.8 per cent in our series. This method combined with preoperative lymphoscintigraphy can be used together in developing country especially in Thailand if we do not have gamma probe. Unidentified mapping should undergo routine standard axillary dissection.

These results confirm that sentinel node procedure is a promising new method to diminish the necessary of axillary dissection in early breast cancer. There is a learning curve with better results as experience increasing. Before being use in routine clinical practice, results from randomized clinical trials are needed.

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