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CHAPTER SIXTEEN

Internal Mammary Sentinel Lymph Nodes in Breast Cancer Patients


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Submitted
The introduction of lymphatic mapping and sentinel node biopsy in the management of breast cancer has refined axillary lymph node staging. Lymph node positive patients who may benefit from axillary clearance can now be identified. Lymph node negative patients can be spared an unnecessary lymph node dissection. The axilla is the generally recognised site of lymph node metastases from breast cancer, however, this is not where all lymph node metastases are located. In 1779, the Dutch anatomist and surgeon Petrus Camper described that breast cancer may drain to lymph nodes along the internal mammary artery. In 1952, Margottini introduced the extended radical mastectomy to remove these lymph nodes. Removal of portions of the first three ribs and the sternum is an integral part of this extensive operation. It has never been shown that this approach improves survival rates. Extended radical mastectomy was abandoned and surgical treatment of breast cancer steadily became more conservative.

The introduction of lymphatic mapping revived the surgical interest in internal mammary lymph nodes. Lymphoscintigraphy can visualise these nodes. Their removal and histological evaluation may identify metastatic disease in otherwise node-negative patients and thus improve staging. Whether this should have therapeutic implications is controversial. We present two cases to illustrate these points.

**Case one**

A 58-year old woman was referred to our hospital with a lower-outer quadrant lesion of the left breast, detected at a mass screening program. The medical history was unremarkable. Physical examination revealed no palpable lesion either in the breast or in the axilla. The ultrasonography identified a 4 mm lesion with malignant characteristics. Ultrasound-guided fine needle aspiration cytology showed adenocarcinoma. The clinical diagnosis was T1N0M0 breast cancer and the decision was made to perform breast conserving treatment and a sentinel node procedure.

Preoperative lymphoscintigraphy was carried out after ultrasound-guided injection of 99.5 MBq 99mTc-Technetium-nanocolloid (Nanocoll, Amersham Cygne, Eindhoven, the Netherlands) in 0.2 ml into the tumour. Dynamic imaging was followed by static imaging at 15 minutes, 2 hours and 4 hours post-injection with a dual-head gamma camera (ADAC Vertex, Milpitas, California, USA). The images at 15 minutes showed no lymphatic drainage. Two left axillary sentinel nodes were seen after two and four hours (figure 1). There was also drainage to the left internal mammary chain where two sentinel lymph nodes were visualised. The nuclear medicine physician marked the location of the sentinel nodes on the skin.

The operation was performed on the subsequent day. Before the incision, 1.3 ml patent blue dye (Laboratoire Guerbet, Aulnay-Sous-Bois, France) was injected into the tumour through a catheter that had been inserted under ultrasound guidance. Two axillary sentinel nodes were identified using the gamma ray detection probe (Neoprobe 2000, Johnson & Johnson Medical, Hamburg, Germany) and harvested. One of these nodes was blue. Frozen section analysis showed no tumour cells.
The location of a sentinel node in the third intercostal space was identified through the intact skin using the probe. A transverse incision was made. The pectoral muscle fibres were split and the intercostal muscles were divided to reveal the pleura. No blue dye was seen but the probe pointed out a small sentinel node adjacent to the internal mammary artery. The node was harvested. The other internal mammary sentinel node was not pursued. A wide local excision of the primary tumour was performed.

Pathological evaluation showed a well-differentiated 0.8 cm invasive ductal carcinoma with estrogen receptors. Serial-sections of the axillary sentinel nodes with hematoxylin-eosin staining and immunohistochemical staining (CAM 5.2, Becton Dickinson, San Jose, CA, USA) confirmed the negative result of the frozen section investigation. However, the internal mammary sentinel node contained tumour deposit with a diameter of 2 mm.

The stage was pT1bN3M0 breast cancer. The patient received adjuvant fractional radiotherapy to the left breast. She also was given radiotherapy to the left internal mammary chain. Adjuvant hormone treatment was also given. She was without evidence of disease eleven months later.

**Case two**

A 35-year old woman was referred to undergo breast-conserving treatment with sentinel node biopsy for a left breast cancer in the upper-inner quadrant. Lymphoscintigraphy showed an internal mammary sentinel node at four hours and no drainage to the axilla (Figure 2). The operation was performed the next day. A dose of 1 ml of patent blue dye was administered into the primary tumour. The axilla was explored but no ‘hot’ or blue node was found. No suspicious nodes were palpated in the open wound. Subsequently, the third intercostal space was opened. A blue lymphatic vessel was visualised but could not be traced. Three ‘hot’ lymph nodes measuring 4, 7 and 10 mm were harvested. Two of the sentinel lymph nodes were free of disease, however, the third sentinel node did contain a tumour deposit. Although this was the largest node, it was the node that was the least radioactive. The primary tumour was a 2.5 cm poorly differentiated lesion with lymphangio-
invasion, with a mitotic index of 36 per ten high-power fields and without hormone receptors. It was removed with a 2 mm minimum margin.

Postoperatively, she was given radiotherapy to the breast, to the ipsilateral axilla and the parasternal region. She also received adjuvant chemotherapy. She was diagnosed with a chest wall recurrence and lung metastases fifteen months later. A CT scan at that time showed an enlarged internal mammary lymph node.

**Discussion**

These two cases demonstrate that internal mammary sentinel node biopsy may have an impact on the management of patients with breast cancer. The first patient was upstaged from stage I to stage IIIB. The second patient was upstaged from stage IIA to stage IIIB.

The incidence of internal mammary lymph node metastases has been quoted to be 6 to 9% in axillary node-negative patients and 28-52% in axillary node-positive patients. Clinical symptoms of internal mammary lymph node metastases are rarely described although they can be mistaken for a local recurrence or may pass unnoticed because of their location inside the chest wall. Treatment of these nodes is subject of debate. Impact of elective radiotherapy to the internal mammary chain on survival has never been convincingly shown. Ongoing randomised studies in Europe and in Canada will provide more data about this topic. The alternative treatment option is elective dissection of internal mammary nodes. Lacour and Meier performed randomised studies of extended radical mastectomy versus radical mastectomy and showed no survival difference. However, Lacour showed a five-year survival benefit in a subgroup of patients with both an inner quadrant primary lesion and a tumour positive axilla: 71% with extended radical mastectomy and 52% with radical mastectomy. Meier found a ten-year survival benefit in patients with an inner quadrant or central primary lesion: 86% with extended radical mastectomy and 60% with radical mastectomy.
The primary lesion site and the tumour-status of the axilla have a limited predictive value for the presence of internal mammary lymph node metastases. With the introduction of lymphatic mapping for breast cancer, patients with lymphatic drainage from a primary tumour to internal mammary nodes can be identified using lymphoscintigraphy. Biopsy of these sentinel nodes can provide relevant information: it allows one to identify patients who indeed have metastatic disease in that regional lymphatic basin with minimal morbidity. Surgical treatment of internal mammary lymph node metastases seems excessive in this era of conservative surgical treatment of breast cancer but radiotherapy could be considered. Common sense suggests that radiotherapy is of no value in case of a tumour-free internal mammary sentinel node, even in the presence of a large primary tumour in an inner quadrant with axillary node metastases.

What about patients who do have metastatic disease in an internal mammary sentinel node? A tumour-positive internal mammary lymph node and a tumour-positive axillary lymph node carry a similar prognosis.\(^\text{12}\) For this reason, such patients seem to be suitable candidates for radiotherapy and adjuvant systemic treatment. Incorporating the tumour-status of sentinel nodes outside the axilla in the management may lead to better patient selection for such treatments and improved regional control and survival.

Result from lymphatic mapping and sentinel node biopsy may have repercussions for the TNM staging system. For instance, until now, the situation has been that a metastasis in an internal mammary lymph node is classified as N3 because it is detected at an advanced stage and thus carries a poor prognosis. However, a metastasis in an internal mammary sentinel node is detected at an early stage. Especially if such patients do not have axillary involvement, the prognosis is probably not much worse than is true for an involved sentinel node in the axilla, which is classified as N1.

In conclusion, the goals of lymphatic mapping in breast cancer extend beyond axilla-conserving surgery. More accurate staging is another option. This may have therapeutic implications and suggests the need for an update of the TNM staging system.

References


