Axillary and internal mammary sentinel lymph node biopsy in male breast cancer patients: case series and review

Xiaoshan Cao¹,² Chunjian Wang¹ Yanbing Liu¹ Pengfei Qiu¹ Binbin Cong¹,² Yongsheng Wang¹
¹Breast Cancer Center, Shandong Cancer Hospital and Institute, Jinan, Shandong, People’s Republic of China; ²School of Medicine and Life Sciences, Jinan University-Shandong Academy of Medical Sciences, Jinan, Shandong, People’s Republic of China

Abstract: Male breast cancer (MBC) is considered as a rare disease that accounts for less than 1% of all breast cancers, and its treatment has been based on the evidence available from female breast cancer. Axillary sentinel lymph node biopsy (SLNB) is now regarded as the standard of care for both female and male patients without clinical and imaging evidence of axillary lymph node metastases, while internal mammary SLNB has rarely been performed. Internal mammary chain metastasis is an independent prognostic predictor. Internal mammary SLNB should be performed to complete nodal staging and guide adjuvant therapy in MBC patients with preoperative lymphoscintigraphic internal mammary chain drainage. We report both axillary and internal mammary SLNB in two cases with MBC. Internal mammary sentinel lymph node did contain metastasis in one case.

Keywords: male breast cancer, internal mammary lymph node, sentinel lymph node biopsy, case report

Introduction

Male breast cancer (MBC) is an uncommon phenomenon, accounting for less than 1% of all breast cancer with an annual incidence of 1/10⁵ which was reported on during the 2014 San Antonio Breast Cancer Symposium.¹ Because of its rarity, MBC has not been studied as extensively as female breast cancer (FBC), and its treatment has largely been based on that of FBC.

In clinically node-negative FBC, several large randomized prospective trials have shown that axillary sentinel lymph node biopsy (ASLNB) substantially reduces the surgical morbidity compared to that of axillary lymph node dissection (ALND).²,³ The feasibility and accuracy of ASLNB replacing ALND have also been proved in MBC.⁴ Internal mammary sentinel lymph node biopsy (IM-SLNB) has not been performed routinely and has remained a subject of discussion both in FBC and MBC, and it has been reported even less in MBC. Four MBC patients were treated in our center from April 2014 to February 2015, and all of them received ASLNB, while internal mammary sentinel lymph node (IMSLN) was detected and investigational IM-SLNB performed successfully in two MBC patients. Here we report these two cases receiving ASLNB and IM-SLNB.

Case report 1

Our first case was a 65-year-old man with a painless lump in his left breast for more than 5 years. He was admitted to our hospital in October 2014. Open-biopsy had been performed 1 week prior in another hospital, and invasive ductal carcinoma of 2.4 cm and grade II–III
was confirmed by routine pathology. Pathology consultation in our hospital indicated: (left) invasive ductal carcinoma, grade III, positive by immunohistochemistry (IHC) for estrogen receptor (ER) (>90% of nuclei stained) and progesterone receptor (PR) (about 10% of nuclei stained) and negative for HER-2 by IHC. The average Ki-67 labeling index was 40%. An elastic, well-defined and mobile axillary lymph node (ALN) about 1.0 cm in diameter was palpable in his left axilla. Ultrasonography revealed several enlarged ALNs with relatively normal structure, and ultrason-guided fine needle aspiration was performed on the largest one (1.2×0.6 cm) with benign cytological finding.

Thirty-seven MBq of 99mTc-labeled sulfur colloid (99mTc-SC) in 1.2 mL volume intraparenchymal injections at the 6 and 12 o’clock positions about 1.0 cm from areola under ultrasonographic guidance 17 hours before surgery, and preoperative lymphoscintigraphy revealed no radioactive IMSLN. Methylene blue (2 mL) was injected subcutaneously away from the open-biopsy cavity 10 minutes before surgery. The first axillary sentinel lymph node (ASLN) was found by the hand-held gamma probe in the second intercostal space. Blue dye was injected subcutaneously around the tumor. Two ASLNs were found with blue dye combined with 99mTc-SC. Intraoperative frozen section histology and touch imprint cytology showed that both of them were positive. Then a complete ALND was performed. After total mastectomy and ALND, the IMSLN was about 6 mm in diameter, and the ex vivo counts were 65. It did contain metastasis after definitive pathology. The routine pathology indicated: (left) invasive ductal carcinoma, grade II. It was positive by IHC for ER (50% of nuclei stained) and PR (about 20% of nuclei stained) and negative for HER-2 by IHC. The average Ki-67 labeling index was 30%. No lymph node was palpable in his left axilla and the ultrasonography also revealed no enlargement of ALNs.

Thirty-seven MBq of 99mTc-SC was injected as in the first case and preoperative lymphoscintigraphy revealed that there was a “hot spot” in his second intercostal space. Blue dye was injected subcutaneously around the tumor. Two ASLNs were found with blue dye combined with 99mTc-SC. Intraoperative frozen section histology and touch imprint cytology showed that both of them were positive. Then a complete ALND was performed. After total mastectomy and ALND, the IMSLN was found by the hand-held gamma probe in the second intercostal space as the lymphoscintigraphy revealed, and it was removed through the intercostal space. The IMSLN was about 6 mm in diameter, and the ex vivo counts were 65. It did contain metastasis after definitive pathology. The routine pathology indicated: (left) invasive ductal carcinoma of 1.8 cm, grade II, ASLN (2/2), ALN (3/18), and IMSLN (1/1). The final pathological stage for this male patient was pT2N3bM0 IIIC.

Case report 2

Our second case was a 56-year-old man who was admitted to our hospital in February 2015 with a painless lump about 2×1.5 cm in the left breast two years and a half. Preoperative core needle biopsy confirmed invasive ductal carcinoma, grade II. It was positive by IHC for ER (50% of nuclei stained) and PR (about 20% of nuclei stained) and negative for HER-2 by IHC. The average Ki-67 labeling index was 18% to 33% (mean 23.4%) of FBC patients, and metastasis...
exclusively situated in the IMLN occurs in 2% to 11% of patients. Patients with both axillary and internal mammary positive nodes have a very poor prognosis. If the IMSLN is positive, internal mammary radiotherapy should be performed, and staging achieved by the status of the ALN alone would lead to under-stage and under-/over-treatment. As we all know, extended radical mastectomy had been abandoned because it did not improve the survival of patients, and current imaging techniques, such as positron emission tomography/computed tomography, ultrasound and magnetic resonance imaging, could only detect metastatic lesions larger than 5 mm, so we recommend IM-SLNB as a minimally invasive technique for the efficient evaluation of the status of IMSLN to obtain complete nodal staging. If there is a high clinical suspicion for IMLN involvement, biopsy needs to be performed to diagnose whether or not it is involved. Gennari et al first reported a patient with MBC who underwent both ASLNB and IM-SLNB in 2004. Although the IMSLN did not contain metastatic cancer, it helped to determine the stage of the breast cancer for this MBC patient.

IM-SLNB is safe and feasible, and it needs to be considered both in MBC and FBC. Gnerlich et al reported no complications in their FBC study, and Caudle et al found only two intraoperative surgical complications, but both were resolved smoothly. Our current study on FBC indicates that the success rate of IM-SLNB is 85.8%, and 9.4% had positive IMSLN. In addition, only 5% of patients had intraoperative surgical complications, including injury to pleura and internal mammary artery. They were repaired intraoperatively, only one had a small pneumothorax on postoperative chest radiography that resolved without intervention and postoperative bleeding. The side effects are negligible when compared with the benefits.

IM-SLNB could guide adjuvant radiotherapy which is more important for MBC than FBC. The 2015 National Comprehensive Cancer Network Breast Cancer Clinical Practice Guidelines strongly recommend consideration of radiotherapy of IMLN for patients who are ALN positive after surgery. But many ALN positive patients did not have IMLN involvement. What is more, breast cancer occurs at an older age in males than in females, these patients may have more frequent cardiovascular and pulmonary comorbidities. Even though with the more modern radiotherapy techniques the toxicity to heart and lungs caused by radiotherapy is estimated to be less, special concern in MBC is still needed. Of note, in our study of women some patients with negative ALN did have IMLN involvement, and it might be the same in men. So, only relying on the status of ALN to perform internal mammary radiotherapy might lead to under-/over-treatment. IM-SLNB could make it possible to personalize treatment for patients thereby avoiding needless internal mammary radiotherapy. Cong et al suggested that patients with positive IMSLN should receive internal mammary radiotherapy, while it could be avoided in those with negative IMSLN. However, there is a need for further studies in IMSLN positive patients in order to confirm that addition of radiation to internal mammary site could improve outcomes.

The low visualization rate of IMSLN is the restriction for both clinical study and daily practice of IM-SLNB. A modified radiotracer injection technique (high volume, intraparenchymal, ultrasonographic guidance) was invented which broke through the bottle-neck of the low internal mammary visualization rate with traditional injection (71% versus 13.8%, P<0.001) in FBC. IMSLN was only detected in two of the four MBC cases in this case report due to the lower visualization rate in males than in females, which may be associated with the fact that men have less glands than women. We recommend that MBC should be diagnosed with core needle biopsy rather than excisional biopsy to avoid gland damage.

**Conclusion**

We suggest that IM-SLNB should be performed in MBC patients with IMSLN detected by preoperative lymphoscintigraphy or intraoperative gamma-probe. IM-SLNB is safe and feasible, and it might help to determine nodal staging and the pathological status of IMSLN in MBC, in case of under-stage and under-/over-treatment. Further studies are needed to confirm the value of IM-SLNB both in female and male patients with breast cancer.

**Disclosure**

The authors have stated that they have no conflicts of interest in this work.

**References**


