Localization of an Occult Primary Breast Cancer with Technetium-99m Sestamibi Scan and an Intraoperative Gamma Probe

Charles E. Cox, MD, Micheline Hyacinthe, MD, and Claudia Berman, MD, of H. Lee Moffitt Cancer Center & Research Institute; and Elisabeth L. Dupont, MD, and Andrew Wagner, MD, of the University of South Florida College of Medicine

Introduction

Breast cancer presenting as axillary adenopathy without radiographic or clinical breast abnormality is a rare entity accounting for less than 1% of all breast cancers.[1,2] In the past, extended searches for an extramammary site were conducted, but this extensive workup was unproductive and therefore not recommended.[3] Most authors currently advise that carcinoma found in an axillary node in a woman should be treated as breast cancer even in the absence of clinical or mammographic findings.[3] The recommended treatment is mastectomy. Tumors that are not recognized by mammography or clinical observation have been treated recently with breast preservation consisting of total breast irradiation with 50 Gy to 55 Gy. A 12% local recurrence rate was found compared with 56% in the nonirradiated breast.[4] A specific and sensitive diagnostic modality to locate an occult tumor is needed for breast conservation.

Case Report

A 34-year-old premenopausal woman presented with a swollen gland of two months' duration under the armpit. A freely movable, firm, round, smooth axillary nodule was found. Menarche occurred in this gravida 4, para 1-0-3-1 patient at age 9, and she had no family history of breast cancer. Physical examination revealed a firm, 2-cm left axillary mass and an indurated, thickened area in the upper outer quadrant of her left breast. No other lymphadenopathy was present. Mammography revealed scattered benign calcifications with no architectural distortion suspicious for malignancy. Fine needle aspiration, which has a sensitivity of 98% at our center,[5] was performed in both lesions. The axillary lesion was an adenocarcinoma, and the thickened area demonstrated fibrocystic changes.

Three therapeutic options were discussed with the patient: (1) mastectomy, (2) whole breast radiation with axillary dissection, and (3) sestamibi localization of the tumor with lumpectomy and axillary node dissection and radiation. She chose breast-conserving surgery. To pinpoint the primary lesion, scintimammography was performed using a dose of 18.0 mCi of technetium-99m sestamibi with five-minute and 60-minute postintravenous injection planar imaging of both breasts and the thorax. There was a small focus of abnormal uptake in the left axilla and another focal uptake inferior and slightly medial to the left nipple (Fig 1).

One hour prior to surgery, the patient was again given intravenous injection at a dose of 18.7 mCi of the radiolabeled isotope. Holding the breast away from the chest wall and directing the hand-held gamma probe away from the chest wall, the location of the lesion was found in the inner lower quadrant of the left breast (Fig 2). The lumpectomy demonstrated an eccentrically placed tumor grossly involving the superior margin of the specimen. The tumor also was identified ex vivo with the hand-held probe. Counts were three times the background. The probe identified the additional positive superior margin as well as the only positive axillary node out of 19 nodes. Touch preparation cytology was used on the lumpectomy specimen and all additional margins.[6] Pathology revealed lesions of 1.1 cm, 5 mm, and 8 mm consistent with infiltrating ductal carcinoma grade III and two small foci of ductal carcinoma in situ. Lymphatic vascular invasion was identified. All final margins were negative. The tumor was estrogen receptor-positive (3+) and progesterone receptor-negative. The one positive lymph node had no capsular invasion but was 90% replaced by tumor. Postoperatively, the patient underwent standard radiation therapy with 46 Gy to the breast and 12 Gy boost to the tumor bed, as well as adjuvant chemotherapy with cyclophosphamide, doxorubicin, and fluorouracil. She had an excellent cosmetic result.

Discussion

According to a report by Khalkhali et al,[7] scintimammography using technetium-99m sestamibi has a sensitivity of 95.8% and a positive predictive value of 81%, whereas mammography and physical examination have a sensitivity of 85% and a positive predictive value of 15% to 30%. Other investigators[8,9] have shown that the uptake of technetium-99m sestamibi is preferential in tumor cells compared with most normal cells. Increased uptake of technetium-99m sestamibi also has been reported in many human tumors (eg, osteosarcoma, recurrent brain gliomas, thyroid and parathyroid lesions, and breast cancers).[10-12] Although the exact mechanism in the preferential uptake of sestamibi in tumor cells is unknown, it probably is related to the level of metabolic activity. Scopinaro et al[13] suggest that the angiogenesis of malignancies, as well as oxidative metabolism by the tumor, accounts for the sestamibi uptake. Ninety percent of the tracer is found in the mitochondria.[14]

The intraoperative probe can successfully measure uptake within both the surgical specimen and the biopsy cavity. The principal drawback of this technique is excessive blood pool background resulting in significant "shine through" or detection of blood pool background in the heart, lungs, or liver. Angling of the hand-held probe away from the chest wall aids in the detection of lesions in the breast. Positioning of the patient is of technical concern in obtaining adequate images of the breast. Small gamma cameras may be more effective than large gamma cameras in obtaining cranial, caudal, and lateral images. Potential improvement in the background-to-tumor ratio within the breast possibly could be attained with selective intramammary arterial injections.

Currently, sestamibi is used to differentiate benign and malignant cells. As a result of our recent experience, however, we believe its use may be expanded to localize occult breast carcinomas, both intraoperatively and postoperatively, using a hand-held probe.

Many studies have shown that these occult breast tumors have the same or even a better prognosis when compared with the more prevalent stage II breast cancers.[1,3,15] Therefore, if the occult breast cancers could be located accurately, breast-conserving therapy would be an option for this patient population.

References

[1,3,15] Therefore, if the occult breast cancers could be located accurately, breast-conserving therapy would be an option for this patient population.