

99mTc-MIBI Scan in Mammary Paget's Disease : A Case Report

Technetium-99m methoxyisobutylisonitrile (99mTc-MIBI) uptake is known to be increased in breast cancer because of increased blood flow from angiogenesis and heightened metabolism. We performed a 99mTc-MIBI scan in a patient with mammary Paget's disease. The patient had underlying invasive cancer in the same side of the breast. 99mTc-MIBI scan exhibited a scintigraphic image of the uptake from the invasive cancer lesion located deeply in the breast toward the epidermis. 99mTc-MIBI showed an uptake in the deeply located invasive cancer lesion as well as nipple lesion. Especially, the delayed phase of Tc-MIBI scan demonstrated the tumor site more accurately. In conclusion, 99mTc-MIBI scan could be a useful adjunct to clinical decision making in the management of Paget's disease of the breast.

Key Words: Breast; Paget's disease, mammary; Technetium Tc 99m sestamibi; Diagnosis

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INTRODUCTION

Recently, a number of studies has been conducted to test the clinical utility of Technetium-99m methoxyisobutylisonitrile (Tc-MIBI) scan in breast cancer. Normal breast epithelial cells and fibroblasts have much lower Tc-MIBI retention than viable breast cancer cells. Similarly, Tc-MIBI uptake in breast cancers appears to be consistently elevated in tumors in comparison to the normal breast tissue (1, 2). This increased Tc-MIBI uptake in breast tumors likely reflects a combination of increased blood flow from angiogenesis (3) and increased Tc-MIBI retention related to heightened metabolism and mitochondrial transmembrane potential (MTP) (4). The aforementioned data support the use of Tc-MIBI as a marker of tumor burden and response in patients undergoing neoadjuvant chemotherapy.

Paget's disease of the nipple has been reported as the presenting sign of breast cancer in 0.5% to 4.3% of all cases. The histogenesis of Paget's cell has been hotly debated by two main theories. The epidermotropic theory postulates that Paget's cells are, in essence, ductal carcinoma cells that have migrated along basement membranes of the underlying duct to the nipple epidermis. The in situ transformation theory regards the Paget's cell as a transformed malignant keratinocyte and considers Paget's disease of the nipple to be an independent in situ

carcinoma. We describe an experience of Tc-MIBI scan and discuss the finding with review of histopathogenesis in Paget's disease of the breast.

CASE REPORT

A 48-year-old woman was referred from the dermatology department one year ago. She visited the local clinic for evaluation of eczematous lesion of the nipple of right breast. The lesion did not improve after one month of treatment with antibiotics and topical agents. Thus, the patient was referred to the dermatology department. When we examined the patient the first time, we could not discriminate the nipple from circumareolar area because of advanced disease. Skin was involved in an area of 5 cm diameter (Fig. 1) and a tissue biopsy was performed. Typical Paget cells were easily identified from the excised tissue (Fig. 2). Mass under the skin lesion was palpated about 4 cm in size on physical examination, but was not evident on mammography except as diffuse clustered microcalcifications. Tc-MIBI scan (Tc-sestaMIBI, 20 mCi, Dupont Pharma. Co.) was performed. Image was obtained at early (5 min) and delayed (50 min) phase. Dual phase showed persistent hot uptake in the area of nipple as well as underlying breast mass. However, axillary lymph node uptake on early scan was



Fig. 1. Typical eczematous skin change of the nipple with involvement of circumareolar tissue.

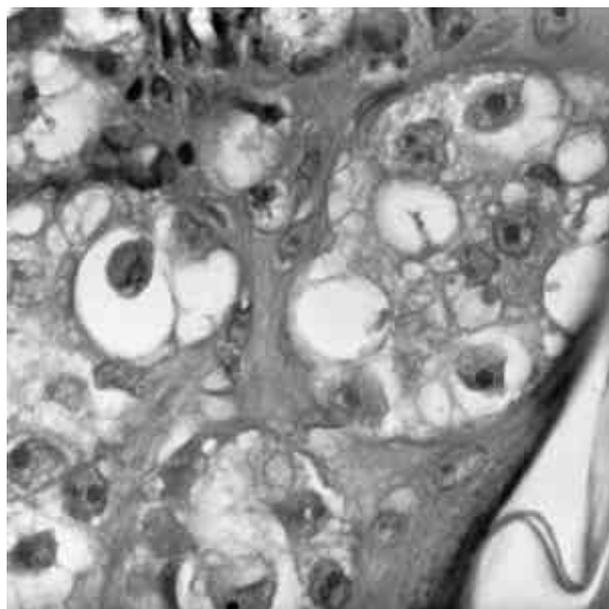


Fig. 2. Characteristic Paget's cells seen through light microscopy. Large, rounded and ovoid intraepithelial cell with abundant pale cytoplasm and enlarged pleomorphic and hyperchromatic nuclei with large nucleoli (H&E, $\times 400$).

washed out on delayed phase, which is not thought to be a metastatic lesion (Fig. 3). Underlying mass was confirmed as invasive ductal cancer by aspiration cytology and the patient underwent modified radical mastectomy.

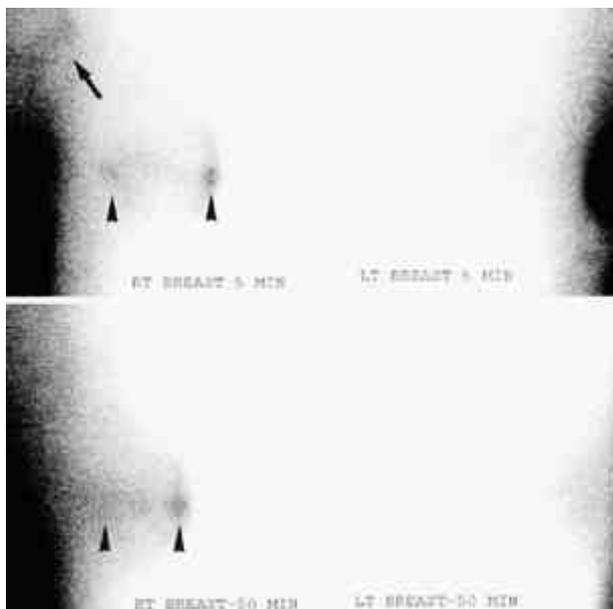


Fig. 3. Lateral view of Tc-MIBI scan. Diffuse hot uptakes (arrow heads) in right breast toward nipple, but not in the left, are persistently noted on early (5 min) and delayed (50 min) scan. However, right axillary uptake on early scan (arrow) is not seen on delayed image, which is indicative of the involvement of axillary lymph node.

The lesion in the breast parenchyma was 4×3.5 cm in size and did not involve the pectoralis fascia. Forty-two axillary lymph nodes were free of cancer cells, and the patient received adjuvant chemotherapy with six cycle regimen of 5-FU, methotrexate, and cyclophosphamide. Patient was free of the disease 12 months after the operation.

DISCUSSION

The clinical usefulness of Tc-MIBI scan in breast cancer patients has been demonstrated by a number of studies (5-7). Tc-MIBI demonstrated a higher sensitivity than conventional mammography in these studies. In the results of a prospective European multicentre trial with 246 breast cancer patients, the overall sensitivity and specificity was 83% and 91%, respectively (5). The nuclear medicine tracer Tc-MIBI is a lipophilic cation whose cellular uptake reflects MTP. Tc-MIBI is retained by cells with negative intracellular intra-mitochondrial electrochemical gradients and is an *in vitro* marker of MTP (8-10). Thus, MIBI preferentially collects in human carcinoma cells in comparison to normal cells, reflecting the heightened metabolic rate and MTP in malignant tissues (9, 11, 12). Processes, that affect MTP, alter cellular Tc-MIBI retention (13-16). Tc-MIBI's dependence upon intact membrane potentials for retention supports its usefulness as an agent for measuring tumor viability (10, 13,

16). Within the body, Tc-MIBI moves from the circulation into tissues, where it becomes bound in mitochondria (8). In vivo, lipophilicity of MIBI results in a large first pass extraction (17), such that its in vivo distribution is dependent upon blood flow as well as MTP. This blood flow related characteristics is the basis for MIBI's most common use as a tracer of myocardial perfusion.

In the case presented here, Tc-MIBI scan exhibited a scintigraphic image of uptake from the invasive cancer lesion located deeply in the breast toward epidermis. Like in our case, Tc-MIBI can exhibit an uptake in deeply located invasive cancer lesion as well as nipple lesion. Especially, the delayed phase of Tc-MIBI scan demonstrated tumor site more accurately. Underlying breast cancer, whether invasive or intraductal, could be found in more than 80% of mastectomy specimens from Paget's disease (18, 19). Most reports on Paget's disease have similarly demonstrated a high incidence of underlying carcinoma at a distance from the nipple lesion within the substance of the breast. The image of Tc-MIBI scan presented here well correlated with the characteristics of Paget's disease. In vivo, Tc-MIBI scan seems to represent the spread of neoplastic Paget's cells probably due to attractions induced by chemotactic factors released by keratinocytes. Tc-MIBI image of this case may be indirect evidence supporting the epidermotropic mechanism in histopathogenesis of Paget's disease of the breast. The same finding has been reported by Mezi et al. (20) during the preparation of this manuscript. Tc-MIBI scan provided useful complementary information about the extent of the disease in the patient with Paget's disease.

In conclusion, Tc-MIBI scan could be a useful adjunct to clinical decision making in the management of Paget's disease of the breast as well as in invasive breast cancer, and could be a complementary method to clarify the histopathogenesis of Paget's disease of the breast.

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