

Paget's Disease of the Nipple: Choice of Imaging Modalities for Breast Localization in Case of Multiple Breast Nodules and Sentinel Node



Suchato C, MD

Abstract

Paget's disease of nipple is rare entity. The majority of cases are associated with ductal carcinoma in situ (DCIS) or invasive ductal carcinoma (IDC) somewhere in the breast. When ultrasonic scan found multiheterogenic masses in both breasts, it is impossible to verify which one or more foci to be malignancy. We suggest to mark with small fish oil capsules at suspected masses before magnetic resonance imaging (MRI) breast with contrast enhancement as well as contrast enhanced spectral mammography (CESM) for comparison. The finding shows CESM is far more superior than (MRI) breast study on detection of sentinel node. CESM is faster, inexpensive and far more convenient for the patient.

Keywords: Paget's disease of the nipple, breast localization, digital mammography, ultrasonic scan, MRI breast contrast enhancement, CESM, sentinel node, contrast enhanced spectral mammography

Chirochana Suchato, MD¹
Mawin Vongsaisuwon, MD²
Kedsuda Thasup, RT¹
Pramaporn Kimhamanon, RT³

Paget's disease of nipple is a rare form of breast cancer; it is only 1-3% of all breast cancer.¹ It arises from small tubular ducts at the nipple. The nipple becomes a dark red color, itchy and irritated. According to the National Cancer Institute, more than 97% of cases have cancer either DCIS or IDC,² somewhere else in the breast. The unusual changes in the nipple are often the first indication of Paget's disease. The development of Paget's disease is unknown. There are two theories that can explain its origin:

1. Tumor arises from small tubular ducts in the breast and spreads to the nipple
2. Nipple becomes cancerous itself and a second breast cancer appears to be completely separate from the Paget's disease.

It is commonly found in women older than 50 years old. A man contracting the disease is rare and usually develops after the age of 70 years. Usually it occurs unilaterally. The immunohistochemical study usually is over expression of the c-erb-B2 oncogene.

Investigation

- Digital mammography either normal or mass, nipple may retract calcification or subareolar mass.
- Ultrasonic scan found heterogenic mass/masses.
- MRI demonstrated contrast enhanced mass or masses.
- CESM is helpful, the sensitivity and specificity is equal to an MRI study³ but CESM is less expensive.

Treatment

Wide excision, lumpectomy, mastectomy and sentinel node biopsy, breast conservative therapy with complete resection of nipple and areolar complex and local radiation therapy which may be used in cases of less extensive disease. For extensive disease, stage 3-4 hormonal, targeted therapy or chemotherapy may be used depending on hormonal tests and IHC for oncogenes.

¹ Imaging Center, Bangkok Hospital, Bangkok Hospital Group, Bangkok, Thailand.

² Surgery Unit, Bangkok Hospital, Bangkok Hospital Group, Bangkok, Thailand.

³ Breast Center, Wattanosoth Hospital, Bangkok Hospital Group, Bangkok, Thailand.

* Address Correspondence to author:
Chirochana Suchato, MD
Imaging Center, Bangkok Hospital
2 Soi Soonvijai 7, New Petchaburi Rd.,
Bangkok 10310, Thailand.
e-mail: chirochana@bangkokhospital.co.th

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Figure 1: Localized dark red lesion at left nipple is seen, no ulceration or extension into areolar region is observed.

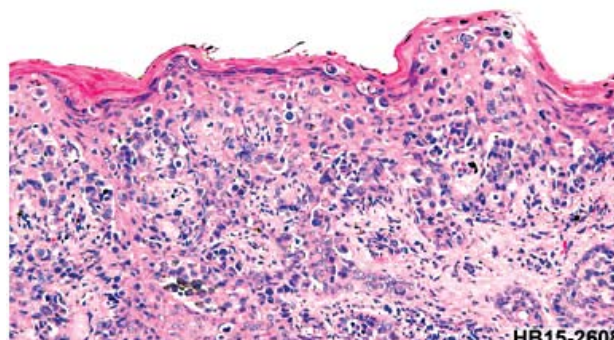


Figure 2: There are abnormal cells, single units and in groups, in the epidermis, some of them house melanon pigment, no abnormal cells in the dermis. Immunohistochemical stains CAM5.2 is positive, HMB45 is negative in tumor cells, Melan A is negative in the tumor cells. Paget's disease of nipple is diagnosed.

Case Report

A 46-year-old woman developed a dark red spot at the left nipple for 5 months (Figure 1). No other symptom is noted. No palpable breast mass is detected. All other findings and all laboratory findings are unremarkable, ultrasonic scan of the breasts reveal hypoechogenic lesions in both breasts. They appear stable for 2 years, suggestive of benign lesions (BIRADS 3), biopsy at left nipple reveals Paget's disease (Figure 2).

Imaging studies between MRI Breast vs Contrast Enhanced Spectral Mammography (CESM)

1. MRI Breast with dynamic study was performed and all techniques, clinical application and interpretation are well described.¹

The findings of MRI Breast with contrast enhanced study revealed two lesions at the medial aspect of the left breast with rapid contrast enhancement on the arterial phase and then declined to gradually washout on delayed phase (Figure 3-4). No contrast enhancement at sentinel node was observed.

2. Contrast Enhanced Spectral Mammography (CESM)

The radiologist was requested by the surgeon to localize this case with Paget's disease at the left nipple who from the previous ultrasonic scan showed multiple hypoechogenic masses in both breasts which appear unchanged for 2 years. How to localize these two lesions of the left breast and other lesions which are not identified by contrast enhancement. To avoid a repeat MRI Breast with contrast

enhancement and given the difficulty in placing markers on the skin, the practical way to approach this case for localization is as follows:

- First step: Markers on the skin of both breasts by using small fish oil pill on the skin by ultrasonic scan.
- Second step: MRI breast without contrast enhancement by using T1W, T2W, and short-tauinversion recovery (STIR). The previous study MRI breast with dynamic gadolinium (Gd) was preformed already, and so we prefer to reduce the cost of a repeat Gd enhancement MRI study.
- Third step: CESM with markers in place (Figure 5). Two masses with contrast enhancement are seen near the marker on the left breast (see arrows). In addition, there is another small contrast enhancement at the sentinel node which is not demonstrated by MRI Breast with Gd study (see arrow). No contrast enhanced mass on the right breast was observed.

CESM was preformed, the detail of technique as well as indications have been described.^{3,4}

Discussion

This is a presentation of Paget's disease of the left nipple which is a rare condition. For this case with follow-up multiple masses at both breasts which appear stable for 2 years, subsequently the patient developed Paget's disease at the left nipple. The planning of investigation for staging and treatment is the most important issue to address. Theoretically, Paget's disease may be cancer in the left breast as either single or multiple foci and possible in

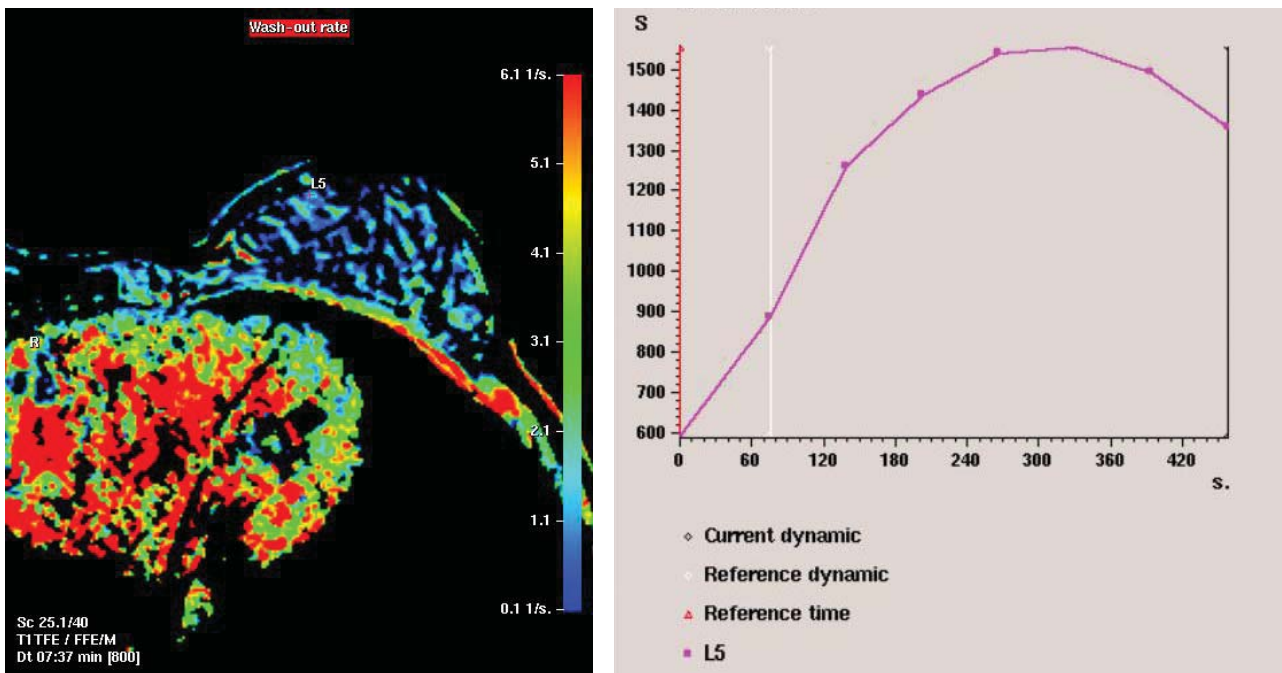


Figure 3: MRI of the breasts with dynamic Gd study reveals contrast enhanced masses at the medial aspect of left breast. MRI Gd dynamic study reveals rapidly increased contrast enhancement on the arterial phase and then this declined gradually on venous and delayed phases (washout) (Figure 4). The findings are suggestive of malignancy. The other masses in either left or right breast are not shown in contrast enhancement.

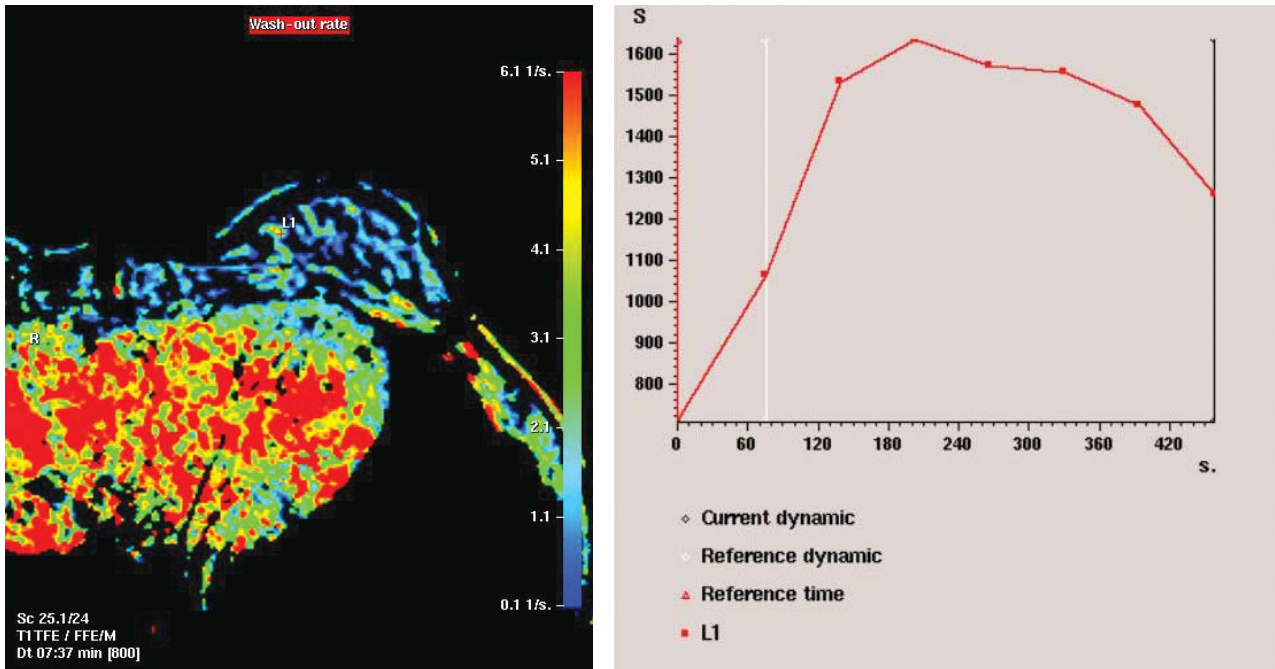


Figure 4: MRI Gd dynamic study sample on the left breast reveals rapidly increased contrast enhancement on arterial phase and then declined gradually on venous and delayed phases (washout). The findings are suggestive of malignancy. Only two lesions at the medial aspect of left breast are contrast enhancement, other lesions of both breasts show negative (they probably represent benign fibroadenomas).

contralateral, although this is even less possible. The second question is which one (or more) of the lesions are cancer. And the third question is how to localize the lesion/s. We suggest the modalities and sequences by ultrasonic scan with markers on the skin and using limitation MRI T1W, T2W, and STIR. and CESM for localized confirmation. As a previous MR Breast with Gd study has already been performed in this case we consider a way to reduce the cost of repeated MR with contrast enhancement. In comparison the findings of MRI and CESM for breast localization are similar. However in this case, CESM could demonstrate positive sentinel node and even microscopic metastasis (Figure 6C). But MRI Breast with contrast enhancement could not detect this. This is maybe possible for other indications of CESM in the detection of sentinel nodes as a surgical requirement for the adjustment in the planning of an operation.

Conclusion

A case presentation of Paget's disease of nipple with multiple hypoechogenic masses at both breasts. The planning for localization to identify the suspected malignancy lesion by using ultrasonic scan with fish oil markers on the skin is performed initially and followed by a limited MRI study. CESM is performed for confirmation. The findings for breast localization using either MRI or CESM are similar. Hence, we prefer CESM than MRI study for breast localization because CESM is relatively inexpensive, less time is needed for examination and it is far more convenient for the patient. In addition, for this case, CESM could detect positive sentinel node which is not detected by MRI of the breast. It may help in staging and may help the surgeon for treatment planning.

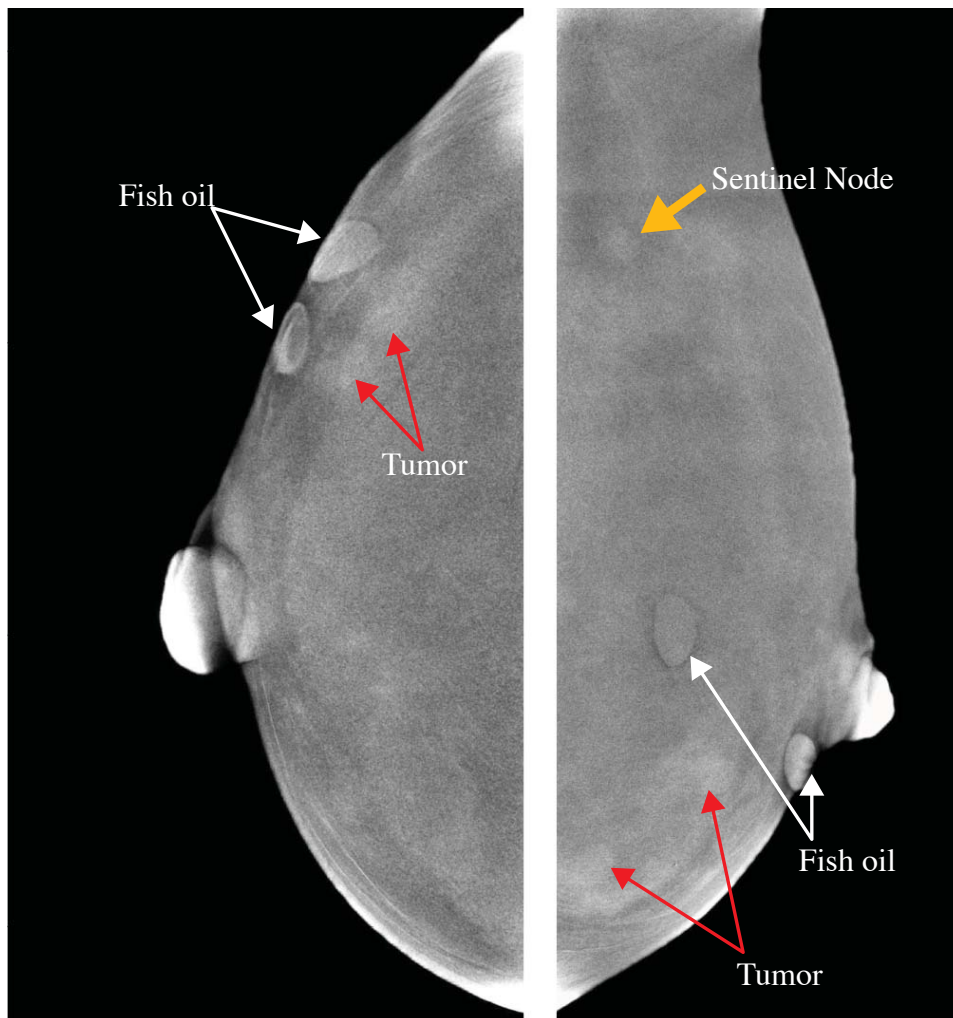


Figure 5: Contrast enhanced spectral mammography (with fish oil marker see arrow) on the skin shows small two tumors with contrast enhancement (see arrow). Other lesions are negative for contrast enhancement.

The immunohistochemical study is performed in S-58-014934-K, the result is as follows:

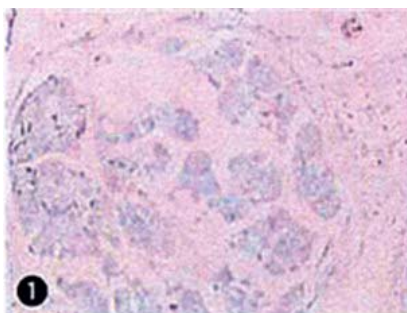


Figure 6A: EGFR -Negative.

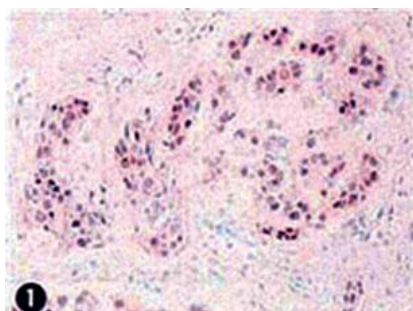


Figure 6B1: Estrogen receptor-Positive 60%.

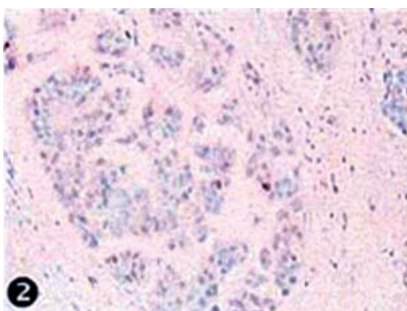


Figure 6B2: Progesterone receptor-Positive 5% (See 2).

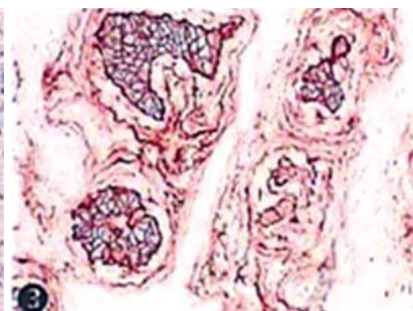


Figure 6B3: c-erbB2 (HER2) Score 3+ = Positive (Circumferential membrane staining that is complete, intense, and within > 10% of tumor cells).

Pathological Diagnosis:

II. Breast mass (left, Wide excision):

-ER: Positive 60%, PR: Positive 5%, Ki67: 20%, p53: positive 5%, c-erbB2 (HER2) Score 3+ = Positive

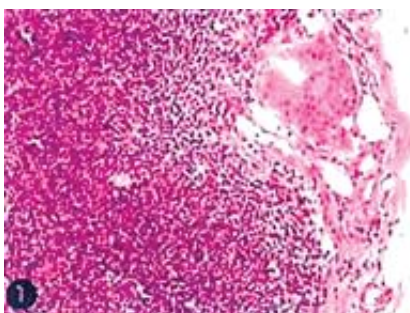


Figure 6C: Sections of sentinel lymph node shows tumor cells (< 2mm) in one lymph node.

Figure 6A-C: The microscopic findings reveal invasive ductal carcinoma of the breast.

Questions

1. Any mass/es is/or are detected in the breast/s?
2. How to localize the suspected malignant mass/es in one or two breast/s?
3. What is the practical method for the detection of malignancy lesion/s when digital mammography and ultrasonic scan are unable to detect the suspected malignancy lesion?
4. What is the ideal for the localization of this case either MRI vs. / or CESM?
5. For this case presentation, what is the imaging modality to detect the sentinel node?

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Answer

1. Ultrasonic scan is the ideal method for detection of breast mass/es but it has its limitations to evaluate whether the tumor is benign or malignant.
2. Ultrasonic scan modality for localization with fish oil pill as markers on the skin.
3. MRI with Gd dynamic study vs. /or CESM. For this case, an ultrasonic scan with markers is in place for localization.
4. CESM is the ideal examination for localization because it is comparatively inexpensive, less time is needed for study and it is more convenient. In addition, the skin markers are difficult in this prone position on an MRI examination.
5. CESM is superior to MRI Breast with Gd enhanced study.