



## Imaging in triple receptor negative carcinoma of the breast.

**KEYWORDS**

Breast, Mammography, Triple negative breast cancer (TNBC)

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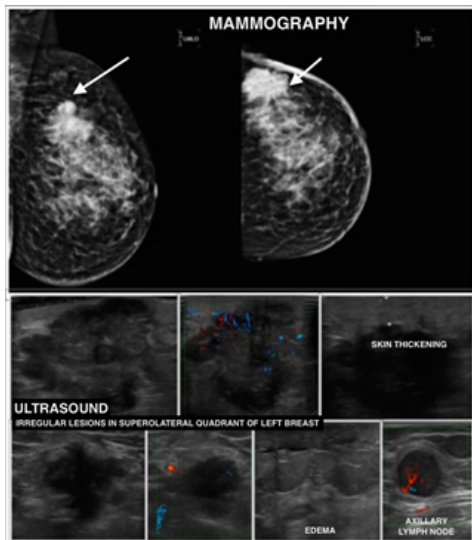
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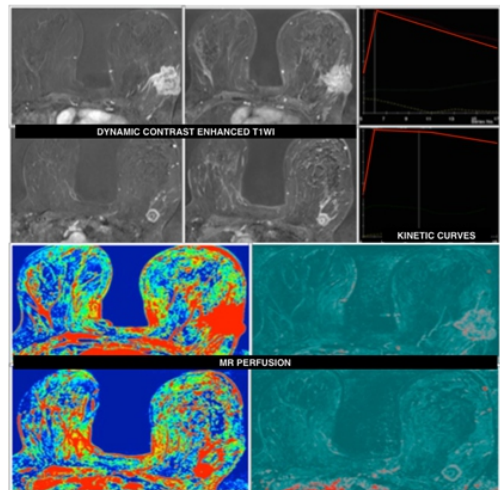
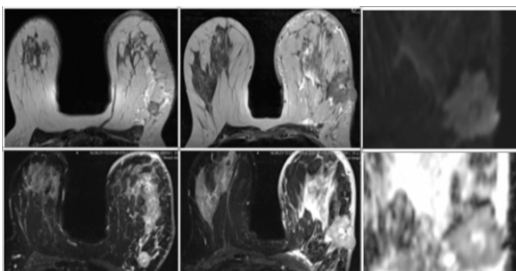
**ABSTRACT** We report a case of a 35 year old woman with a palpable painless lump in her left breast. Mammography revealed a suspicious lesion which was further evaluated by ultrasound, and MRI. Excision biopsy revealed triple receptor negative breast carcinoma, a distinct cancer subtype with a poor prognosis. This case highlights the imaging features of triple negative breast carcinoma (TNBC) with emphasis on some features that can help us to differentiate this type of breast cancer from others. Although triple-negative breast cancer (TNBC) has been studied extensively in the oncology and pathology literature, there are few reports on imaging features.

A 35-year-old woman presented with a palpable mass in the left breast. Initial evaluation with mammography showed an irregular lesion with spiculated margins in the superolateral quadrant of left breast with overlying skin thickening. Ultrasound showed two collocated solid cystic lesions at 3 o' clock position of left breast with irregular margins. On color doppler, intra-lesional and peri-lesional vascularity is seen along with skin thickening and architectural distortion. Left axillary lymph nodes with loss of fatty hila and raised vascularity were also seen (Fig. 1).

On dynamic contrast enhanced T1WI, the lesions showed inhomogeneous enhancement, predominantly in the periphery, with a quick rise and delayed wash out on the kinetic curves. MR Perfusion shows delayed wash out of contrast in both the lesions (Fig. 3).



Magnetic Resonance Imaging (MRI) showed two lesions in the superolateral quadrant of left breast, appearing heterogeneously hyperintense on T2WI and STIR images showing restriction of diffusion on diffusion weighted imaging (Fig. 2).



With these imaging features, BIRADS category 5 was given. Excision biopsy was done and histological examination came out positive for triple negative breast cancer.

**DISCUSSION:**

TNBC accounts for 11%–20% of all sub-types of breast cancers [1, 2], but accounts for 23%–28% of locally advanced disease [3, 4] and about 18% of TNBCs are occult on initial mammography [5–7]. Hence, understanding the imaging features is of considerable importance. On mammography, TNBC most commonly presents as a mass, with margin type reported to be circumscribed and absence of calcifications in 49%–100% of cases [5, 7–9]. Alternatively, TNBC presents as focal asymmetry, or as calcifications associated with a mass [6, 7].

TNBC lacks the typical suspicious mammographic features of breast cancer; namely irregular mass shape, spiculated margins and associated suspicious calcifications [10]. Therefore, mammography alone is usually a sub-optimal tool for its initial diagnostic evaluation.

The distinctive ultrasound features of TNBC include a well-

circumscribed margin of lesions [6–9] with associated posterior acoustic enhancement [7, 9]. Ultrasonographic well-circumscribed margins and acoustic enhancement are typically encountered in benign breast neoplasms, cysts or abscesses. However, posterior acoustic enhancement may also indicate an internal fluid component, as in tumour necrosis, a feature frequently reported on pathological assessment of TNBC.

Ultrasound is the mainstay of evaluation of the ipsilateral axillary, infraclavicular, internal mammary and the supraclavicular nodes [12]. Demonstrating the extent of nodal disease is critical for surgical and radiation planning, as well as appropriately routing patients who will benefit from neoadjuvant chemotherapy (NAC).

Dogan et al. [7] reported on the mammographic, ultrasound and magnetic resonance (MR) findings. TNBC were detected in 91% and 93% of patients by mammography and ultrasound, respectively, but magnetic resonance imaging (MRI) detected all tumours that are discovered on pathology specimens. According to their study, the peripheral enhancement pattern—which is a feature highly predictive of malignancy—was the most common enhancement pattern, and was found in 76% of triple-negative carcinomas [7]. Type of imbibition was rim enhancement, and MRI dynamic curve was fast wash in first two minutes and then plateau. The MR appearances reflect this aggressive biology. Chen et al. [11] commented on the presence of multi-focality (21%), large tumour size (mean  $4.1 \pm 2.7$  cm) and prominent skin enhancement suspicious of dermal lymphatic invasion in 34% of tumours <5 cm in diameter, with 79% of patients stage T2 or above at presentation. They also reported strong and/or heterogeneous enhancement in 93% of cases, rim enhancement in 41% and a quantifiable choline peak in 78% of the patients who underwent MR spectroscopy.

Improved understanding of TNBC biology has led to increasing use of NAC with TNBC being more chemosensitive than ER- positive tumours [13]. It has been shown that measurement of tumour size by MR correlates better with pathology [28]. Studies suggest that tumour sub-type and the type of NAC may influence the accuracy of MRI in determining the response and the extent of residual disease [13–16]. It is well recognised that all imaging modalities, including MRI, will miss small foci of disease. Non-concentric tumour shrinkage and the use of agents that reduce tumour vascularity decreasing contrast uptake within residual cancer are confounding problems. Indeed, the use of MRI to monitor response to anti-angiogenic agents has resulted in the lowest predictive accuracy of all chemotherapy regimens [14] as the reduction in tumour vascularity results in poor delivery of contrast agent and hence sub-optimal or non-visualisation of the tumour. Further work is required to monitor response in this clinical setting including the use of other MR parameters and alternative imaging modalities. Diffusion-weighted MRI (DW-MRI) detects changes in the apparent diffusion coefficient (ADC) of tissue and water, secondary to alterations in tissue and intra-cellular structure. ADC values have been reported to alter as early as a few days after commencing NAC [17] and may help detect NAC response sooner. Future work in this area may help determine whether diffusion has differing levels of sensitivity for assessing NAC response depending on breast tumour phenotype.

**CONCLUSION:** TNBCs appear in younger women and may carry benign features on mammography and ultrasound imaging, which in turn may cause delay in their accurate diagnosis. All cases are visualised on MRI where they appear as mass type of enhancement with well defined borders, regular shape and rim type of enhancement, also more often have persistent and plateau type of dynamic curve, and less likely have wash out type of curve. MRI also helps in staging these lesions and provides a reliable baseline for NAC follow-up. However, determination of residual tumour size post-NAC is still problematic and may be limited by the chemotherapy regime employed. DW-MRI is emerging as a helpful method to identify NAC response earlier than conventional breast MRI.

## REFERENCES:

1. Rakha, E. A., El-Sayed, M. E., Green, A. R., Lee, A. H., Robertson, J. F., & Ellis, I. O. (2007). Prognostic markers in triple-negative breast cancer. *Cancer*, 109(1), 25-32.
2. Lin, N. U., Vanderplas, A., Hughes, M. E., Theriault, R. L., Edge, S. B., Wong, Y., ... & Weeks, J. C. (2009). Clinicopathological features and sites of recurrence according to breast cancer subtype in the National Comprehensive Cancer Network (NCCN). *Journal of Clinical Oncology*, 27(15\_suppl), 543-543.
3. Dolle, J. M., Daling, J. R., White, E., Brinton, L. A., Doody, D. R., Porter, P. L., & Malone, K. E. (2009). Risk factors for triple-negative breast cancer in women under the age of 45 years. *Cancer Epidemiology and Prevention Biomarkers*, 18(4), 1157-1166.
4. Millikan, R. C., Newman, B., Tse, C. K., Moorman, P. G., Conway, K., Smith, L. V., ... & Nyante, S. (2008). Epidemiology of basal-like breast cancer. *Breast cancer research and treatment*, 109(1), 123-139.
5. Yang, W. T., Dryden, M., Broglio, K., Gilcrease, M., Dawood, S., Dempsey, P. J., ... & Arun, B. (2008). Mammographic features of triple receptor-negative primary breast cancers in young premenopausal women. *Breast cancer research and treatment*, 111(3), 405-410.
6. Wang, Y., Ikeda, D. M., Narasimhan, B., Longacre, T. A., Bleicher, R. J., Pal, S., ... & Jeffrey, S. S. (2008). Estrogen Receptor-Negative Invasive Breast Cancer: Imaging Features of Tumors with and without Human Epidermal Growth Factor Receptor Type 2 Overexpression. *Radiology*, 246(2), 367-375.
7. Dogan, B. E., Gonzalez-Angulo, A. M., Gilcrease, M., Dryden, M. J., & Yang, W. T. (2010). Multimodality imaging of triple receptor-negative tumors with mammography, ultrasound, and MRI. *American Journal of Roentgenology*, 194(4), 1160-1166.
8. Ko, E. S., Lee, B. H., Kim, H. A., Noh, W. C., Kim, M. S., & Lee, S. A. (2010). Triple-negative breast cancer: correlation between imaging and pathological findings. *European radiology*, 20(5), 1111-1117.
9. Kojima, Y., & Tsunoda, H. (2011). Mammography and ultrasound features of triple-negative breast cancer. *Breast Cancer*, 18(3), 146-151.
10. Bi-Rads-IRM. A. C. R. (2003). Première édition française basée sur la première édition américaine. American College of Radiology (ACR). ACR-BI-RADSMagnetic Resonance Imaging. ACR Breast imaging reporting and data system, Breast Imaging Atlas. Reston, Va: American College of Radiology.
11. Chen, J. H., Agrawal, G., Feig, B., Baek, H. M., Carpenter, P. M., Mehta, R. S., ... & Su, M. Y. (2007). Triple-negative breast cancer: MRI features in 29 patients. *Annals of oncology*, 18(5), 504.
12. Yang, W. T., Ahuja, A., Tang, A., Suen, M., King, W., & Metreweli, C. (1996). High resolution sonographic detection of axillary lymph node metastases in breast cancer. *Journal of ultrasound in medicine*, 15(3), 241-246.
13. Buchholz, T. A., Lehman, C. D., Harris, J. R., Pockaj, B. A., Khouri, N., Hylton, N. F., ... & Newman, L. A. (2008). Statement of the science concerning locoregional treatments after preoperative chemotherapy for breast cancer: a National Cancer Institute conference. *Journal of Clinical Oncology*, 26(5), 791-797.
14. Chen, J. H., Feig, B., Agrawal, G., Yu, H., Carpenter, P. M., Mehta, R. S., ... & Su, M. Y. (2008). MRI evaluation of pathologically complete response and residual tumors in breast cancer after neoadjuvant chemotherapy. *Cancer*, 112(1), 17-26.
15. Loo, C. E., Straver, M. E., Rodenhuis, S., Muller, S. H., Wesseling, J., Vrancken Peeters, M. J. T., & Gilhuijs, K. G. (2011). Magnetic resonance imaging response monitoring of breast cancer during neoadjuvant chemotherapy: relevance of breast cancer subtype. *Journal of Clinical Oncology*, 29(6), 660-666.
16. Moon, H. G., Han, W., Lee, J. W., Ko, E., Kim, E. K., Yu, J. H., ... & Oh, D. Y. (2009). Age and HER2 expression status affect MRI accuracy in predicting residual tumor extent after neo-adjuvant systemic treatment. *Annals of oncology*, 20(6), 683.
17. Theilmann, R. J., Borders, R., Trouard, T. P., Xia, G., Outwater, E., Ranger-Moore, J., ... & Stopeck, A. (2004). Changes in water mobility measured by diffusion MRI predict response of metastatic breast cancer to chemotherapy. *Neoplasia*, 6(6), 831-837.