PATHOLOGY CONSIDERATIONS IN PATIENTS TREATED WITH NEOADJUVANT CHEMOTHERAPY

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KEYWORDS

• Breast cancer • Neoadjuvant therapy • NAT • Preoperative therapy • Histology
• Pathologic diagnosis • Tumor markers

ABSTRACT

Neoadjuvant therapy (NAT) was first used to treat women with locally advanced disease but is currently offered to women with earlier-stage and operable breast carcinoma. NAT allows more women to be eligible for breast conservation surgery and provides an opportunity to assess the response of carcinomas to therapy. This review focuses on predictors of therapeutic response in pretreatment biopsy, evaluation of post-treatment breast and lymph node specimens, classification systems to evaluate degree of response to NAT, and reporting of post-treatment specimens.

Pathologic Key Features
Analysis of Breast Carcinoma in Neoadjuvant Setting

- Identification, thorough sampling, and microscopic documentation of the tumor bed are essential, particularly in cases of complete or near-complete response.
- Microscopically, the tumor bed appears as a loose vascularized fibrotic area often associated with edema, myxoid change, and lymphohistiocytic infiltrate.
- The extent, largest contiguous focus, cellularity, and treatment effect of any residual tumor should be analyzed carefully to grade the extent of response in both the breast and lymph nodes.
- Tumor bed transected at the margin should be reported, particularly in specimens where residual invasive carcinoma or ductal carcinoma in situ (DCIS) is identified.
- Repeat studies on residual tumor for hormone receptors, human epidermal growth factor receptor 2 (HER2) and proliferation marker (eg, Ki-67) can provide additional prognostic and therapeutic information.

OVERVIEW

Neoadjuvant therapy (NAT) is offered to women with locally advanced carcinomas to reduce tumor burden and make patients eligible for surgical treatment. Clinical trials have shown no difference in the locoregional control and metastasis free survival for patients who receive adjuvant chemotherapy vs NAT.[1–6] However, patients who achieve a pathologic complete response (pCR) have improved long-term survival, disease-free survival (DFS), and overall survival (OS) compared with patients who have partial or no response to NAT.[7–10] Individual patients may benefit from this information by being able to change treatment when no response is evident or receive additional treatment if response is not complete. Alternatively, patients with good responses benefit by knowing their prognosis and making decisions about types of treatment, including prophylactic

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surgery. Tumor response has also been used as a short-term endpoint for clinical trials. Information about the effectiveness of a treatment is available in months to 1 to 2 years, in contrast to the endpoints of recurrence or death—events that typically do not occur for many years or even decades after adjuvant treatment. Finally, the ability to correlate pretreatment and post-treatment tumor samples directly to treatment response has provided a wealth of information about tumor biology and will hopefully yield better methods of predicting response as well as identify additional targets for treatment.

Patients undergoing NAT are diagnosed by a core needle biopsy. Pretreatment tumor size and extent are determined by imaging studies. A clip or clips must be placed at the time of diagnostic core needle biopsy and/or during the first

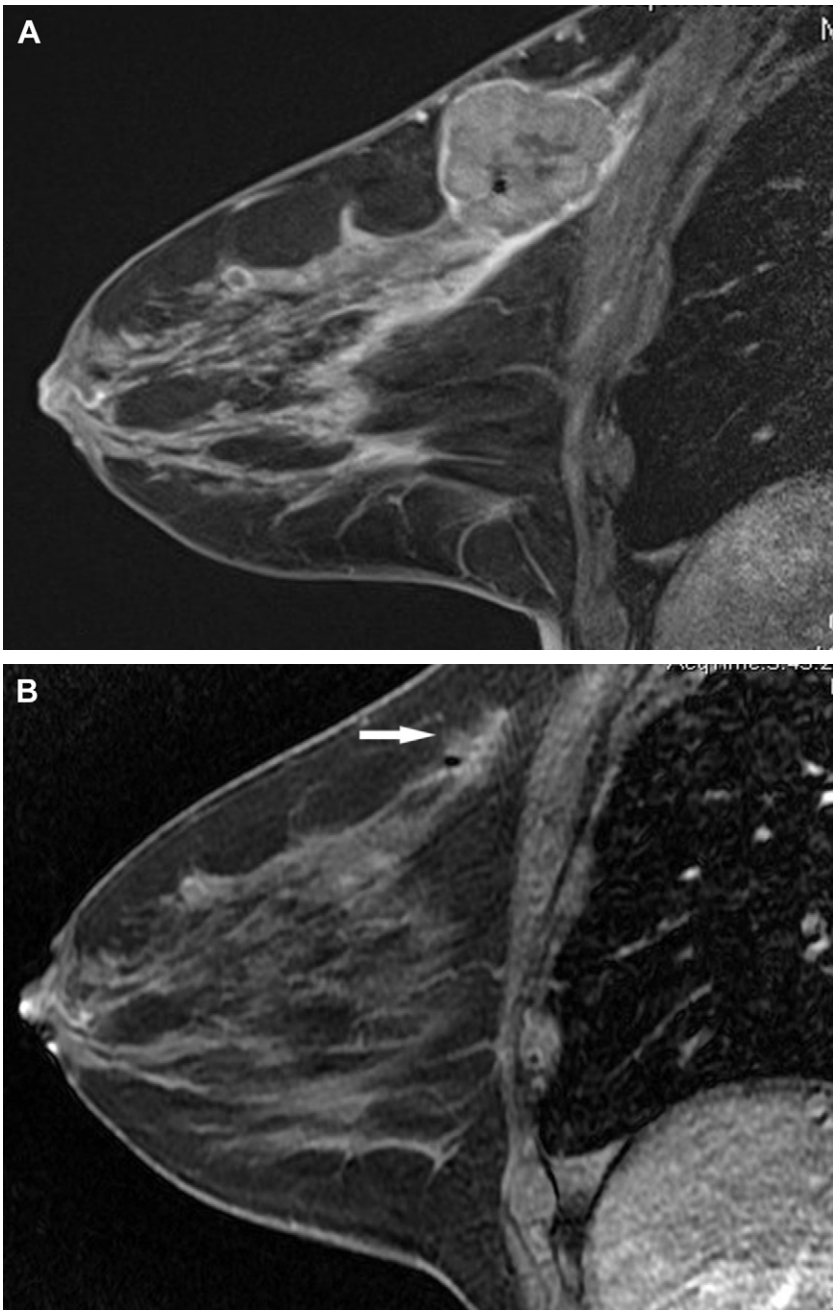

Fig. 1. Pretreatment and post-treatment contrast enhanced MRI images of breast carcinoma. (*A*) Pretreatment maximum intensity projection image of a patient presented with a large palpable breast mass that abutted but did not involve the skin or chest wall. (*B*) The postchemotherapy maximum intensity projection image shows complete resolution of the prior mass (*arrow*). Microscopic evaluation did reveal, however, scattered residual tumor in the area of prior abnormality (tumor bed).