CASE REPORT

Use of Oncotype DX Assay in Stage I Breast Cancer: A Case Report

Merry L. Tetef, MD

Case Report

A 58-year-old postmenopausal woman underwent a routine screening mammogram, which revealed a 7 mm mass in her left breast. Breast MRI revealed 2 adjacent lesions. On lumpectomy she was found to have 2 adjacent invasive ductal carcinomas measuring 10 mm and 4 mm, both high grade, both high Estrogen Receptor (ER), high Progesterone Receptor (PR), HER 2 negative, and Ki67 intermediate at 24%. One sentinel node was negative and she therefore had multifocal Stage IA breast cancer. Given the high grade nature of the cancer, Oncotype Dx 21-gene recurrence score was performed on the larger lesion to clarify the potential benefit of chemotherapy. The Recurrence Score returned at 32, in the high risk range, with a 10-year risk of distant recurrence with tamoxifen alone of 21%. Therefore, she was treated with chemotherapy based on the oncotype result, and she received docetaxel and cyclophosphamide for 4 cycles followed by whole breast radiation therapy, then aromatase inhibitor therapy with anastrazole. She remains in remission and as of now has completed 1 year of adjuvant anastrazole.

Discussion

Adjuvant endocrine therapy for hormone dependent non-metastatic breast cancer improves survival and is fairly well tolerated. In addition, endocrine therapy can offer chemoprevention against new breast cancer for women who have residual breast tissue after surgery. Therefore, endocrine therapy is advised for the adjuvant therapy of hormone sensitive breast cancer.

However, some women with non-metastatic hormone sensitive breast cancer will also benefit from adjuvant chemotherapy. For those women with hormone receptor positive, HER2-positive tumors, the combination of chemotherapy and HER2 blockade can improve both recurrence free and overall survival. Such therapy can improve outcome for even small tumors, and most women with hormone sensitive HER2 positive tumors 5 mm or greater in size will benefit from chemotherapy with HER2 blocking agents followed by endocrine therapy.

The role of chemotherapy for women with hormone receptor positive, HER2 negative tumors is less defined as such tumors are heterogeneous with varying biological subtypes with differing responses to chemotherapy. Over time, as the biology of breast cancer has become better defined, pathologic and molecular features are being used to determine the patients who will benefit from chemotherapy. These tools allow chemotherapy, with its associated potential toxicities, to be used in the patients who will have the best likelihood of benefit.

In general, chemotherapy is more effective in cancers that have faster growth rates. The standard pathologic feature of tumor grade has been used to reflect cancer growth rates, but this has been found to not be adequate on its own to predict chemotherapy responsiveness. There can be inter-observer variability in assessing tumor grade, particularly for grade 2 tumors. Ki67 testing can also reflect tumor growth rates, but there is significant inter-laboratory variability in this tumor staining and therefore this test cannot be relied upon as the conclusive feature to determine the benefit of adjuvant chemotherapy.

Genomic expression studies of breast cancers, which simultaneously measure the expression of thousands of genes, have identified several breast cancer subtypes that differ in prognosis and potential therapeutic targets.[1] The luminal A subtype has high expression of ER-related genes, low HER2 related genes, and low proliferation genes. In contrast, the luminal B subtype has a relatively lower expression of ER-related genes, variable HER2-related genes, and does have more expression of proliferation genes. The luminal A tumors are unlikely to benefit from chemotherapy, while luminal B tumors have a worse prognosis and are more likely to benefit from adjuvant chemotherapy.

A number of biomarker assays, which use genomic expression of tumors, have been developed as prognostic and/or predictive tools, to help determine the appropriate systemic therapy for an individual patient. The Oncotype Dx Recurrence Score is one such assay, used to identify patients with hormone sensitive breast cancer who are most or least likely to benefit from chemotherapy, in addition to endocrine therapy.[2] The Recurrence score quantifies the likelihood of breast cancer recurrence and also predicts the magnitude of benefit from chemotherapy in patients with node negative disease. The use of the Recurrence Score in node positive disease can help predict the benefit of chemotherapy [3] but the other histologic features that affect risk of recurrence in higher stage disease

also should be considered when deciding the role of chemotherapy in node positive disease. Another genomic assay, the 70 gene profile called Mammaprint, can be utilized in both the node negative and 1-3 node setting to assess high or low risk of recurrence and therefore consider which patients might benefit from adjuvant chemotherapy.[4]

There are a number of other biomarker assays which can be used to decide if an individual patient should receive chemotherapy. For the patient discussed above, Ontotype testing was performed which revealed a high risk Recurrence Score with an associated estimated 9% absolute decrease in distant spread with chemotherapy. After reviewing these statistics, the patient chose to be treated with chemotherapy prior to receiving endocrine therapy. In this setting of early stage I breast cancer, genomic testing revealed a high risk of recurrence despite low volume disease, reflecting the importance of individualized systemic breast cancer therapy for early stage disease. Although basic pathologic assessment is the critical first step in evaluating early breast cancer, genomic testing often adds valuable personalized data to optimize systemic therapy.

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