

CLINICAL VIGNETTE

The Need to Biopsy Initial Site of Metastatic Recurrence in Patients with Breast Cancer

Steven Applebaum, M.D.

A 56-year-old woman with a breast mass biopsy, in August of 2005, confirmed the diagnosis of an invasive ductal cancer, which was estrogen receptor (ER) positive, progesterone receptor (PR) positive, and negative for amplification of HER-2, which was confirmed on both immunohistochemical (IHC) testing and on FISH testing. She had back pain and bone scan confirmed the presence of limited bone metastasis. She requested and underwent bilateral mastectomies. The pathology from the surgical specimen confirmed a 5 cm cancer with eight axillary nodes removed, all of which were involved with metastatic cancer. The cells were again confirmed to be ER positive, PR positive, and HER-2 negative. She received six cycles of chemotherapy with cyclophosphamide, doxorubicin and 5-FU followed by hormonal therapy with anastrozole.

She did very well clinically for years with no evidence of progression and enjoyed an excellent quality of life with no limitations (ECOG performance status of 0). However, in February of 2014, she developed fairly rapidly progressing symptoms of cough and shortness of breath. Imaging showed the presence of a large lung mass, with a significant pleural effusion and worsened bone metastasis. A biopsy of a bone lesion confirmed the presence of breast cancer. However, the cancer cells were now noted to be ER negative, PR negative, and HER-2 positive.

She was declining rapidly, requiring oxygen despite a thoracentesis, so she was started promptly on therapy with docetaxel, trastuzumab, and pertuzumab. She has had a dramatic response with marked shrinkage of the lung mass, resolution of the effusion, and is no longer requiring oxygen. The anastrozole she had been taking has been discontinued.

This case exemplifies the need to biopsy new metastasis in patients with breast cancer, as the progressive disease may express a different phenotype from the original cancer, which can have dramatic implications for therapy. In this case, her initial cancer was ER positive and HER-2 negative and well-controlled on hormonal therapy for many years, but her progressive disease proved to be completely different, now being ER negative and HER-2 positive. This was previously felt to be a rare occurrence, and practicing oncologists used to presume the metastatic disease would have the same behavior as the original cancer, and thus biopsy was unnecessary.

More recently however, the question of the need to biopsy new sites of disease has been readdressed, largely driven by newer, targeted therapies such as trastuzumab, as well as novel hormonal agents that can be used in the second line if the cells maintain their hormonal sensitivity. Also, improved techniques for image-guided biopsies in interventional radiology has allowed for less invasive means to obtain tissue.¹ Lastly, advancements in pathologic techniques allow for improved testing on tissue that previously may have been inadequate to fully analyze.

This question was recently addressed in a phase III trial published in February 2012. Investigators at the University of Ottawa were able to consent 137 women who presented with newly noted metastatic or progressive disease and with a prior diagnosis of early stage breast cancer to perform a biopsy of the metastatic site with the end-point to see if a change in management could be attributed to the biopsy. The secondary goal was to see the overall discordance of the new site of cancer to the prior known disease, specifically in terms of ER, PR and HER-2.

A total of 121 biopsies were completed, confirming breast cancer in 117. Ninety-four of these (80%) had sufficient tissue for immunohistochemical staining, and of these, 83 (88%) were sufficient for HER-2 testing by FISH. The total discordance rate was 38% with the most common change being in the PR. The more clinically significant changes in ER occurred in 16% and in HER-2 at roughly 10%. A total of 17 women had a change in therapy due to the biopsy, which included addition of trastuzumab in patients who "gained" HER-2 positivity, which happened in 6 women.

While these numbers may seem relatively small, the potential for dramatic change in outcome warrants biopsy in this setting. Certainly the patient presented had a dramatic clinical response based on new information from the biopsy.

REFERENCES

1. **Amir E, Miller N, Geddie W, Freedman O, Kassam F, Simmons C, Oldfield M, Dranitsaris G, Tomlinson G, Laupacis A, Tannock IF, Clemons M.** Prospective study evaluating the impact of tissue confirmation of metastatic disease in patients with breast cancer. *J Clin Oncol.* 2012 Feb 20;30(6):587-92. doi:

10.1200/JCO.2010.33.5232. Epub 2011 Nov 28.
PubMed PMID: 22124102.

Submitted November 9, 2014