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CLINICAL VIGNETTE

Metastatic Breast Cancer Following an Initial Diagnosis of Ductal Carcinoma in Situ

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Case Report

An 80-year-old woman presented with 6 months of bloody right nipple discharge. Mammography revealed ill-defined asymmetry in the entire upper outer quadrant of the involved breast without a discrete mass, with scattered benign appearing calcifications. Biopsy revealed intermediate grade ductal carcinoma in situ. Right mastectomy revealed 8 cm of intermediate ductal carcinoma in situ (DCIS) with no invasion, highly positive Estrogen Receptor (ER) and Progesterone Receptor (PR), and one negative sentinel node. The patient declined endocrine therapy for chemoprevention and was followed with routine physical examination and breast imaging.

Five years after her diagnosis of DCIS she underwent a spine MRI for back pain, which was determined to be degenerative but was also found to have an incidental lung nodule. Subsequent chest CT revealed multiple bilateral lung nodules, while PET/CT did not show any disease outside of the lung. Biopsy of the largest lung nodule revealed invasive ductal carcinoma, ER and PR positive, HER-2 negative. She was started on letrozole and has had stable disease for 6 months.

Discussion

DCIS is defined as in situ, or non-invasive, disease, and as such is not felt to pose a risk of systemic metastasis. Treatment for DCIS is based on the management of the local process, with surgery and radiation therapy used to treat the known non-invasive disease to prevent a local recurrence. In contrast to the treatment of invasive breast cancer, in which systemic treatment is used to prevent systemic spread, systemic therapy in the management of DCIS consists of endocrine therapy that is used for chemoprevention to decrease the risk of developing a new breast cancer in the remaining breast tissue and not to prevent a systemic recurrence.

Our patient developed invasive, metastatic breast cancer after a prior diagnosis of DCIS. It is surmised that she therefore must have had areas of microinvasion not detected at her initial pathology. Given that her initial DCIS extended over the large area of 8 cm, this disease extent increases the risk of microinvasion that might be occult on pathologic review.

However, when microinvasive DCIS has been studied, prognosis has been good with no increased risk of systemic spread^{1,2}. These conclusions are based on a small number of patients as microinvasive DCIS is not a common presentation of breast cancer.

The risk of distant invasive breast cancer after a diagnosis of DCIS is very small, with one study reporting a risk of 2%³. So are there other factors that can be used to help determine why this patient developed metastatic, invasive breast cancer?

The mammographic appearance of calcifications on mammography in small invasive breast cancers has been correlated with prognosis⁴. Casting-type calcifications were found to correlate with a worsened prognosis in small screening detected invasive breast cancers. When evaluated in DCIS, such casting-type calcifications correlated with increased risk of in situ breast cancer events but not increased risk of invasive disease⁵. For our patient, her mammogram at the time of diagnosis of DCIS revealed only benign appearing calcifications.

There is no clinically established classification of DCIS that helps predict prognosis and risk of invasive disease. Molecular subtypes of invasive breast cancer have been identified based on gene expression profiling, with prognosis and treatment now often being based on such subtypes of invasive cancer. A cohort study examined the relation between these subtypes in DCIS and prognosis in 382 cases of DCIS³.

The subtypes evaluated were Luminal A, Luminal B/HER2 negative, Luminal B/HER2 positive, HER2 positive/ER negative, and triple negative. Eight of these women with DCIS had distant recurrences in the absence of a local recurrence. There was no correlation of risk of distant recurrence and molecular subtype. The study did find an increased risk of developing breast cancer more than 10 years after a diagnosis of triple negative DCIS but this was based on a small number of events as fewer than 10% of the patients had triple negative DCIS. Of note is that our patient likely had the Luminal A subtype of DCIS (although HER2 testing and gene expression were not performed on her initial cancer).

HER2 positive DCIS is felt to potentially have an increased risk of local recurrence compared with HER2 negative DCIS. The National Surgical Adjuvant Breast and Bowel Project (NSABP) on study B-43 is evaluating the use of radiation therapy following lumpectomy for DCIS with or without the use of trastuzumab for HER2 blockade to potentially decrease the risk of local recurrence. This study is not using systemic therapy of trastuzumab to decrease the risk of distant disease as HER2 positive DCIS is felt to be a local process.

The literature does not explain why this patient with DCIS developed the unusual complication of subsequent metastatic breast cancer. Perhaps if she had chosen to receive endocrine therapy for chemoprevention at her diagnosis of DCIS, this might have prevented systemic spread. Currently with the rarity of invasive systemic spread of breast cancer after a diagnosis of DCIS, endocrine therapy will continue to only be used in the setting of DCIS for chemoprevention of a new breast cancer in residual breast tissue.

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