CLINICAL VIGNETTE

Invasive Lobular Breast Cancer with Metastasis to the Stomach

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Case Report

A 46-year-old woman underwent bilateral mastectomies for a node positive, hormone receptor positive grade 2 invasive lobular cancer. She received adjuvant chemotherapy with Cyclophosphamide, Methotrexate and 5FU, but declined endocrine therapy. Twenty-three years later at age 69 preoperative laboratory testing in preparation for knee replacement surgery, found anemia. Imaging revealed extensive bone metastases and para-aortic nodal metastases. Bone marrow biopsy revealed metastatic breast cancer, Estrogen receptor (ER) positive, Progesterone Receptor (PR) positive, HER2-neu negative. Genetic testing was negative for mutations in the BRCA1, BRCA2, CHD1, PTEN and TP53 genes. She was treated with letrozole and denosumab for 4 years, after which imaging revealed progressive disease with a new gastric mass in the cardia, stable para-aortic nodes and improved bone metastases. Upper gastrointestinal endoscopy revealed the mass in the gastric cardia was metastatic invasive adenocarcinoma consistent with her breast cancer, ER positive, PR positive, HER2 negative. She had no local symptoms related to the gastric metastasis. Her treatment was then changed to fulvestrant with palbociclib.

Discussion

Accounting for approximately 10% of invasive breast cancer cases, invasive lobular carcinoma (ILC) is the second most common type of breast cancer, with invasive ductal carcinomas (IDC) the most prevalent. Patients with ILC present on the average 3 years older than those with IDC and more frequently have ER and PR positive disease. ILC is more strongly associated with exposure to female hormones than is IDC, including early menarche, late menopause, and age at first live birth.[1]

Arising from the lobular epithelium, ILC is often insidious in onset as it does not invoke a desmoplastic response, while small cells tend to infiltrate the stroma in long single-file sheets. E-cadherin loss is the hallmark on pathology. ILC may not be apparent on mammography due to its incohesive growth pattern and lower likelihood to produce calcifications. This growth pattern often makes ILC difficult to detect clinically. These features contribute to ILC often being diagnosed at a higher stage than IDC, with larger tumors and more frequent nodal involvement.[2]

In comparison to IDC, patients with ILC have statistically improved disease free survival and overall survival early in their disease, but higher risk for late recurrence, as seen in our patient.[3] There are no significant differences in overall survival between IDC and ILC.

Patients with ILC have a different pattern of metastatic spread compared to IDC, with location of initial metastasis more often to bone, the GI tract, and ovaries as compared to IDC.[3] One review of 761 patients with metastatic breast cancer[4] identified a 5.7% incidence of initial metastasis to the GI tract in ILC as compared to a 0.3% incidence in IDC. During the course of metastatic disease, 9.7% of those with ILC versus 0.6% of IDC developed GI metastases.

A number of genetic mutations are associated with an increased risk of breast cancer and can now be identified on various gene panels. The high penetrance genes BRCA1, BRCA2, TP53 and CDH1 have differing clinical presentations of breast cancer. Germline mutations of BRCA1 and TP53 are predominantly associated with IDC. BRCA2 mutations are associated with both IDC and ILC, while CDH1 mutations are associated exclusively with ILC.

Located on chromosome 16q22, CDH1 encodes for the E-cadherin protein, which mediates cell-to-cell adhesion. Loss of CDH1 expression is observed in the majority of ILC but is unaffected in IDC. CDH-1 was initially identified as the susceptibility gene in diffuse gastric cancer, which demonstrates inactivation of E-cadherin and similar histopathologic features to those of ILC.[1] Women with CDH1 mutations have an approximate 50% risk of breast cancer and are recommended to start breast cancer screening with mammography and MRI starting at age 30. In addition, prophylactic total gastrectomy is recommended between ages 18-40 for CDH1 mutation carriers. The loss of E-cadherin as seen in gastric cancer may contribute to the tendency of ILC to metastasize to the stomach.

The patient described in this case report did not have a CDH1 mutation, but did present with late gastric metastases, as can be seen in ILC. With the approximate doubling in progression free survival when CDK4/6 inhibition with palbociclib is combined with fulvestrant therapy, this woman should have a better clinical outcome than prior to the use of CDK4/6 inhibitors. Unfortunately metastatic ILC remains an incurable disease.

REFERENCES

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