CLINICAL VIGNETTE

Long-Term Survival in the Setting of Metastatic Breast Cancer to Bone: A Case Report

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Case Report

A 48-year-old premenopausal woman presented with a palpable left breast mass and underwent a left modified radical mastectomy; the pathology revealed a 6.0 cm infiltrating ductal carcinoma involving the nipple and lower inner and outer quadrants of the breast with multifocal lobular carcinoma in situ. One sentinel node was positive with an additional 7 negative axillary nodes for total of 1/8 positive nodes. The disease was estrogen receptor (ER) positive, progesterone receptor (PR) positive, and her 2 negative by immunohistochemistry. After surgery, she underwent a metastatic workup with a PET/CT scan, which revealed 3 bony metastases, one in her 4th lumbar vertebra, and two in her left iliac bone. CT-guided biopsy of one of the iliac bone lesions confirmed metastatic breast cancer, hormone receptor positive. She was treated initially with chemotherapy with 8 cycles of epirubicin and docetaxel along with pamidronate and a complete response on imaging. She then was maintained on endocrine therapy with leuprolide, anastrazole, and pamidronate for 1 year at which point she underwent a bilateral salpingo-oophrectomy to render herself menopausal, and the leuprolide therapy was discontinued. The pamidronate was then stopped when imaging remained negative for bone metastasis.

She remained on anastrazole for 12 years at which point she developed left hip pain. Pelvis MRI revealed a lytic lesion in the left iliac bone. PET/CT scan revealed an isolated mixed lucent and sclerotic lesion in the left iliac bone measuring 3.2 cm. Pelvic bone biopsy revealed metastatic carcinoma consistent with breast cancer, ER strongly positive, and her 2 negative.

She received radiation therapy to her isolated pelvic bony metastasis and was started on therapy with fulvestrant and palbociclib; she has remained without disease progression after 3 months on this systemic therapy.

Discussion

This patient's disease course brings up a number of points for discussion. The first is in regards to initial systemic therapy for metastatic breast cancer. For hormone receptor positive metastatic breast cancer, both chemotherapy and endocrine therapy can be used as systemic therapy. When this patient was initially diagnosed, the use of chemotherapy as initial systemic treatment for stage IV breast cancer was standard of care. In her case, chemotherapy did result in a complete response on imaging, and therefore, she was changed to endocrine therapy for maintenance. Current practice for the treatment of metastatic hormone dependent breast cancer is to reserve chemotherapy for patients with symptomatic visceral disease. Therefore, had she presented with the same situation today, with asymptomatic bone only metastases, she would not have been offered chemotherapy but rather would have been treated with first-line endocrine therapy.

A woman's menstrual status determines the endocrine therapy options that are available to her. The selective estrogen receptor modulator (SERM) tamoxifen can be used in women who are either premenopausal or postmenopausal. Another less commonly used SERM is toremifene, which is approved for treating metastatic hormone sensitive breast cancer in postmenopausal women.

Ovarian ablation is effective endocrine therapy in premenopausal women and has been shown in a meta-analysis to have equal therapeutic efficacy to tamoxifen.[1] In this study, progression free survival and overall survival were equal with either tamoxifen or ovarian ablation.

Another class of drugs, the aromatase inhibitors, are only effective in women without ovarian function. These agents work by inhibiting the enzyme aromatase, therefore preventing the peripheral conversion of androgens to estrogen. The aromatase inhibitors are more effective than tamoxifen, as documented in a meta-analysis of 2560 patients from 6 trials that demonstrated an improvement in response rate and clinical benefit with the aromatase inhibitors, and a trend towards improved survival compared to tamoxifen.[2] For the patient discussed in this case study, she was not yet definitively menopausal at the completion of her chemotherapy treatment, and therefore was treated with ovarian suppression with leuprolide in order to give her aromatase inhibitor therapy.

Bone metastasis can result in a variety of skeletal-related complications, including bone fractures, the need for palliative radiation or surgery, hypercalcemia, and cord compression. The bisphosphonates and the RANK L inhibitor denosumab have been shown to decrease the risk of such skeletal-related complications, while also reducing bone density loss associated with the aromatase inhibitors. For that reason, our patient did receive the bisphosphonate pamidronate until her bone metastases resolved on imaging.

For women with metastatic breast cancer to bone that becomes refractory to initial aromatase inhibitor therapy, a variety of treatment options exist. Premenopausal women who have disease progression on tamoxifen ideally will have ovarian ablation or suppression in order to receive one of the many treatment options for postmenopausal women. Single agent therapy with a different aromatase inhibitor or with tamoxifen can be used. Fulvestrant is an effective agent that works by blocking/degrading the estrogen receptor and can be used as second line therapy.

There are other classes of drugs that when combined with endocrine therapy can improve disease free survival. The cyclin-dependent kinase (CDK) 4/6 inhibitors when combined with aromatase inhibitors[3] and fulvestrant[4] have doubled progression free survival compared to the endocrine therapies as single agents. The CDK 4/6 inhibitors have dramatically improved the outcome for women with metastatic disease and are used in patients that do not require chemotherapy. Palbociclib, the only CDK 4/6 inhibitor that is currently FDA approved, is often used as first line therapy given the compelling improvement seen in progression free survival.

One other drug that has shown efficacy when combined with aromatase inhibitors is the mtor inhibitor everolimus. The Bolero-2 trial[5] evaluated exemestane with or without everolimus in metastatic breast cancer, and the everolimus group had more than double progression free survival.

Metastatic breast cancer to bone can have an indolent course and can occur many years after initial diagnosis. Given the variety of available effective sequential single and combination endocrine therapies and bone modifying agents that can palliate symptoms and improve progression free and potentially overall survival, women with bone only metastatic breast cancer often live many years with good quality of life in the setting of metastatic disease.

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