CLINICAL VIGNETTE

A Case of Long Survival Following Local Regional/Sternal Breast Cancer Recurrence In a Postmenopausal Woman With Hormone Receptor Positive HER2 Negative Disease

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Case Report

A 59-year-old female presented with right-sided inflammatory breast cancer. The pathology was well differentiated grade I infiltrating mucinous adenocarcinoma, ER+, PR+, HER2 negative by FISH. The stage was III B (T4bN2m0), and the patient was initially managed with a modified radical mastectomy where 5 of 13 lymph nodes were positive for disease. She received five cycles of TAC chemotherapy (docetaxel, doxorubicin, and cyclophosphamide) and radiation therapy, and was started on adjuvant tamoxifen therapy.

Three years after resection while on tamoxifen, the patient had a biopsy proven recurrence on the right chest wall with similar tumor characteristics. Following complete surgical excision, systemic therapy was changed to the aromatase inhibitor anastrozole. Three years later a second recurrence occurred with a soft tissue mass, shown to be recurrent mucinous adenocarcinoma on biopsy. CT imaging revealed anterior chest wall invasion involvement of internal mammary lymph nodes with focal uptake at the right border of the sternum on bone scan.

The patient was considered to have metastatic disease and was begun on zoledronic acid for bone involvement, and switched to monthly fulvestrant. Monitoring over the next three years, with periodic CT and bone scans, noted a persistent mass with no progression. The breast cancer tumor board recommended updating the imaging studies, and if stable with no other metastases, to proceed with surgery to attempt a complete resection of the residual mass.

Discussion

While case reports and clinical experiences of prolonged survival of patients with HER2 positive metastatic breast cancer treated with long term trastuzumab therapy are becoming more frequent, [1, 2] such outcomes are less commonly seen for other breast cancers[3]. This patient's survival for over 9 years following diagnosis of recurrent, hormone receptor positive, HER2 negative breast cancer raises several clinical questions. Does sternal involvement represent disseminated, blood born metastatic disease precluding long term survival even with aggressive attempts at local control? What is the optimal agent and duration of therapy duration for breast cancer patients with bone metastases? Also, emerging data is challenging concepts regarding the optimal sequence of hormone therapy for postmenopausal patients with bone metastases.

Based on a series of non-randomized studies at the MD Anderson Cancer Center [4, 5] a management strategy of aggressive local regional therapy followed by systemic chemotherapy was initiated for breast cancer patients with single site metastases. In an initial report, about half of patients with visceral or soft tissue disease experienced recurrences while all those with bone as their solitary site had recurred [4]. While the number of cases was limited, this finding suggested bone may represent a particularly challenging local recurrence site. In this regard, sternal metastases are considered to represent stage IV disease according to the AJCC staging system.

A recent retrospective series noted long-term survival in eight patients with isolated sternal recurrences. With a median follow-up of six years, seven of the eight patients with sternal metastases were alive with one death from metastatic breast cancer ten years after sternal recurrence. Two patients are in continuous complete remission at seven and 14 years from sternal recurrence. [6] These remarkable results from contemporary US based oncology practices suggest sternal involvement could represent direct local/regional extension rather than systemic spread and carry a much better prognosis. These findings and related case reports[7, 8] are the basis for our recommendation for surgical resection of our patient's stable disease mass.

The patient received monthly intravenous zoledronic acid therapy for three years in an attempt to reduce skeletal related events. Although efficacy data is limited to one year and the safety data is largely limited to about two years duration[9], however, we are reluctant to discontinue this therapy, but would stop following surgical resection. A non-bisphosphonate alternative can be considered. In a head to head phase III clinical trial, denosumab was associated with 20% fewer skeletal events in patients with breast cancer and bone metastases compared to zoledronic acid. Although side effect and convenience differences favored denosumab, osteonecrosis of the jaw was comparable with both agents [10]. Since our patient has stable disease on zoledronic therapy we did not consider a switch to an alternative agent [9].

The patient is currently receiving monthly fulvestrant therapy, which was begun following progression on tamoxifen and later on the aromatase inhibitor anastrozole. Fulvestrant was originally approved on a 250 mg monthly schedule. However, in September 2010 the FDA approved a 500 mg dose of fulvestrant with an additional two week dosage for loading replacing the previous lower dose regimen[11]. On the basis of results available with the lower dose regimen where only equivalence to tamoxifen in a first line setting had been demonstrated, many clinicians consider fulvestrant as a "downstream" intervention as we did in this case. However, recent results potentially change that categorization.

Approval of the higher fulvestrant dose was based on data from the CONFIRM (Comparison of Faslodex ® in Recurrent or Metastatic Breast Cancer) a phase III study which demonstrated that fulvestrant 500 mg reduced the risk of disease progression by 20% (P=0.006) when compared to fulvestrant 250 mg without increased toxicity[12]. The FIRST (Fulvestrant fIRst-line STudy comparing endocrine Treatments) trial provides additional support for this regimen. This trial compared the fulvestrant high dose regimen of (500 mg/month plus 500 mg on day 14 of month one) to anastrozole as first-line endocrine therapy for advanced hormone receptor positive breast cancer in postmenopausal women. First-line high dose fulvestrant had a comparable clinical benefit rate and overall response rate as anastrozole and was associated with significantly longer time to progression[13]. These findings were updated by a San Antonio Breast Cancer Symposium oral presentation where the median time to progression was 23.4 months for fulvestrant compared with 13.1 months for anastrozole (P=0.01) [14].

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Most postmenopausal patients with early stage breast cancer will receive adjuvant aromatase inhibitor therapy. Fulvestrant may represent a reasonable first-line therapy for those with recurrent disease especially since its FDA label indicates utility for metastatic disease following anti-estrogen therapy. Our plan will be to continue fulvestrant even if resection with clear surgical margins can be achieved.

In summary, this case represents the unique clinical course of breast cancer patients with sternal involvement and highlights the issues regarding selection and duration of therapy to reduce skeletal related events. Finally, recent results are reviewed supporting earlier use of fulvestrant in its newly approved higher dose in breast cancer patients.

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