Bad Disease with Reasonable Outcome

Sir,

Breast cancer with an abnormally high expression of HER2 on its cell surface is characterised by a more aggressive tumor biology, with adverse prognosis. Median survival time of breast cancer after the diagnosis with apparent bone marrow metastasis is few months.[1] Breast cancer also constitutes 2-5% patients with leptomeningeal carcinomatosis.[2] Unfortunately, even with multimodality therapy, the median survival is only 12 weeks; although in one series, patients live an average of 7.5 months after diagnosis.[3]

A 35-year pre-menopausal lady presented to hematology clinic in September 2015 with anemia and worsening lower backache radiating to lower limbs without neurological deficit for two months. There are no other constitutional symptoms or family history of malignancy. Her baseline investigations revealed low hemoglobin. She underwent bone marrow biopsy, which revealed heavy infiltration by metastatic glandular cells with some areas of normal tri-lineage hematopoiesis. Immunohistochemistry was positive for cytokeratin 7 (adenocarcinoma), most likely the breast primary malignancy.

She was referred to oncology department for further management. CT scan revealed liver studded with multiple small irregular hypodense lesions, minimally enhancing irregular lesion seen in the right medial breast and multiple osseous lytic bone lesions without fracture. Later, MRI spine showed irregular diffuse metastatic involvement of multiple vertebral bodies with no evidence of cord compression. PET CT scan revealed hypermetabolic disease in multiple bones, liver and right breast and left axillary nodes. Mammogram showed irregular, spiculated mass 1.6 cm at the lower inner quadrant of the right breast with minimal distortion, BIRAD 5. Biopsy of breast lesion revealed IDC grade 2, estrogen and progesterone receptors negative, and HER-2/neu overexpression 3+ positive, FISH positive and Ki 67 of 20%.

She was treated with palliative radiation to the thoracolumbar spine and after its completion was started on combination of chemotherapy with dual anti HER-2/neu therapy with docetaxel, pertuzumab, trastuzumab and zoledronic acid as part of systemic treatment. Subsequent PET CT scan, after completion of three cycles showed complete metabolic resolution. After completion of six cycles, bone marrow biopsy revealed cellular marrow with no morphological evidence of disease. She was continued on maintainance therapy with dual anti HER-2 therapy and zoledronic acid for more than a year. In March 2017, she presented with short history of diplopia and dizziness. On examination, there was no peripheral vision in right eye, with normal vision in left eye. MRI brain showed evidence of leptomeningeal metastasis. She received whole brain radiation of 30 Gy over 10 fractions and planned for intrathecal trastuzumab *via* Ommaya reservoir. She received her first intrathecal dose but unfortunately developed immediate complication, which recovered with conservative management. Later, it was decided to omit intrathecal trastuzumab and to continue with trastuzumab and zoledronic acid. Her subsequent and recent brain imaging revealed improvement in CNS disease; whereas, systemic imaging revealed stable disease. It has been for more than two years from the time of initial diagnosis that patient is doing well with good performance status, tolerating the treatment and the systemic disease is well controlled on maintenance therapy.

The therapeutic approach, in patients with good performance status, is the treatment by dual anti HER-2/neu blockade in combination with taxanes as the first line therapy, which provides a significant survival advantage of 15.7 months.[4] Patients responding well are treated with maintainance dual anti HER-2/neu therapy until disease progression. HER2-positive brain disease appears to be more sensitive to local radiation than HER2-negative tumors. It is believed that patients sensitive to trastuzumab should still be offered the drug even with brain disease, despite its poor penetration to the brain.[5] Hence, after CNS metastases pertuzumab is discontinued and trastuzumab is continued traditionally until disease progression.[6]

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