

Breaking survival barriers in breast cancer- A case of CNS metastasis

G S Chowdhary¹, Anmol Sharma²

From ¹MD (Medicine), Department of Medicine, Command Hospital Western Command, Chandimandir; ²MBBS, Armed Forces Medical College, Pune, India.

Correspondence to: Dr. G S Chowdhary, Command Hospital Western Command Chandimandir, Panchkula, India. E-mail: gschowafmc@yahoo.com

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ABSTRACT

One in every eight women worldwide will be diagnosed to be suffering with breast cancer in their lifetime. It is vital not only to diagnose the disease early but also to refer it to a tertiary care center for the most appropriate or standard anti-cancer treatment without delay. The outcomes of such therapy can be a game changer for the patient. Screening mammography is only having a small reduction in mortality of breast cancer. Here, we present a clinical report of one patient who had Her2 Neu positive disease with early central nervous system (CNS) metastasis and responded extremely well to anti her2 Neu therapy with chemotherapy and has survived over six years now on treatment.

Keywords: Her 2 Neu receptor, Mammography, Trastuzumab.

Worldwide around 14 million new cancer cases were diagnosed in 2012 according to GLOBOCAN data [1]. So, out of 7.6 billion or 7600 million world population 5.42 % developed cancer annually. Over 60% of these cases were from under developed or developing world. Every year cancer kills over 8.2 million people globally. Notably ischemic heart disease has killed 8.8 million worldwide at the same time. After lung, liver, colon and stomach cancer, breast cancer is the fifth leading cause of, cancer related death worldwide. Annually, approximately 1.7 million new breast cancer cases are recorded with 99% being women.

Metastasis in breast cancer can occur at any stage of its natural history, with 5% being metastatic at presentation. The expression of a transmembrane protein 'Her 2 Neu' is one of the molecular bases of breast cancer propagation. Her 2 Neu positivity is found in around 18-20% of breast cancer patients and this phenotype indicates a more aggressive clinical behavior with early systemic metastasis with cranial spread reflecting the worst prognosis [2]. The treatment of her 2 Neu positive breast cancer with Trastuzumab and anthracycline based chemotherapy is known to reduce the rate of loco-regional recurrence by 50% and improve survival by nearly 30% [3,4].

However one third of patients with Her 2 Neu positive breast cancer will develop central nervous system (CNS) metastasis when treated with Trastuzumab as this drug controls extra-cranial disease but does not cross the blood brain barrier. We report an interesting case of recurrent CNS metastasis in a primary breast carcinoma to bring forth important clinical and pathological cues for early diagnosis of such cases and to highlight the effect of adequate treatment on neurological sequelae and overall prognosis of the patient.

CASE REPORT

A 43-year-old premenopausal lady, a known case of diabetes since 2008 had presented in Apr 2011, to the outpatient department due to an increasing lump on her left breast. She revealed the history of this lump having been present for 2 months. On physical examination, a lump located in left upper outer quadrant of size 2.5 x 2.1 cm was appreciated. The lump was firm, non tender, mobile with normal overlying skin. A clinically significant solitary left axillary node was also palpable. There was no complaint of nipple discharge, no history of trauma and the patient was otherwise in good health. She was at clinical stage T2N1Mx disease with a biopsy showing histological evidence of invasive breast cancer, which was ER +, PR +, and Her 2neu positive on immuno-histochemistry.

Upfront, she underwent a breast conserving surgery with left axillary lymph node dissection which on pathological examination showed an infiltrating ductal carcinoma with negative margins and 15 of 16 lymph nodes +++. Her pathological stage was pT2N3a. She received adjuvant chemotherapy with Trastuzumab for one year including post BCS radiotherapy and hormonal therapy with ovarian suppression. The patient remained disease free for 23 months whereas she presented with headache and visual problems and no other deficit. Perimetry confirmed right homonymous hemianopia, which reflected towards CNS pathology, confirmed as metastatic poorly differentiated adenocarcinoma on histology. The growth was ER +, PR -, HER 2neu ++ (IHC) FISH-amplified. The patient was administered Trastuzumab beyond progression as per standard norms along with chemotherapy with Lapatinib and capecetabine. The patient also received holocranial post op

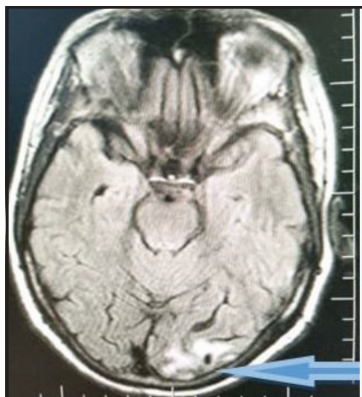


Figure 1: Left occipital metastasis.

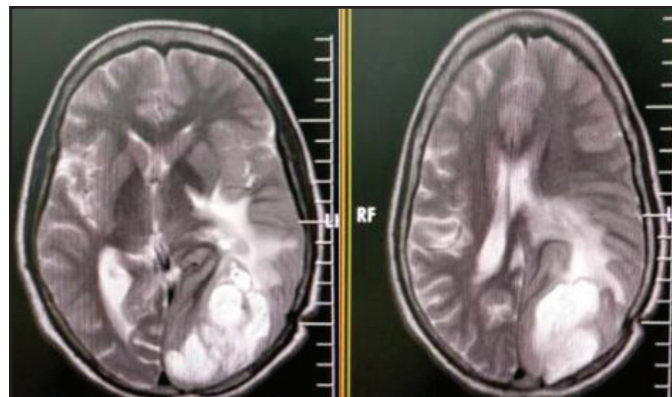


Figure 2: Left occipital metastasis recurrence before and after second surgery.

radiotherapy 30Gy/ 10# /12 days along with steroids and anti-epileptic drugs.

She continued on follow up and remained asymptomatic for another 24 months when she again developed headache and dizziness in Feb 2015. Neuroimaging showed recurrent CNS disease with no extra cranial disease. The MRI showed a left occipital region mass of 52x40x37 mm, left Parieto-occipital mass of 51x30x40mm size and a few occipital nodules with a 5.8 mm midline shift (Fig. 1). The repeat PET CT – confirmed a Left Occipital lesion with secondary Gliosis and no extra cranial disease. It also revealed an atrophic pancreas. The patient was admitted for repeat surgery and craniotomy was performed with maximal safe tumor resection. (Fig. 2).

She was managed with steroids, anti-epileptics and antibiotics. She continued to be on Inj Trastuzumab with Docetaxel based chemo therapy and remained asymptomatic till May 2017. Trastuzumab was discontinued, and a third surgical intervention to tackle the occipital mass was performed in view of an excellent performance status. A newer anti Her2 Neu treatment with a drug antibody conjugate (TDM-1) Trastuzumab –Ematsine was administered as Lapatinib at a dose of 1250 mg daily. The patient continues to remain asymptomatic in ECOG PS01, seizure free and is able to carry out her daily activities. She has received nine doses of TDM-1 till date and continues to be on follow up.

DISCUSSION

Breast carcinoma involves one third of all cancers in women. It is uncommon to have brain metastasis in breast cancer and this occurs later in the natural history of the disease with an incidence of 10-15% despite treating the primary by surgery followed by radiotherapy or chemotherapy. Traditionally metastatic breast cancer, without CNS metastasis, has a median survival of 24-36 months. The aim of treatment is to reduce pain from metastatic sites, limit progression and tempo of disease with improvement of quality of life with possible improvement in overall survival. The median 1-year survival of CNS metastatic breast disease as per literature is 20% [5,6].

Brain metastasis remains one of the most challenging clinical scenarios to tackle in case of a patient with a primary breast carcinoma. It is coupled with differential diagnosis including astrocytoma, multiple sclerosis, oligodendroglioma, cerebral venous thrombosis, CVA and radiation necrosis. Despite extensive treatment of the primary, few cases do progress to metastasize and it remains a challenge to catch them early and start treatment before permanent neurological damage. It is vital that a thorough neurological examination be carried in cases of primary breast carcinoma to screen for CNS metastasis. Her 2 neu receptors are known to be amplified in primary breast carcinoma and is involved in the disease's pathogenesis and pose a poor prognosis to women found positive for this mutation.

Although such cases remain undiagnosed, a few reports have been published discussing various modalities of treatment and their prognosis. Recent studies have reported cases of breast carcinoma with brain metastasis which responded well to endocrine therapy including high dose medroxyprogesterone acetate with complete resolution of CNS metastasis [7]. Reports of middle aged female with secondary's in brain and scalp on letrozole showing complete resolution of neurological symptoms and no residual deficit were also recorded [8].

CONCLUSION

This case report highlights the importance of accurate diagnosis in patients with persistent headache, continuing anti Her 2 Neu treatment beyond progression, aggressive surgical cyto-reduction of oligo metastatic disease. Also exploring newer agents especially for younger patients with an excellent performance status thereby, bringing improved patient survival.

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