



Correlation Of Brain Metastasis and Hormonal Status in Breast Carcinoma

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Abstract

Background

Breast cancer is the second most common cause of brain metastatic tumor. Brain metastasis occurs in 14% of patients with median interval of 32.5 months between the diagnosis and the brain metastasis presentation. (1) The development of brain metastasis holds poor prognosis with median survival ranges from 9 months to 10 months.

Material and Method

Our study population consists of 60 histologically proven patients with breast cancer brain metastases (BCBMs) were studied retrospectively in our department between year January 2015 and August 2019.

ER, PR and Her2neu status were evaluated.

Results

Most common site was supratentorial 38 (63.3%) followed by Infratentorial 22 (36.6%).

Out of 60 patients Her2 neu positive were 26 (43.3%), Triple negative were 14 (23.3%) and ER and PR positive were 20 (33.3%).

Out of 60 patients 8 were solitary and 52 were multiple brain metastatic sites.

Other Metastatic sites includes bone, lung, liver

Conclusion

In our study it is concluded that there is strong correlation of brain metastasis with Her2neu positive and triple negative and brain metastasis occurs more in supratentorial area than in infratentorial.

Keywords: Breast cancer, brain metastases, hormonal status

INTRODUCTION

Breast cancer is the second most common cause of brain metastatic tumor. One of the most feared consequences after a diagnosis of advanced breast cancer is development of metastases to the brain as this diagnosis can affect physical function, quality of life, personality, independence and ultimately one's sense of self.

The incidence brain metastasis is 14 % in breast cancer patients (1) with a median interval of 32.5 months

between the diagnosis and the brain metastasis appearance.

10 -30 % of patients with metastatic breast cancer develop brain metastases during the course of their disease. (2-4) The development of brain metastasis holds poor prognosis with a median survival range from 9 months to 10 months. (1,5 6).

The affinity to develop breast cancer brain metastases (BCBMs) varies by subtypes. Patients with triple negative or human epidermal growth factor receptor 2

(HER2)-positive cancers have a particularly high rate of brain metastases. Approximately 34% of patients with HER 2 + breast cancer will develop CNS metastases.

Current standard treatment opportunity for CNS metastases includes local treatments such as surgery, whole brain radiotherapy (WBRT), stereotactic radiosurgery, hormonal therapy. Targeted therapy and chemotherapy have been reported to be efficient for approximately 30 -40 % of patients. (7,8)

Here, we reevaluate the biology of BCBMs and how it informs the rational design of new therapeutic approaches and agents. We discuss administration of novel targeted and immunotherapies by breast cancer subtypes.

MATERIALS AND METHODS:

60 histologically proven patients with metastatic breast cancer who were diagnosed and treated at our institute between January 2015 and August 2019 were included in this retrospective study.

We assessed sociodemographic and clinicopathological data including patient demographics, histological type, biomarker status, site of metastases.

Status of ER, PR & HER 2 NEU were determined by immuno histochemistry. Staining in 1-10% of the tumor cells was considered as focally positive and staining in >10% of cells was considered as positive for ER and PR. HER2 status was also determined by using immunohistochemistry (IHC) and equivocal positive results were confirmed using fluorescent *in situ* hybridization (FISH).

RESULTS:

A total of 60 patients were included in this study. Their median age at initial diagnosis of breast cancer was 54.4 years (range 39-79). The histological type of most patients was invasive ductal carcinoma (75%). In this study 62% of patient belonged to urban locality as compared to 38% of patients belonging to rural areas along with 50/60 (83.3%) of patients being hindu and only 10/60 (16.6%) were Muslims in religion. This disparity in religion may be attributed to the cultural practices followed by muslim women, which reduces the risk of breast cancer in these females, although there is no scientific study done till date proving this.

24 out of 60 patients (40%) presented with clinical signs related to the CNS event. The most common symptoms were headaches (46%), nausea and vomiting (22%), paresis (18.4%), aphasia and dysarthria (6.8%) and seizure (6.8%). 36 patients (60%) did not present any symptoms related to their brain metastases and diagnosis was made as part of routine screening with MRI or CT scan.

Most common site was supratentorial 38(63.3%) followed by Infratentorial 22(36.6%).

Out of 60 patients Her2 neu positive were 26 (43.3%), Triple negative were 14(23.3%) and ER and PR positive were 20 (33.3%).

Out of 60 patients 8 were solitary and 52 were multiple brain metastatic sites.

Other Metastatic sites includes Bone, lung, liver

DISCUSSION:

Brain metastases are strongly related to hormonal status. Biomolecular markers are becoming the paramount factors for systemic therapy of breast cancer patients such as hormonal therapy, chemotherapy, or targeted therapy.

The recent management of patients with BM depends on the performance status, the number, size and localization of the metastases and the status of the disease outside the brain. (9,10) There is no specific treatment guidelines for BCBMs. The main intension is to alleviate symptoms when treating such tumors.

In ancient series, median overall survival for patient with breast cancer and brain metastases treated with whole brain radiotherapy (WBRT) alone was inferior and less than 6 months (11). The execution of better local treatment option like stereotactic radiosurgery has improved the outcome of patients with brain metastases. Overall survival and functional autonomy as compared with WBRT alone. (12)

In our study, apart from triple –negative breast cancer, HER2 –positive breast cancer is the most likely one to metastasize to the brain, similar results were found in a study conducted by. (13, 14) Brain metastases Strongly associated with overexpression of Her2neu. It occurs early and more in Her2neu + and triple negative than ER positive. HER2 overexpression occurs in 15 % -25 % of all breast cancers and is

associated with a high recurrence rate, a short disease-free survival, a propensity for brain metastases and reduced overall survival. (15-19)

Recent studies have shown that anti-HER2 treatment can improve survival after BCBM diagnosis. (7,8,20) It is uncertain whether such improvement is due to extracranial diseases control or indirect intracranial tumor response. However, it has been reported that HER 2-targeting agent trastuzumab can penetrate the impaired blood-brain barrier at the site of metastasis. (21)

In our study, about 60 % of the patients with brain metastases did not present any CNS symptoms. Majority of brain metastases occurs in supratentorial region most commonly frontal region.

Almost half of patients with advanced triple negative breast (TNBC) develop brain metastases with poor survival compared to non-TNBC subtypes and new treatment options are immediately needed. Patients with BRCA1 germline mutation are known to develop TNBC (22) and approximately 20 % of TNBCs harbor a BRCA 1 and 2 mutation. (23) The Olympi AD phase III trial (24) comparing the oral PARP inhibitor olaparib to single agent chemotherapy (capecitabine, vinorelbine, or eribulin) in TNBC with germline BRCA mutation showed improved PFS for the targeted agents (7.0 versus 4.2 months). A phase II trial, including a brain metastases cohort, is currently recruiting comparing cisplatin combined with veliparib to cisplatin monotherapy in TNBC +/- BRCA mutation (NCT02595905). A trial of Eribulin, a microtubule inhibitor already FDA approved in metastatic breast cancer, is currently recruiting for a phase II study exploring its efficacy in treatment of brain metastases (NCT02581839).

TNBC is the most immunogenic of the subtypes making checkpoint inhibition of programmed cell death protein 1 receptor (PD-1) and programmed cell death protein 1 receptor ligand (PD-L1) attractive therapeutic targets like pembrolizumab (25), atezolizumab (26) and avelumab. (27)

Conclusion:

Detection of breast cancer brain metastasis at an early stage might improve patient outcome and quality of life. The landscape for managing breast cancer brain metastasis improving significantly, due in large part

due to a better understanding of the biology of brain metastasis.

In our study it is concluded that there is strong correlation of brain metastasis with Her2neu positive and triple negative and brain metastasis occurs more in supratentorial area than in infratentorial.

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