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Different Presentation of Treatment in Carcinomatous Meningitis of Breast Cancer: Report of 3 Cases

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Abstract **Background:** Carcinomatous Meningitis (CM) refers to the multifocal seeding of the leptomeninges by malignant cells. CM occurs in approximately 5% of patients with breast cancer. Herein, we suggest that Intrathecal (IT) can use in treatment of breast cancer patients with CM before of any treatment until can prevent of going patient to debilitating phase of this disease. **Patients and Methods:** Three patients with high risk breast cancer with CM: A 62 year-old Kurdish woman with a history of lung tuberculosis. Her cerebrospinal fluid was positive for malignant cells. She treated with IT chemotherapy and died 3 months after diagnosis of CM. A 48 year-old woman in premenopausal states had a left axillary mass for last 4 months. After one year of followed up she complaints with refractory headache. In cerebrospinal fluid (CSF) analysis with diagnosis of CM treated with brain irradiation and multiple courses of IT chemotherapy. After six months she is well still and in follow up with previous drug list and monthly IT chemotherapy. A 63 year-old woman was presented at the emergency department of our hospital. After 4 months of her treatment she complained from decrease of consciousness and in CSF analysis with positive cytology. She treated with IT chemotherapy and She died about 2 weeks ago with exacerbation of brain tumor. **Conclusion:** According to the poor prognosis of this disease it is better that in high risk breast cancer patients like Non-Hodgkin lymphoma (NHL) high risk patients. IT prophylaxis was done for these high risk patients because by this way, we can prevent of going patient to debilitating phase of this disease.

Keywords: *Breast Cancer, CM, IT Chemotherapy, NHL*

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1. Introduction

Breast cancer is the most common cancer (27% of all cancers) and common cause of death (16%) which occurs due to cancers among women, either in developed or developing countries [1]. Leptomeningeal metastasis occurs in approximately 5% of patients with breast cancer [2].

Leptomeningeal metastasis or neoplastic meningitis refers to the multifocal seeding of the leptomeninges by malignant cells. It is known as leptomeningeal carcinomatosis or CM when these cells originate from a solid tumor. CM is frequently diagnosed in patients with breast cancer, lung cancer, lymphoma or leukemia as well as tumors of the central nervous system (CNS), mostly medulloblastoma [3]. When it is related to a systemic lymphoma, it is called lymphomatous meningitis, and when associated with leukemia, it is termed leukemic meningitis, the seeding of cancer cells into the CNS via the cerebrospinal fluid (CSF) [2]. The diagnosis of CM is made by the combined picture offered by the clinical examination, neuroimaging studies, and CSF results [4]. IT treatment requires invasive procedures, preferably repeated lumber puncture, and limits the use of chemotherapy agents due to the cerebrospinal damage [5]. Herein, we suggest that IT can use in treatment of breast cancer patients with CM before of any treatment until can prevent of going patient to debilitating phase of this disease.

2. Case Reports

2.1. Case 1

A 62 year-old Kurdish woman with a history of lung tuberculosis referred to our clinic. She cured about tuberculosis approximately 10 years ago from first her visit to our clinic. She had left breast mass with pathology diagnosis of invasive breast cancer with bone metastasis during last 18 months. In immunohistochemistry (IHC), she was triple-negative (ER-negative, PR-negative, HER2-negative) and androgen receptor (AR) negative. She treated with six courses of FAC (5-FU, cyclophosphamide, adriamycin) regimen. At last 18 months follow up she treated with monthly of zolindronic

acid (bisphosphonate) with sirulimus (MTOR inhibitor) and capecitabine. She presented with severe refractory headache that was unresponsive to oral analgesics including morphine. Both CT and MRI scans with contrast were normal, however her CSF was positive for malignant cells. The patient's headache responded to whole brain radiotherapy. She treated with IT chemotherapy. She died 3 months after diagnosis of CM.

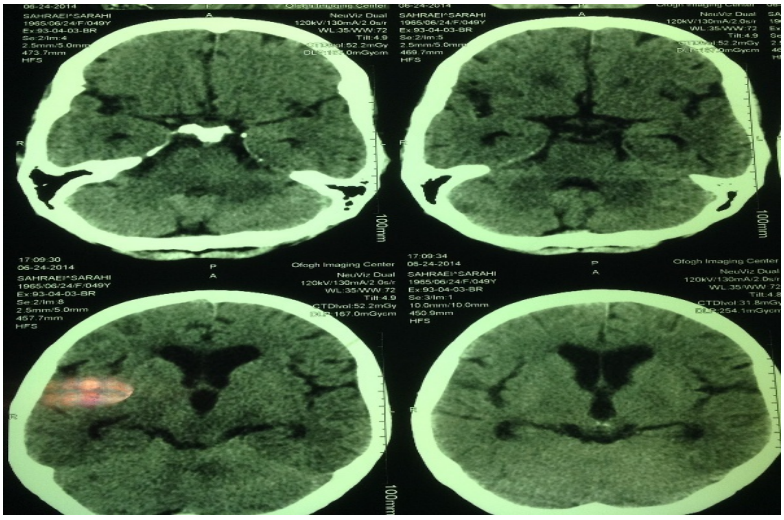

Figure1. Brain CT scan shows ventricular widening due to meningeal seeding

2.2. Case 2

A 48 year-old woman in premenopausal state had a left axillary mass for last 4 months without any other significant complaints that referred to our surgical clinic. According to the patient swelling was significantly increasing in size for last two months. She did not have any contributory past or family history. On examination, her general health was good and vital signs were normal without any systemic abnormal. Local examination revealed a 3x4 cm mass in the left axilla. The mass surface was nodular and skin overlaying was normal, too. Both breast and right axilla and both supraclavicular fosse were normal. Fine needle aspiration cytology (FNAC) of the left axillary mass was done in a private clinic then was reported as metastatic adenocarcinoma although she suspected to infiltrating ductal carcinoma of the breast. Patient was further investigated and all routine blood examination results like brain, chest and abdomino-pelvic CT scan were normal. Bilateral mammogram and MRI breasts showed normal architecture without any abnormalities. Looking at the physical findings and investigation results patient was diagnosed as a case of left occult breast cancer with left axillary lymph node metastasis. Patient was planned for right mastectomy and right axillary clearance. There was no lump in the mastectomy specimen and histopathological examination of right axilla revealed infiltrating ductal carcinoma involving 5 nodes out of 10 lymph nodes.

There was no tumor in the mastectomy specimen. ER and PR were positive in the axillary nodes. Subsequently patient was subjected to 6 cycles of docetaxel and adriamycin chemotherapy. She was treated with radical radiotherapy (50GY#25) and hormonal therapy (tamoxifen 20 mg daily). After 1 year of followed up she complaints with refractory headache. In CSF analysis with diagnosis of CM (carcinomatous meningitis) treated with brain irradiation and multiple courses of IT chemotherapy. After six months she is well still and in follow up with previous drug list and monthly IT chemotherapy.

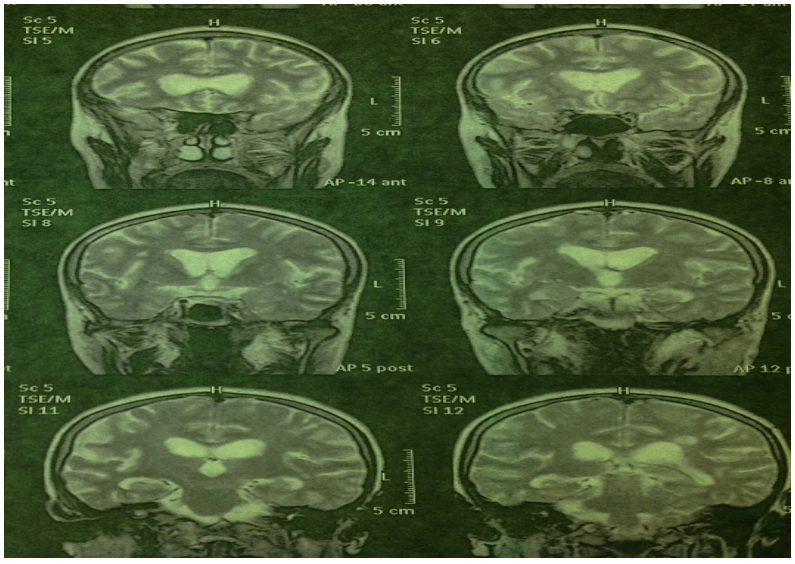

Figure 2. Meningeal thickness show in the brain MRI

2.3. Case 3

A 63 year-old woman presented at the emergency department of our hospital and was reported that 1 year ago she had felt a small lump in her right breast; over the last 2 months the breast had become much bigger, heavy, itchy, and hot, and had taken on a cellulites-like appearance. After total right radical mastectomy with diagnosis of inflammatory triple negative breast cancer and 6 courses of chemotherapy, and after 3 years of follow up, she suffered of left breast inflammatory mass and with diagnosis of left breast cancer that at this period treated with neoadjuvant chemotherapy. After 4 months of her treatment she complained from decrease of consciousness and in CSF analysis with positive cytology. Figure 1 and Figure 2 show images of meningeal before IT and Figure 3 shows meningeal after IT. She died about 2 weeks ago with exacerbation of brain tumor.

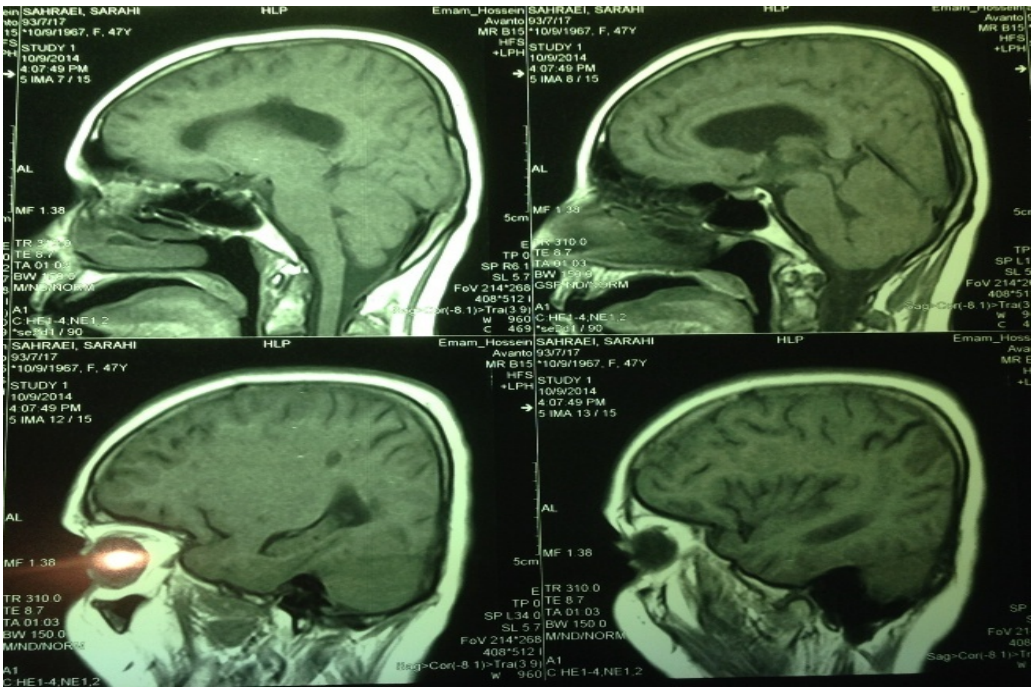

Figure 3. Last Brain CT scan shows decreased widening of ventricle and lightening in meningeal seeding

3. Discussion

The most common neurological symptom in 118 patients with CM, 54 % of patients had headache, followed by cranial nerves symptoms (42 %), cerebellar signs (35 %), nausea/vomiting (30 %), parhesis (26 %), mental changes (19 %), meningism (11 %), seizures (9 %) and radicular pain (7 %) [6]. In this study, two cases had headache and one case had mental changes. Median survival after the diagnosis of CM is about 18 weeks [7]. We can increase life time if we use IT after the diagnosis CM. Drugs can be instilled into the subarachnoid space by lumbar puncture or via an intraventricular reservoir system. The latter is the preferred approach because it is simpler, more comfortable for the patient and safer than repeated lumbar punctures. It also results in a more uniform distribution of the drug in the CSF space and produces the most consistent CSF levels [8]. Trastuzumab is a murine antibody that recognizes the extracellular domain of the HER2/Neu receptor and has been used successfully for the treatment of breast cancer [9]. Although CM from breast cancer shows the best prognosis among CM from various malignancies, median overall survival is no more than 6 months following diagnosis of CM from breast cancer [10]. Treatment of CM relies mainly on IT and/or systemically delivered chemotherapy, combined with other treatment modalities, such as irradiation or debulking surgery of meningeal metastases. There are no standard chemotherapy regimens for CM because neither prospective nor retrospective studies have shown any anticancer drugs to be highly effective against CM [11]. Time for alive in this disorder is less than a few months, so it is progressive neurologic dysfunction, but may be extended by early detection and intervention.

4. Conclusion

According to the poor prognosis of this disease it is better that in high risk breast cancer patients like NHL high risk patients. IT prophylaxis was done for these high risk patients (inflammatory breast histology, Triple negative, unusual presentation extra- breast) because by this way, we can prevent of going patient to debilitating phase of this disease.

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