

## Case Report

# PROLONGED SURVIVAL OF A PATIENT WITH LEPTOMENINGEAL AND BONE MARROW METASTASIS FROM BREAST CANCER

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## ABSTRACT

Leptomeningeal metastasis and bone marrow infiltration with profound cytopenia are uncommon in breast cancer. Leptomeningeal seeding from breast cancer usually shows extremely poor prognosis with median overall survival of 3 to 5 months. I here report a case of breast cancer with both of leptomeningeal and bone marrow metastasis. The first symptom was headache with nausea, vomiting, and diplopia. Generalized seizure developed during the admission to neurology. Repeated cerebrospinal fluid (CSF) analysis found metastatic carcinoma. magnetic resonance imaging (MRI) of brain finding also corresponded with leptomeningeal carcinoma. <sup>18</sup>F-FDG PET-CT showed diffuse bone marrow (BM) uptake and peripheral blood smear revealed leukoerythroblastic feature. Repetitive administrations of intrathecal chemotherapy were performed. She survived 39 months till November 2016.

**Keywords:** *Leptomeningeal Metastasis, Bone Marrow Metastasis, Breast Cancer*

## INTRODUCTION

The prevalence of breast cancer has increased in Korea. Park *et al.*, (2009) reported that younger breast cancer patients less than 50 years are more common in Korea than the United States. The majority of metastatic breast cancer patients experience bone metastasis and a few of them have invasion to BM. However, it is not common that the invasion cause profound cytopenia.

Lin *et al.*, (2004) reported 10-16% of stage IV patients had brain metastasis and the incidence of leptomeningeal metastases were less than parenchymal ones.

Cytopenia often make chemotherapy difficult and leptomeningeal seeding usually have very poor prognosis. I here report a patient who survived relatively long with both of these conditions.

## CASES

A 37-year-old woman visited a clinic with dizziness, nausea and diplopia in September 2013. She had generalized tonic-clonic seizure on admission for the investigation. The MRI of her brain showed leptomeningeal enhancement and the analysis of her CSF revealed malignant cells. <sup>18</sup>F-FDG PET-CT found that left breast cancer and multiple bone metastasis. The diffuse uptake suggested invasion to BM (Figure 1). Her peripheral blood smear showed leukoerythroblastosis with thrombocytopenia and anemia. The nadir of platelets and hemoglobin were 30,000/ $\mu$ L and 7.5g/dL on October 14, 2013. The biopsy of left breast mass revealed breast cancer which had estrogen and progesterone receptor expression without Her-2 receptors.

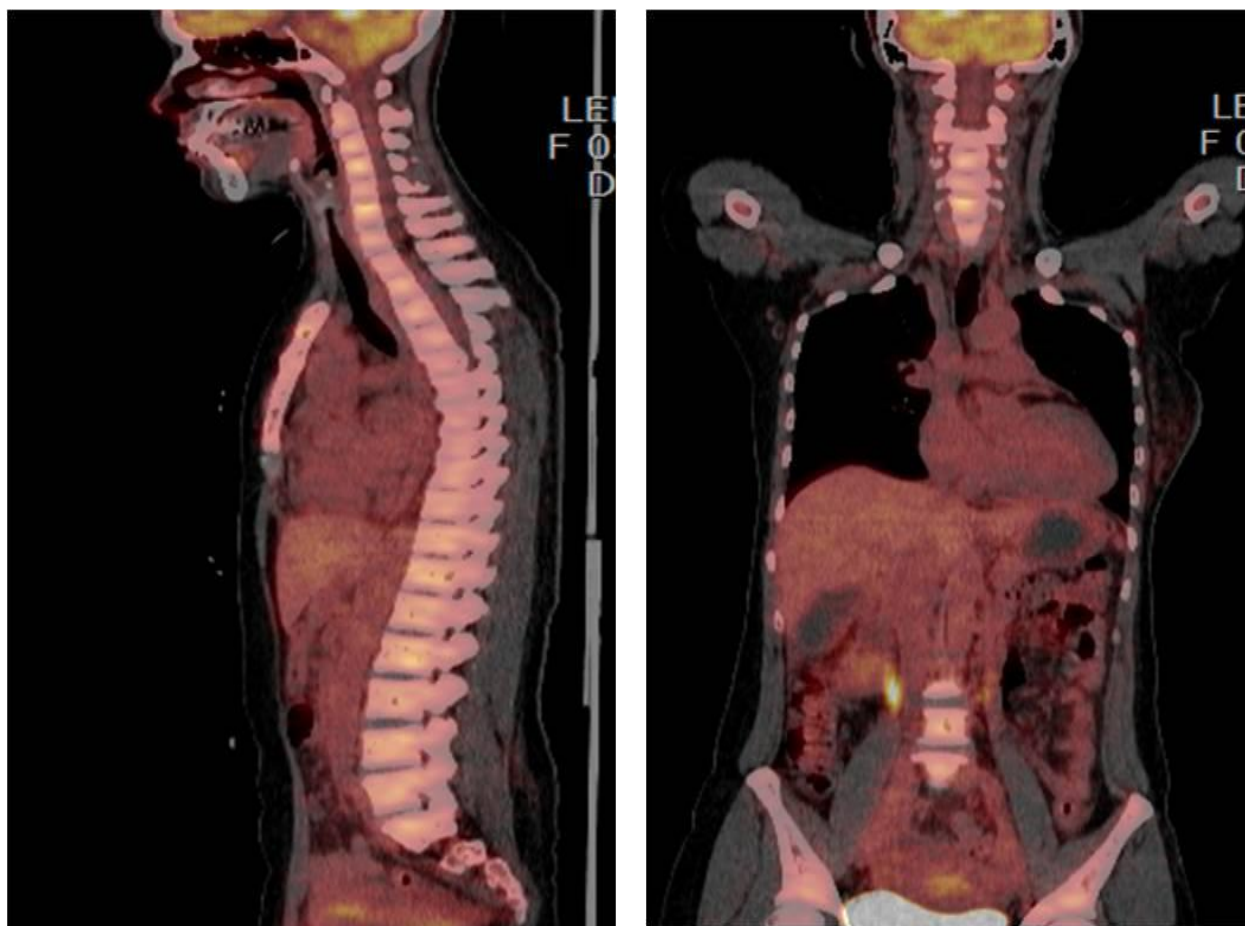
Intrathecal administration of methotrexate (MTX) 12.5mg started on Oct 2. The 2<sup>nd</sup> intrathecal chemotherapy of cytarabine, MTX and hydrocortisone was administrated on Oct 5. Five cycles of intrathecal chemotherapy made her CSF clear from the malignant cells although she kept having seizure despite of anticonvulsant agents.

We started intravenous docetaxel (90mg/m<sup>2</sup>) on Oct 18. The number of her seizure decreased since 23 Oct. She experienced grade 4 neutropenia but recovered quickly from it. Even preexisting anemia and thrombocytopenia improved. Total 9 cycles of intravenous docetaxel were given till April 10, 2014. <sup>18</sup>F-FDG PET-CT showed no uptake in left breast, axillary lymph nodes and bones. Brain MRI also showed no enhancement.

We treated her with tamoxifen and zoledronic acid from June 2014 to October 2015. She was in good

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general conditions as an outpatient. But headache started again and her brain MRI revealed leptomeningeal progression. She was treated with whole brain radiation therapy and letrozole with goserelin. She took bilateral oophorectomy for artificial menopause on March 4, 2016. But she had seizure again and we implanted Ommaya reservoir into her brain. She had been administered 10 cycles of intrathecal MTX from March to June 2016. She started to take arimidex and everolimus in March on admission. She improved and discharged with the medicine but discontinued everolimus due to pneumonitis in May 2016. In August, her headache aggravated and 5 cycles of intrathecal MTX were administered via the Ommaya. Although, imaging for response evaluation found stable disease, the level of her consciousness gradually had decreased. We decided to take care of her in our hospice center and discontinued arimidex in September 2016. She survived 39 months till November 20, 2016.



**Figure 1:  $^{18}\text{F}$ -FDG PET-CT Shows Multifocal Hypermetabolic Lesions in Bilateral Cerebral and Cerebellar Cortex; Diffuse Bone Marrow Uptake Suggested Bone Marrow Infiltration**

### DISCUSSION

When we treat a metastatic cancer patient with impaired BM function, it makes risk-benefit evaluation difficult that major side effect of cytotoxic chemotherapy is BM suppression. Gaurav *et al.*, (2015) reported that a breast cancer patient who had BM metastasis and pancytopenia (WBC 3,200/ $\mu\text{L}$ , Hb 6.8g/dL and platelet 3000/ $\mu\text{L}$ ) and been treated with infusion of doxorubicin successfully. Kopp *et al.*, (2011) studied 22 breast cancer patients with BM invasion causing cytopenia and reported that 21 patients were treated with cytotoxic chemotherapy. There were only 5 patients who had grade 3 or 4 toxicity including neutropenic fever and bleeding. They said that active chemotherapy could improve BM function and prolong survival.

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Leptomeningeal metastasis is estimated to afflict around 2-5% of metastatic breast cancer patients. The patients with leptomeningeal metastasis generally have very short survival time between 2 and 5 months. Emilie *et al.*, (2013) investigated 103 patients with leptomeningeal metastasis from breast cancer. There were 11 patients who survived longer than 1 year although the median overall survival was 3.8 months. All the 11 patients were treated with combination of intrathecal liposomal cytarabine and systemic chemotherapy. The intrathecal liposomal cytarabine infusions continued till progression of disease. Jo *et al.*, (2013) studied 95 patients with leptomeningeal metastasis from breast cancer in Korea. The median survival was 3.3 months. There were 7.8% patients who survived longer than 12 months and systemic chemotherapy, good performance, stable extracranial disease were related with longer survival. Leptomeningeal metastasis and bone marrow invasion with cytopenia are challenging conditions to treat. However, there are a few patients who get favorable responses. We need further investigation to clarify contributing factors to longer survival and improve results of overall patients.

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