Leptomeningeal Carcinomatosis: A rare complication of BRCA-mutation related triple negative breast cancer

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INTRODUCTION

Leptomeningeal carcinomatosis is metastasis to the CSF and Leptomeninges seen in patient with advanced solid tumors. Diagnosis is made with CSF studies positive for malignant cells and/or contrast enhanced MRI of brain and spine which typically shows linear and nodular enhancement of the leptomeninges. We present the case of a woman with BRCA-mutation related triple negative breast cancer (TNBC) with leptomeningeal carcinomatosis (LMC) and discuss the incidence, diagnosis and management.

CASE

We present the case of a 43-year-old woman with a family history of breast cancer (aunt had BRCA1 mutation) who was treated with neoadjuvant chemotherapy followed by bilateral mastectomies for a locally advanced TNBC. She too tested positive for BRCA 1 mutation. Two years later she presented with metastatic disease with involvement of bones, lungs and liver. Ten months into palliative chemotherapy she presented with headaches. Computed tomography (CT) showed right frontal lobe edema with leptomeningeal enhancement. Cerebrospinal fluid (CSF) cytology was positive for malignant cells, and a diagnosis of LMC was made and intrathecal chemotherapy initiated. She died 12 Months later.

CT head showing right frontal lobe edema with leptomeningeal enhancement.

DISCUSSION

LMC/ carcinomatous meningitis/ leptomeningeal metastasis is metastasis to the leptomeninges and CSF. Most often seen with hematologic malignancies (in 5-15% of acute leukemias and high-grade lymphomas) and less with solid tumors (in 5-8%). It has been reported with breast, lung, GI malignancies and melanoma with breast cancer being the most common culprit. Subtypes like HER2 positive and TNBC have 4 times increased incidence than others. Lung metastasis as the first site of relapse and BRCA + status are risk factors. The median time from Breast cancer diagnosis to LMC is 32 months. Typical presentation is waxing and waning multifocal neurological signs (e.g., headaches, nausea, vomiting, altered mental status, diplopia, facial pain, leg weakness, cerebellar signs, seizures). Symptoms can be subtle, delaying diagnosis. Hydrocephalus is another complication. Infectious meningitis, treatment side effects, toxic and metabolic encephalopathies should be excluded. Improvements in neuroimaging and survival times have contributed to increased incidence of LMC. Positive CSF cytology (gold standard of diagnosis) with or without leptomeningeal enhancement on imaging studies is diagnostic. Serial CSF sampling may be needed due to high (20%) false negative rates. MRI abnormalities are noted in 75% - 90% of patients with positive CSF cytology. Due to poor drug penetration of the blood brain barrier, treatment is difficult and involves intrathecal chemotherapy (methotrexate, cytarabine, thiopeta or sustained release liposomal cytarabine), focal radiation to symptomatic sites (for relieving obstruction to CSF flow) and ventriculoperitoneal shunt (for hydrocephalus). Prognosis is poor with median survival of 3-6 weeks if untreated and 2-4 months with treatment.

CONCLUSION

LMC is an uncommon but well-known complication of end stage breast cancer and is commonly associated with TNBC and BRCA mutation carriers. It can present with non-specific, waxing/waning neurological symptoms. Hence a high index of suspicion for this diagnosis should be maintained in patients with advanced breast cancer. Serial CSF cytology should be performed in suspicious cases. Positive CSF cytology establishes the diagnosis even in the absence of leptomeningeal enhancement on neuroimaging. This disease carries an extremely poor prognosis in spite of treatment.

REFERENCE


