



Meningeal Carcinomatosis: From Body to Brain, an Elusive diagnosis

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ABSTRACT

Meningeal carcinomatosis refers to metastatic spread of extracranial primary cancers into the pia mater and/or arachnoid mater of the meninges (also known as leptomeningeal metastases). It is diagnosed in approximately 5% of patients with advanced cancer, with breast cancer being the most common primary source. A 60 year old woman with known stage 4 breast cancer presented to community hospital for evaluation of shortness of breath and altered mental status, onset 2 days prior. On admission to ICU, she was profoundly hypotensive, tachycardia, and found to have right lower extremity DVT. Once anticoagulated and stabilized, she was moved to the floor, whereafter she experienced dizziness, visual hallucinations, and auditory hallucinations. CT Head was performed as initial screening for altered mental status. Empiric antibiotics given, and once blood cultures revealed multi-drug resistant organism (*Klebsiella* ESBL and group *F. streptococcus*), this was switched to ertapenem and vancomycin. MRI of the Brain and Thoracic spine were obtained for better visualization of abnormal findings. Patient underwent a lumbar puncture to check for malignant cells in an attempt to confirm diagnosis of suspected meningeal carcinomatosis. MRI of the Brain and spine showed an erosive skull base lesion, as well as metastases at T7 and T11. Lumbar puncture yielded a 2mL sample of pink, hazy CSF with an elevated WBC of 7.0, elevated RBC of 7,160, and elevated protein of 126.7. Differential of CSF cell count noted 76% neutrophils, 15% lymphs, 9% monocytes. Patient was thereafter transferred to a tertiary care facility to initiate inpatient palliative radiation and evaluation of possible Ommaya reservoir. Meningeal carcinomatosis is a rare complication of malignancy that may take several attempts to pinpoint on imaging or laboratory findings. High suspicion and overall clinical picture can be just as diagnostic.

CASE PRESENTATION

The patient was a 60 year old female with a past medical history of recurrent deep vein thrombosis, breast cancer with bony metastasis, and anemia of chronic disease who presented to the emergency department from home with a 1 week history of altered mental status.

Prior to her hospitalization, the patient was receiving Anastrozole and Abemaciclib treatment for her stage four breast cancer. Six months prior to this admission she had been discharged from another hospital for a left lower extremity deep vein thrombosis, pulmonary embolism, and subsequent thrombectomy. She was then sent to a rehabilitation center for six weeks, and sent home with home physical therapy

During the current admission there was reported that the patient had begun to experience altered mental status including increased and progressive confusion, generalized weakness. In addition to this she had a two-day history of vomiting and decreased oral intake.

The review systems was positive for the patient experiencing fatigue, shortness of breath, leg swelling, and nausea

On admission the patient had the following vitals:

Temperature: 97.5 heart rate: 121 Respiratory Rate: 20 Blood Pressure: 87/61

On exam the patient was alert and oriented to self in place alone, they had a right ear pressure ulcer with dried blood around her. She had sinus tachycardia, bilateral 2+ pitting edema, purple striae on her abdomen, an upper middle back pressure ulcer, along with redness and skin breakdown in the area of her buttock.

Hospital Course

In the hospital the patient received a chest X Ray suspicious for right sided infiltrates and negative blood cultures. The patient was initially placed on prophylactic antibiotics. The patient also had a troponin of 0.15 which peaked at 0.32. Subsequent ECG showed sinus tachycardia with repolarization abnormalities suggestive of ischemia in lateral leads. Cardiology was consulted. The patient had a creatinine of 4.4, nephrology was consulted, and she was placed on IV fluids. On admission the patient had a sodium of 129, a potassium of 3.3, and a lactic acid of 3.5. Her hemoglobin was 7.3 and she was transferred to the ICU due to hypotension with her blood pressure going as low as 50/30. In the ICU the patient's blood pressure improved on IV fluids and she was also given 3 units of blood. She was also found to have a PE and right lower extremity DVT, thus the patient was placed on a heparin drip which was then transitioned to Eliquis which had been stopped prior to this hospital admission. In the ICU her electrolyte abnormalities were also normalized.

Patient was eventually downgraded from the ICU. On the floor she developed paroxysmal atrial fibrillation, was placed on Lopressor and Cardizem, and her heart converted to sinus rhythm. To investigate the patient's altered mental status, an MRI of the brain was obtained with no signs of metastasis, however there was significant motion abnormalities. The patient was eventually placed on 25 mg of Seroquel which did improve her mental status. The patient also had urine culture test positive for *klebsiella* ESBL and *candida albicans*. The patient was evaluated by infectious disease and placed on vancomycin and ertapenem.

On the floor the patient's hemoglobin again dropped to 6.8. An EGD was performed showing an esophageal ulcer, and the patient was transfused an additional unit of packed red blood cells. Eventually the patient did develop a second clot in her superficial femoral, popliteal, and peroneal veins. An IVC filter was eventually placed.

Lastly during her hospital stay the patient had a CT abdomen/pelvis showing lytic bone lesions, along with a CT head showing it destructive changes of the left skull base which was not appreciated on the previous MRI brain due to the motion artifact. A repeat MRI of the brain and thoracic spine showed metastatic lytic bone lesions at the left skull base, T7 vertebrae, and T11 vertebrae. At this point suspicion for meningeal carcinomatosis was high and the patient was transferred to another hospital for further evaluation and management of the metastasis.

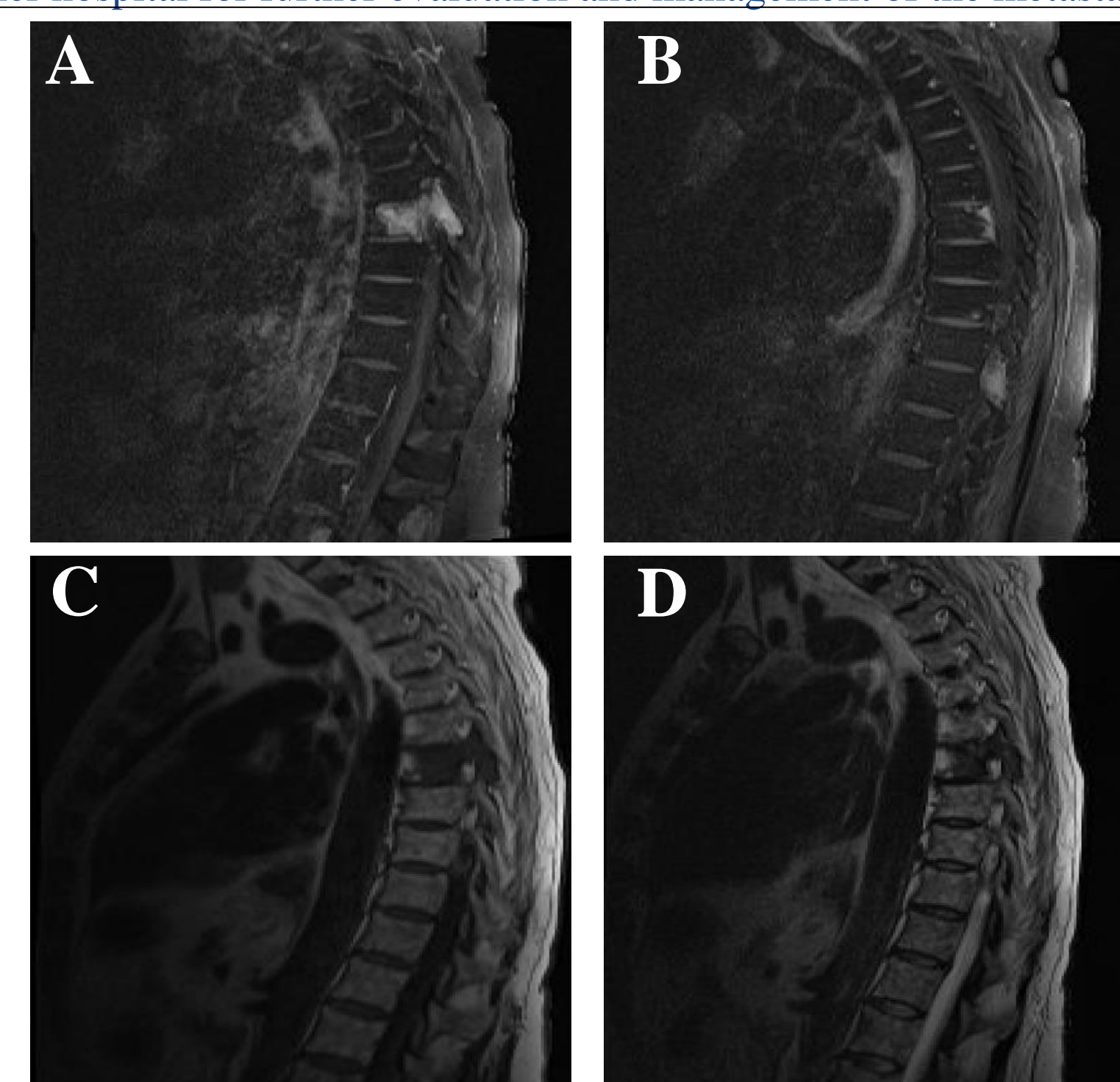


Fig.1: MRI imaging of the lumbar spine. A) Prominent T7 lesion seen on T2; B. Smaller portion of T7 lesion, as well as a Schmorl's node at T9 and bulky lesion between T11; C) Same T7 lesion, seen as hypodense on T1; D) Additional view of T7 and T11 lesion on T1.

RESULTS

The patient's urine culture grew multi-drug resistant *Klebsiella pneumoniae*. Despite switching her antibiotic regimen based on susceptibility studies, patient remained somewhat altered at baseline.

MRI imaging of the Thoracic Spine with and without Contrast showed several abnormalities (Figure 1). There was a heterogeneous enhancing infiltrating mass seen at T7 vertebral body. Another enhancing metastatic lesion was seen at T11 on the right lamina and pedicle. A benign incidental finding was a Schmorl's node seen on T9. MRI imaging of the Brain did not yield any signs of metastatic lesions within the brain parenchyma; however, a small lytic lesion was seen on the clivus by the foramen magnum (Figure 2).

CSF cytology from lumbar puncture showed no evidence of malignant cells. Though the cell count had a neutrophilic predominance, sample was not suggestive of bacterial or viral meningitis as a source of the patient's altered mental status (Figure 3). The large amount of red blood cells in the sample would be consistent with a traumatic LP.

Though malignant cells were not discovered on lumbar puncture, the abnormal imaging findings and overall clinical picture was consistent with meningeal carcinomatosis. In discussion with the Hematology/Oncology consultant, the decision was made to transfer the patient to an inpatient facility where she could receive palliative radiation treatments.

Neurosurgery service at receiving facility was consulted for potential placement of Ommaya intraventricular catheter for administration of chemotherapeutic agents. Unfortunately, patient quickly decompensated and ultimately expired a few days later secondary to COVID-19.

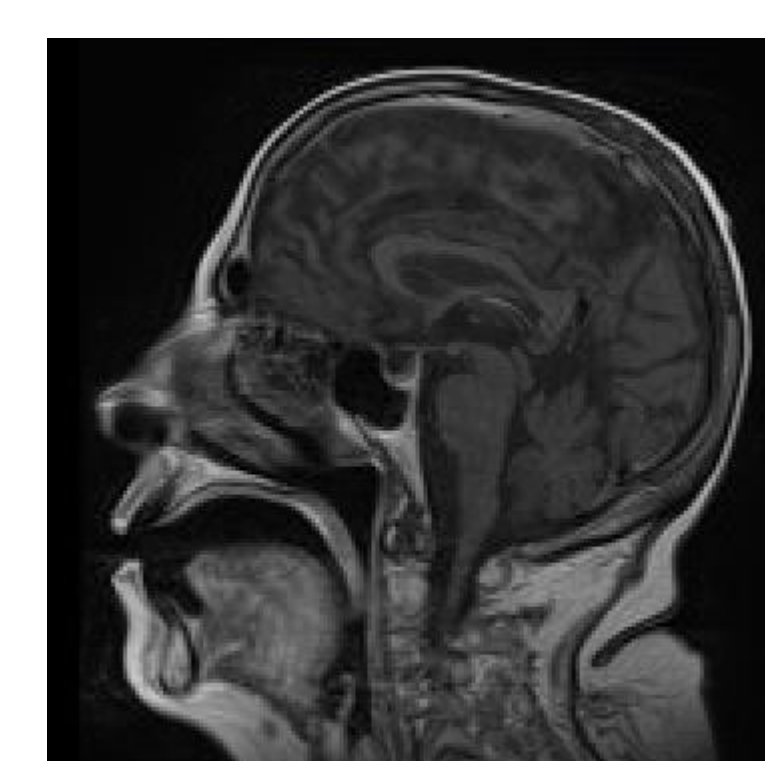


Fig 2. MRI Brain shows destructive lesion at left clivus and foramen magnum.

CSF Findings	
Color	Pink
Appearance	Hazy
WBC	7.0
RBC	7,160
Neutrophils	76%
Lymphocytes	15%
Monocytes	9%
Glucose	71
Protein	126.7

Fig. 3 Lumbar puncture findings, with abnormal values printed in red.

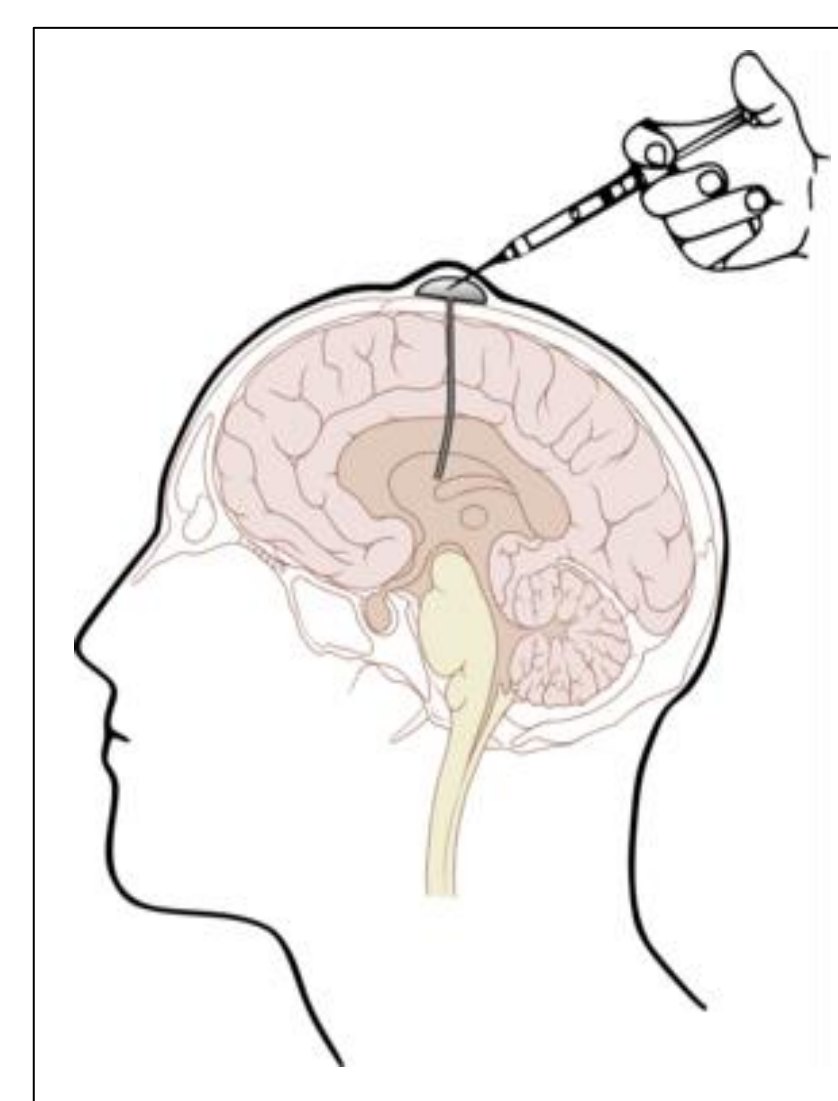


Fig. 4: Schematic of Ommaya reservoir once surgically implanted in a patient.

DISCUSSION

Breast cancer is the most common form of cancer to progress to meningeal carcinomatosis, with a prevalence of 5-8% (1). Given its rarity, research on this condition is somewhat limited. However, it appears the disease can progress by location invasion or hematologic spread. Recent studies suggest upregulation of complement C3 by cancer cells, leading to compromise of the blood-brain barrier, and thereby allowing access for mitogens to enter the CSF and promote leptomeningeal progression (1,2). In addition to breast cancer, meningeal carcinomatosis is seen in other solid tumors-- frequently lung cancer and melanoma-- and hematologic cancers, most often of these being leukemia (1).

Diagnosis of this condition is further complicated by a diverse array of symptoms based on what specific areas of the central nervous system are affected. Our patient exhibited urinary incontinence, altered mental status, nausea, headache, and confusion, though symptoms such as psychosis, paresthesias, seizure, dysphagia, and SIADH have also been reported (1,3).

Classically, malignant cells seen on lumbar puncture are the diagnostic test of choice. However, as also exhibited by our patient, malignant cells in CSF are not required to make the diagnosis. Furthermore, as much as 10% of patients with meningeal carcinomatosis persistently do not show malignant cells on LP throughout their clinical course (4). The decision to not repeat the lumbar puncture in our patient was based more in patient comfort given her advanced age and already significant imaging. Another limitation of the CSF sample is size; most recommend a sample of at least 10 ml to accurate cytology whereas only 2 ml CSF were collected from our patient (1).

Despite earlier diagnosis due to advances in neuro-imaging, meningeal carcinomatosis is still indicative of a poor prognosis overall. Untreated, patients with meningeal carcinomatosis live about 6 weeks after diagnosis on average; with chemotherapy and radiation, this may be extended to about 3-6 months (4).

CONCLUSIONS

- A rare complication of breast cancer is meningeal carcinomatosis (also often called leptomeningeal carcinomatosis) and is seen in about 5% of oncology patients
- Breast cancer, lung cancer, and melanoma are most common neoplasms to progress to meningeal carcinomatosis.
- Lumbar puncture for meningeal carcinomatosis may be negative or require ventricular sampling.
- Abnormal MRI alone may be sufficient to make the diagnosis.
- Ommaya reservoir is a continuous sampling option for CSF fluid and administration of chemotherapy in otherwise stable individuals

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