CASE REPORT

Symptomatic improvement with whole patient care for Leptomeningeal Carcinomatosis diagnosis: A Case Report

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Received: 9/3/2024 Accepted: 12/12/2024 Published: 12/31/2024

Am j Hosp Med Sept;8(4): 2024. DOI: https://doi.org/10.24150/ajhm/2025.013

Keywords: Leptomeningeal Carcinomatosis, Brain Metastasis, Metastatic Breast, Case Report

ABSTRACT

Leptomeningeal Carcinomatosis (LC) is the metastasis of solid and hematological tumors to the pia and arachnoid mater, as well as the subarachnoid space. While uncommon, this complication is associated with mortality and remains difficult to treat. This case describes a 53-year-old female who presented with isolated left-sided facial droop and bilateral hearing loss. Her past medical history was significant for left breast carcinoma status post lumpectomy, lymph node dissection, and breast radiation. During the hospital stay, right-sided facial paralysis developed which prompted MRI brain and spine revealing possible leptomeningeal carcinomatosis, further confirmed by lumbar puncture results. The purpose of this case report is to highlight the presenting clinical picture and outpatient treatment following hospitalization in hopes to call attention to this disease and inspire an early consideration of LC as a differential diagnosis among treating physicians.

INTRODUCTION

Solid and hematological tumors have been shown to metastasize to the leptomeninges, which are composed of the pia and arachnoid mater, along with the subarachnoid space[1]. This metastasis is termed Leptomeningeal Carcinomatosis (LC), also known as leptomeningeal disease or leptomeningeal cancer. LC is thought to develop by tumor cell seeding of the leptomeninges either

directly from brain tissues, hematogenously, or via cerebrospinal fluid (CSF)[1].

The leptomeninges are present throughout the central nervous system. The arachnoid mater consists of an outer barrier cell layer and inner trabeculae layer with a basement membrane separating the two[2]. Within the barrier layer, there are several *zonulae occludens, zonulae adherens,* and *macula adherens* that work to exclude large molecules such as proteins from diffusing from the blood to the CSF[2]. The pia mater is composed of fibroblasts with differing cell layer thickness along the spinal cord, leaving areas along the cord fenestrated and therefore exposed to subarachnoid space[2]. Certain portions of the central nervous system, especially near the third and fourth ventricles, contain leptomeningeal spaces which allow contact to the systemic circulation[3]. The need for further exploration of tumor spread, as well as the sequestering effects of the blood brain barrier against certain anti-cancer therapies, contribute to the challenge of developing effective treatment for LC[4].

Approximately 1-8% of cancer patients in the United States develop LC[5]. Patients tend to present once LC has become advanced, with common symptoms including headache, confusion, cognitive impairment, cranial nerve deficits, vascular ischemia and infarct, weakness, and bowel and bladder dysfunction[1].

The tumors which are most commonly associated with LC development include breast, lung and melanoma, with breast cancer being the most prominent overall[1]. Incidence varies between primary tumor type, ranging from 5-30%[1]. There is an increased risk of developing LC the longer one harbors a primary tumor as this can allow for the cancer to develop central nervous system metastasis[5].

Evaluation includes imaging, such as magnetic resonance imaging (MRI) brain and spine, as well as CSF studies. CSF cytology is the gold standard for diagnosis for LC showing the presence of malignant cells[5]. Upon lumbar puncture, the first draw has a sensitivity of 50-60% with the second draw increasing sensitivity to 80%[5]. In the absence of malignant cells in cytology, protein levels should be evaluated as above 45 mg/dL can be seen in 63-90% of patients with LC[5]. Imaging can reveal structural abnormalities within the brain, more commonly when metastasis occurs from a solid primary tumor rather than a hematological primary with MRI is preferred over computed tomography (CT)[5].

Treatment strategies include whole brain radiation therapy (WBRT), central nervous system (CNS) penetrant systemic therapy and palliative care. However, it is important to note that current literature supports only limited improvement in survival time with treatment (4-12 weeks average) and average survival without treatment is 4-6 weeks[1,4]. Patients with breast cancer can have longer survival time as there are more targeted therapies, however survivability rates remain low at 13-25% in year one, followed by 6% at year two[5]. Given the current limitations in treatment, exploration of effective care strategies through case reports may allow for improved provider understanding regarding disease course and strategies for patient support.

CASE PRESENTATION

A 53-year-old female presented with an isolated left-sided facial droop that occurred in February 2024. A week prior the patient

also had sudden and complete bilateral hearing loss, which prompted her to go to an urgent care where she was prescribed 4mg of steroids for reported bilateral fluid accumulation behind eardrums. History was obtained through the help of family members and writing on a whiteboard. Her nausea was managed by ondansetron (Zofran). Patient denied any accompanying facial, upper extremity, or lower extremity altered sensation. She denied concurrent headaches, vision changes, or back pain. No reports of incontinence.

Past medical history includes stage IV ER positive, PR negative, HER2 1+ carcinoma of the left breast (rpTX, pNX, pM1) originally diagnosed September 2021 with later Tempus xF revealing BRCA1 germline mutation. The patient reported receiving lumpectomy, lymph node dissection, and breast radiation in Spain. Review of records shows that she declined systemic chemotherapy at that time and chose to pursue complementary and alternative medicine treatment which included: ozone therapy, hyperthermic treatments, and various vitamin infusions in Spain. Patient believed to be in remission until imaging revealed CNS and left iliac metastasis in October 2022 when she presented with progressive right-sided weakness. The patient reported being on Tamoxifen at the time of presentation. The new course of treatment included: 1. Letrozole and ovarian suppression and 3 days of Ribociclib that was discontinued by the patient due to side effects. 2. Left frontal lobe metastasis resection performed October 2022 followed by stereotactic radiosurgery to resected cavity and remaining three brain mets. 3. Right lateral cerebellar dural lesion treated with stereotactic radiosurgery in June 2023. 4. Continued holistic treatment of vitamin infusion. Review of imaging revealed ependymal enhancement shown on both lateral ventricles in November 2023. Patient reported being asymptomatic at that time.

Over the course of the patient's hospital stay, they developed right-sided facial droop occurring overnight. The patient was started on dexamethasone (Decadron) 4 mg every 6 hours and underwent spine and brain MRI with/without contrast.

Findings revealed a new left occipital periventricular mass, temporal mass, with leptomeningeal enhancement involving superior cerebellum, and cauda equina as shown in attached **Figures 1** and **2.** The patient then underwent a lumbar puncture revealing malignant cells present, consistent with cerebrospinal fluid involvement by metastatic breast carcinoma, WBC count of 47, normal glucose of 65, and protein CSF of 173.8 mg/dL.

Figure 1: MRI which shows new left occipital periventricular enhancing mass.

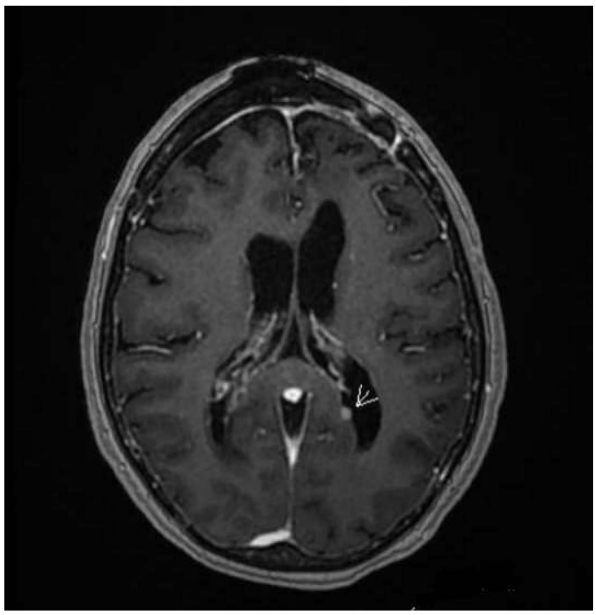
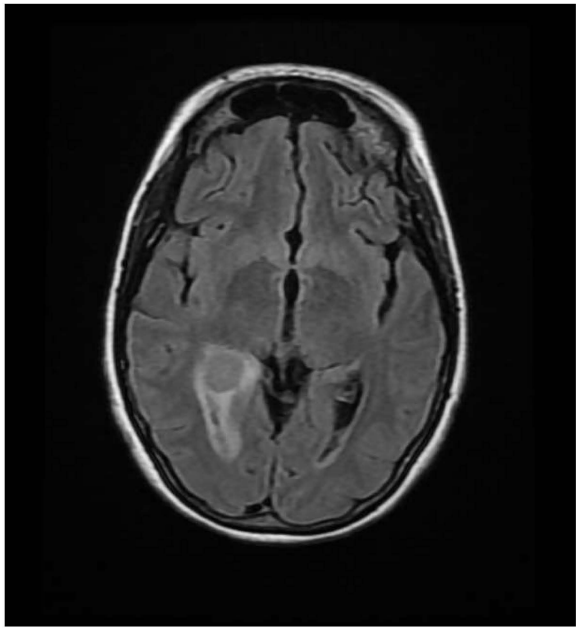


Figure 2: MRI which shows right temporal mass.



Day 3 on dexamethasone (Decadron), the patient began to regain facial control, demonstrating the ability to raise eyebrows, initiate tear production, and drink from a straw. Hematology oncology advised no surgical resection at that time but initiated 10 whole brain radiation treatments WBRT. Pain was controlled at the time with oxycodone 5 mg q8h PRN and acetaminophen (APAP) 500 mg q6h. The patient received 4/10 WBRT in hospital before being discharged home. Hematology oncology deferred intrathecal chemotherapy until WBRT concluded.

Post discharge, the patient followed outpatient oncology finishing all 10 WBRT sessions within 13 days. A porta catheter was placed and was started on trastuzumab deruxtecan in March 2024. Documentation from day 8 into chemotherapy, the patient's facial paralysis was reported as completely resolved. The patient also followed up with audiology, where they reported profound sensorineural loss 250-8000 Hz. Patient developed chest pain where CTA was urgently captured showing pulmonary emboli in the right upper and right lower lobes. Enoxaparin sodium (Lovenox) 1 mg/kg was started that same day followed by apixaban (Eliquis) 5 mg twice a day. The patient's chest pain resolved 9 days later. Patient completed 2 cycles of chemotherapy and repeat imaging was completed and compared to initial hospital stay imaging.

Findings of the MRI head with/without contrast showed marked improvement from prior imaging revealing a decreased right posterior medial lesion size of 0.9 x 0.6 cm from original size of 1.8 x 1.6 cm. The prior enhancement of the ventricular wall was also resolved. There was improved focus in the right internal auditory canal and improved enhancement in the internal auditory canal. Superior cerebellar, interpeduncular cistern, and nodular enhancement in occipital horn with leptomeningeal disease also resolved. MRI lumbar/spine showed no new findings from prior imaging.

Oncology documentation reports that the patient is tolerating the cycles of chemotherapy well with reported increased energy and only nausea as a common complaint. She is currently about to begin her 6th cycle of trastuzumab deruxtecan. There has been no resolution of hearing loss, but resolution of facial droop.

DISCUSSION

This case highlights the variable and often insidious nature of LC presentations. The patient's initial symptoms of isolated left-sided facial droop and bilateral hearing loss are atypical and underscore the necessity for high clinical suspicion, especially in patients with a known history of malignancy[1,4]. The development of right-sided facial paralysis

further complicated the clinical picture, necessitating advanced imaging and lumbar puncture with cytology, which confirmed the diagnosis of LC. This reinforces the importance of considering LC in differential diagnoses when patients with a history of cancer present with new neurological deficits[4].

MRI of the brain and spine played a pivotal role in diagnosing LC, revealing characteristic leptomeningeal enhancement[1]. The subsequent lumbar puncture, showing atypical cells with elevated white blood cell count and protein levels in the cerebrospinal fluid, was crucial in confirming the diagnosis. These findings are consistent with other reported cases, where MRI and CSF analysis are the cornerstone of LC diagnosis[4]. However, the subtle nature of the initial presentation in this patient highlights the importance of thorough and repeated imaging and the need for a high index of suspicion in similar cases.

The treatment approach in this case involved a combination of corticosteroids, whole-brain radiation therapy (WBRT), and systemic chemotherapy. The patient's initial response to corticosteroids, with significant improvement in facial paralysis, illustrates the potential for symptomatic relief even in advanced LC. WBRT was administered promptly, and the patient completed 10 sessions, which is consistent with current treatment protocols aiming to control neurological symptoms and improve quality of life.

The initiation of trastuzumab deruxtecan post-radiation therapy represents a modern therapeutic approach targeting HER2-low cancer cells, reflecting advances in targeted therapies. The patient's favorable response, marked by significant improvement in MRI findings and resolution of neurological deficits, is encouraging. However, the development of complications such as pulmonary emboli underscores the complexity of managing LC and the need for vigilant monitoring and supportive care.

While the prognosis for LC remains poor, this case demonstrates that with prompt and aggressive treatment, patients can achieve significant symptomatic relief. The marked improvement in the patient's MRI findings and improvement of leptomeningeal disease indicate that targeted therapies, combined with traditional modalities like radiation, can offer meaningful clinical benefits.

The patient's journey also highlights the importance of a multidisciplinary approach, involving oncology, radiology, neurology, and supportive care teams to address the multifaceted needs of LC patients. Ongoing research into novel therapeutic agents and approaches is crucial to improve outcomes for patients with this challenging condition[1,4].

Other case reports have mentioned the role of palliative care with the improvement of pain management[6]. This case report highlights the optimistic symptomatic improvement that encompasses more than pain control. The role of palliative medicine was approached to the patient during her time in the hospital, but the patient and family declined the consultation. The patient had great support from her family and religious figures as she was constantly surrounded with loving and encouraging moments during her hospital stay.

It is important to note that this patient was highly motivated at obtaining symptomatic improvement and working toward regaining her facial control. She was seen nearly every

morning walking in the hallways and continuing to work on her occupational therapy exercises throughout the day.

Incidence of leptomeningeal carcinomatosis (LC) has increased, largely attributed to focused imaging and improvement of treatment modalities for primary tumors, yet mortality remains prevalent. This case report describes a patient who preferred a more holistic approach to cancer treatment when approaching her primary malignancy, and expanded her preferences to include chemotherapy as her diagnosis evolved to include leptomeningeal carcinomatosis. This patient's symptom and imaging improvements with a multidisciplinary approach highlights the benefits of early incorporation of LC into provider differential diagnoses and further reinforces the need for continued advancements in treatment of LC.

Informed patient consent was obtained during the hospitalization stay. IRB approval was not applicable for this report.

Notes

Conflicts of Interest: None declared.

Funding: None declared.

Acknowledgements: None

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