CASE REPORT OPEN ACCESS

A Rare Presentation: Leptomeningeal Disease Involving the Left Cerebellar Hemisphere and Lumbosacral Region in Breast Cancer

Rida Aziz[1], Arifa Shahzadi[2], Hamza Tanzeel[3], Ayesha Siddiqa[4], Areeba Aziz[5]

[1]1CMH Medical College, Lahore, [2]Sughra Shafi Medical Complex, Narowal, [3]Riphah International University, Lahore, [4]Ghausia foundation, Lahore, [5]THQ Civil Hospital, Sialkot

ABSTRACT

Leptomeningeal disease (LMD) is a rare condition that occurs in fewer than 5% of breast cancer patients. In certain instances, individuals exhibit symptoms of LMD when initially diagnosed. We present a case involving a 48-year-old female who experienced a sudden onset of weakness in her left upper and lower limbs, leading to an extensive LMD diagnosis. A series of investigations were initiated to uncover the root cause of LMD. Subsequent MRI scans covering both the entire brain and the spinal cord confirmed the presence of metastatic breast carcinoma, thus providing insight into the origin of her condition. Following this, the patient underwent a regimen of radiation therapy to address the metastases and then started a comprehensive neuro-rehabilitation program aimed at improving her overall well-being and quality of life.

Keywords: Breast Neoplasms, Brain Neoplasms, Neurological Rehabilitation.

Corresponding author:
Dr. Rida Aziz
CMH Medical College,
Lahore, Pakistan.
Email: rida_aziz_29@yahoo.com
Doi: 10.36283/PJMD13-2/016

How to cite: Aziz R, Shahzadi A, Tanzeel H, Siddiqa A, Aziz A. A Rare Presentation: Leptomeningeal Disease Involving the Left Cerebellar Hemisphere and Lumbosacral Region in Breast Cancer. Pak J Med Dent.2024;13(2): 106-111. Doi: 10.36283/PJMD13-2/016

INTRODUCTION

Leptomeningeal malignancy, known by numerous names, including leptomeningeal metastases and neoplastic meningitis, specifies the outspread of the tumor to the cerebrospinal fluid (CSF) and infiltration of subarachnoid space[1]. The word leptomeningeal indicates the thin meninges, the arachnoid, and the pia mater, in the middle of which the CSF is present[2]. The preponderance of LMD is approximately 11% in patients with advanced tumors throughout the illness and results in cumulative neurologic dysfunction, which results in mortality for untreated patients after 4 to 6 weeks[3].

Three solid cancers give rise to LMD i.e., breast tumor, lung tumor, and adenocarcinomas. Leptomeningeal malignancy is spotted in about 2-5% of breast cancer patients with a poor prognosis and substantial morbidity, ultimately leading to mortality, if left untreated[4,5]. Despite progress in focused radiation and chemotherapeutic treatments, the prospects for survival following a diagnosis of leptomeningeal involvement are quite

bleak, with an average life expectancy typically spanning only 3 to 6 months. The likelihood of survival varies significantly depending on the underlying cause, and notably, individuals with breast cancer exhibit the most favorable prognosis, with a 13% to 25% chance of survival at one year and a 6% chance at two years [6]. Malignant cells can infiltrate any region of the central nervous system and accelerate the onset of symptoms. Consequently, leptomeningeal disease can manifest with a wide array of initial clinical indications (Table 1) [7, 8]. Cerebrospinal fluid (CSF) investigations, and (MRI) of the brain are the basis for confirmation of the disease[9].

Trastuzumab deruxtecan (T-DXd) proved effective for breast cancer patients with brain metastases (BM), regardless of BM status or leptomeningeal carcinomatosis (LMC). The treatment demonstrated efficacy in controlling intracranial tumors, with a manageable adverse event profile. Notably, T-DXd showed potential survival benefits for patients with BM and a poor prognosis (low Karnofsky performance status score). In a small subgroup with LMC, the therapy achieved sustained systemic disease control [10]. We present a rare case of cancer metastasis in this study, which not only extends to the Conus Medullaris and Cauda equina but also to the left Cerebellar Hemisphere, Adrenal glands, and the Cervix.

Table 1: Indications of Leptomeningeal disease

Clinical Presenting Symptoms	Nature of Symptoms	Clinical Manifestations of LMD in Various Central Nervous System Regions	Radiographic Findings
Headache	Persistent, severe	Cancer cells in cerebrospinal fluid	Contrast-enhanced MRI may show meningeal enhancement
Neck Stiffness	Stiff neck, discomfort	Cancer cells infiltrate the meninges	MRI may reveal leptomeningeal enhancement
Nausea and Vomiting	Persistent nausea, vomiting	Cancer cells infiltrate cerebrospinal fluid	MRI can show meningeal thickening or nodularity
Changes in Vision	Blurred or double vision	Cancer cells affect optic nerves	MRI or CT scans may show abnormalities in the optic pathways
Difficulty with Balance	Poor coordination, unsteadiness	Cancer cells disrupt cerebellar function	Imaging may reveal cerebellar or brainstem abnormalities
Weakness in Limbs	Muscle weakness, paresis	Cancer cells compress spinal cord	MRI may indicate spinal cord compression or nerve root involvement
Seizures	Seizure activity	Irritation of brain tissue by cancer cells	EEG may show abnormal electrical activity

Altered Mental State	Confusion, cognitive decline	Cancer cells affect brain function	MRI or CT scans may show brain parenchymal involvement
Cognitive Impairment	Memory loss, executive dysfunction	Cancer cells infiltrate brain tissue	Neuropsychological testing may detect deficits

CASE REPORT

A 48-year-old female sought medical attention at the OPD of our Physiotherapy department, Sahara Hospital, Narowal after experiencing a sudden onset of left-sided paralysis along with symptoms of headache and vomiting. The patient was experiencing various other symptoms, including double vision (diplopia), loss of vision, changes in hearing, and weakness in the left side of the face for the last month after taking the Whole brain radiation therapy (WBRT) treatment. Common spinal symptoms in her case involved weakness in the lower motor neurons, tingling sensations (paresthesia), pain radiating along nerve roots (radicular pain), discomfort in the neck or back, and potential dysfunction in bladder or bowel control. Her medical history was notable for metastatic breast cancer, which had previously led to facial palsy, bilateral mastectomy, ovarian ablation, and six cycles of chemotherapy. Additionally, she had a history of brain metastasis, which had been treated with WBRT which was not very effective and all the other symptoms appeared after receiving that therapy. Her medication regimen included Cap Risek 20 mg, Tab Tamoxifen 20 mg, Syp Motillium, Cap Celbex 100 mg, and Risek Sachet on an as-needed basis.

Upon examination, it was evident that sensations on the left side of her body were absent, accompanied by a complete loss of motor function, resulting in hypotonic muscles. In stark contrast, the right side of her body exhibited intact sensations, albeit with reduced strength rated at 3/5, and normal muscle tone. Her balance was severely compromised, and coordination of movements was notably impaired. She also faced speech difficulties, with impaired cognition and hearing loss in her left ear as well as blurred vision as the patient couldn't see clearly.

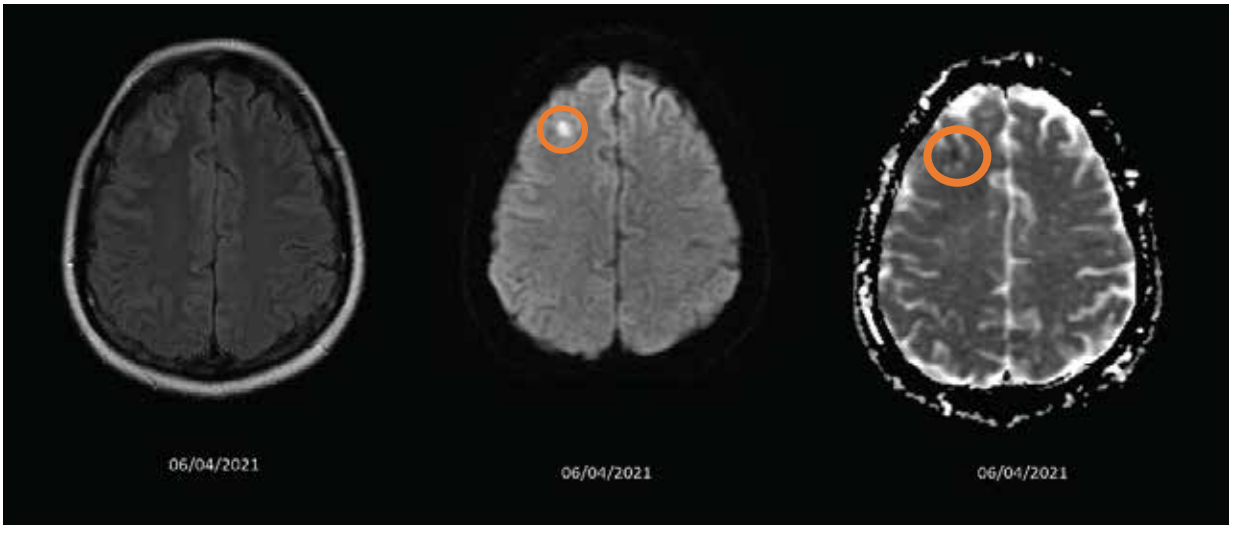

Figure1: The T2/FLAIR-weighted MRI images, along with diffusion and apparent diffusion coefficient (ADC) map, reveal a lesion exhibiting high signal intensity (Blue Circle) on T2/FLAIR in the corticocortical transition of the right inferior frontal gyrus. The lesion demonstrates restricted diffusion of water molecules, as indicated by hyperintensity (Green Circle) on the diffusion-weighted imaging (DWI) sequence and hypo intensity (Black Circle) on the ADC map.

A previous MRI report from the past year had revealed a small homogeneously enhancing lesion measuring approximately 7x8 mm in the left cerebellar hemisphere, displaying mild surrounding vasogenic edema. Leptomeningeal metastatic disease was identified, involving the cauda equina and conus medullaris, extending from the T^{11} vertebra down to the S2 vertebra. Subsequently, a

 DOI: https://doi.org/10.36283/PJMD13-2/016

follow-up MRI of the brain and whole spine was recommended. This latest imaging showed a mild interval increase in the size of the left cerebellar lesion, measuring about 12.19 x 9.08 mm, with no significant diffusion restriction or perilesional edema. Additionally, a new nodular enhancing lesion was identified in the left cerebellar hemisphere, Dural-based in nature. Extensive T2 and FLAIR hyper-intense signals were observed in bilateral periventricular and deep white matter, with no diffusion restriction, suggestive of chemotherapy-induced leukoencephalopathy (Figure 2). The MRI of the whole spine indicated an extension of leptomeningeal disease, now involving the upper thoracic region.

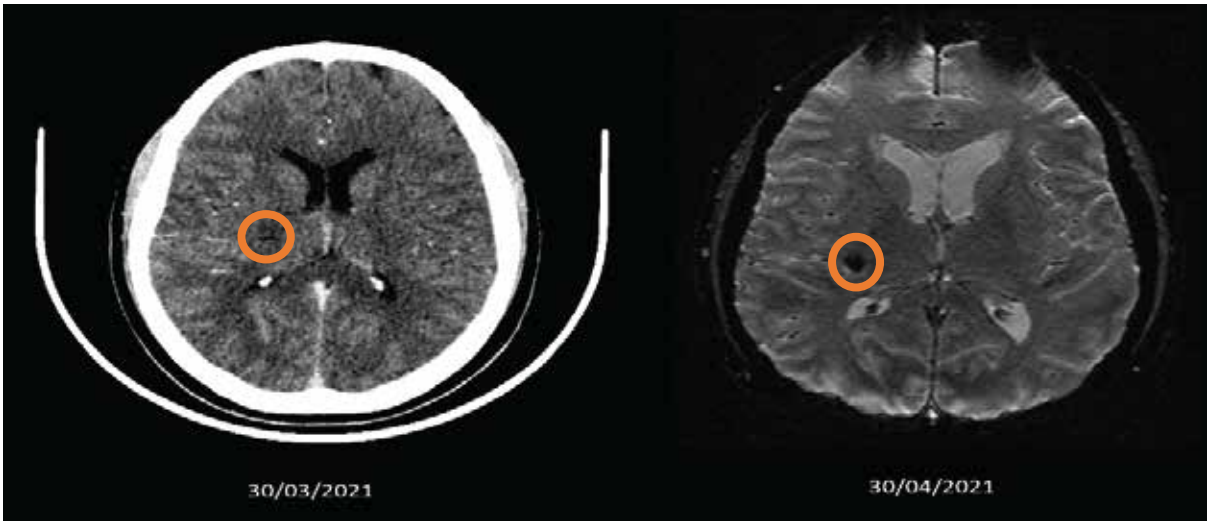

Figure 2: The left side displays an axial computed tomography image with iodinated contrast, revealing a hypodense region (Green Circle) in the right posterior putamen-capsular area, lacking notable enhancement. On the right, a magnetic resonance image using a susceptibility-weighted sequence (SWI) shows a region of hypo intensity (Blue Circle) in the same location, suggesting the presence of hemosiderin deposition.

Following consultation with the oncologist and initial treatment, we initiated a comprehensive rehabilitation protocol to address the left-sided paralysis. Our approach encompassed a range of therapeutic interventions, aiming to restore sensations, enhance motor control, and improve the overall quality of life. We employed techniques such as Electrical Muscle Stimulation, sensory retraining exercises, and Mirror Therapy to reestablish sensory feedback and proprioception. To regain motor control, we implemented motor relearning strategies and applied the passive range of motion exercises. This multifaceted rehabilitation approach was designed to address the patient's specific needs holistically, focusing on her physical and functional recovery.

Rehabilitation protocols included: a) Electrical Muscle Stimulation: Stimulation parameters ranged from 200-1000 µs for pulse duration, 2-60 Hz for the frequency, and 10-200 mA in amplitude. 10-15 minutes, 2 times per day for 4 weeks. b) Sensory retraining exercise: Two types of superficial sensitivity were analyzed: pinprick and light touch. c) Mirror Therapy to re-establish sensory feedback and proprioception: 30 minutes, 3 days a week for 4 weeks. d) Motor relearning strategies: The motor assessment was performed using the ASIA scale, with the grading of the strength of key muscles from 0 to 5. Task-specific training, repetitive practice, feedback, and error correction were practiced in this training. The total duration of intervention was 1 hour per session and frequency of 4 weeks, with 5 sessions per week. e) Balance Exercises: Berg Balance Scale was performed before and after performing the balance exercises such as weight shift, sit-to-stand exercises, Single Leg Stance, heel-to-toe walk, and tandem stance, 2 days a week for 4 weeks.

After one month of dedicated rehabilitation, the patient reported reduced pain in her lumbosacral region, improved sitting posture, and enhanced postural alignment. She had also regained sensations and exhibited some motor activity. Furthermore, her static and dynamic balance showed significant improvement, facilitating her ability to perform activities of daily living, including standing, walking, and bathing.

In summary, our patient's overall quality of life demonstrated substantial improvement following the implementation of a comprehensive physical therapy regimen which is assessed through the SF-36 Health Survey. The difficult circumstances postulat

ed by metastatic breast cancer and its neurological indicators, our integral approach successfully restored her physically and functionally, giving her new hope and increasing her level of well-being has been improved.

DISCUSSION

The pervasiveness of brain upheaval, including the minacious specter of LMD, is of great worry. A roughly calculated 70k- 400k people are thought to be newly diagnosed with brain metastases in the United States alone[11]. Critically, 10-40% of patients only encounter these metastases even after surviving the wearing clinical course of the disease[12].

This case highlights the significant impact of leptomeningeal disease (LMD) in making stride solid tumors. The sudden left hemiplegia of a 48-year-old patient is a crisp reminder of the impact of this rare finding that can affect people with a variety of malignancies. It is practiced to situate these findings within broader medical knowledge and to make comparisons with kindred research in this field.

Currently, the archetype for LMD is based on neuroimaging, cerebrospinal fluid (CSF) cytology and clinical evaluation. The focal means of LMC diagnosis include advanced MRI techniques using gadolinium, panoramic analysis of CSF cellular composition, and brain MRI using T1- and T2-weighted sequences with contrast agents. Nevertheless, the indisputable identification of malignant cells within the CSF remains the most important diagnostic benchmark. Although MRI results can reveal abnormalities in the majority of patients with cytology-positive CSF, it is important to recognize that the sensitivity of MRI alone fluctuates from 65 to 75%. Therefore, clinical indicators combined with MRI or serial CSF studies should be considered to make the final diagnosis of LMC[13].

The prognosis for patients contending with LMC is, regrettably, confined to a mere three to four months. Treatment encompasses a spectrum of options, including radiation therapy (RT), Craniospinal irradiation (CSI), shunt diversion procedures to manage hydrocephalus, cytotoxic chemotherapy regimens, as well as innovative approaches centered around Antifolate metabolites, immunotherapy, and the choice between Ommaya and lumbar puncture administration. These therapeutic interventions all share a common goal: to enhance patient outcomes and enhance their overall quality of life[14].

The individual encountered a relapse of breast cancer within 4-6 months following the initial treatment. Instead of Trastuzumab, which is not suitable for postmenopausal patients, the patient was prescribed anastrozole as an alternative. Strength training revamps the strength and endurance of the muscle groups being used. Upskill compensatory strategies allow patients to remain mobile and engage in maintaining balance and self-care activities. Therapeutic exercises are mostly integrated with teaching compensatory strategies and appropriate use of assistive devices to develop complex interventions to maximize autonomy. Patients are taught to use an assistive device (usually a cane or walker) when walking or climbing stairs to compensate for decreased sensory input[15].

As neural deterioration progresses, physical therapists and health care professionals can help reduce cancer-related fatigue, alleviate deconditioning, adjust sleep patterns, optimize nutrition, utilize non-invasive neurostimulation techniques, and implement energy-saving strategies. You should know strategies to effectively treat the implementation and associated symptoms. The majority of patients with LMD do not require inpatient rehabilitation or acceptance to a long-term care facility due to the severity of functional impairment or duration of chemotherapy. Nevertheless, granting access to appropriate rehabilitation facilities remains paramount to enable the proclamation of effective interventions and essential education in the realm of cancer rehabilitation.

In conclusion, this case highlights the importance of a comprehensive approach to patient care that addresses the myriad needs of LMD patients and includes medical interventions and holistic rehabilitation programs. The path forward necessitates concentrated efforts in research, education, and the assurance of accessible therapeutic facilities to enhance the quality of life for individuals grappling with this intricate and debilitating condition.

CONCLUSION

Treatment of LMD secondary to breast cancer and also involving the lumbosacral region is a challenging disease to treat. LMD is a rare fundamental sign of breast cancer and early diagnosis can avoid morbidity and improve the prognosis. Important initial neuro-rehabilitation protocol is necessary for the patient's Functional Independence Measure.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest.

ACKNOWLEDGEMENTS

I extend my sincere gratitude to my supervisor, for their expertise and guidance. Special thanks to Ana Cláudia Kutax Buiar, Fernanda De Almeida Vieira, Ricardo Pasquini Neto, Mariana Cristina Gomes-Morila for giving us the consent to use the MRI Images of this case study and Arifa Shehzadi & Areeba Aziz for their valuable contributions by providing the detailed case history.

AUTHORS CONTRIBUTION

RA: Conceived and designed the study, collected Images, and drafted the initial manuscript. AS: Contributed to the literature review, provided critical intellectual input, and assisted in revising the manuscript for important intellectual content. HT: Conducted the patient interviews, gathered clinical data, and contributed to the interpretation of findings. AS: Reviewed and edited the manuscript for language and style, ensuring clarity and coherence. AA: Assisted in data putting, provided additional insights during manuscript revision, and ensured the scientific rigor of the study.

REFERENCES

1. Lukas RV, Buerki R, Mrugala MM. Management of Leptomeningeal Disease From Solid Tumors. Oncology (Williston Park). 2016; 30(8):724-730 DOI: https://link.gale.com/apps/doc/A460901264/AONE?u=anon~bb0b19cd&sid=g.
2. Chamberlain M, Soffietti R, Raizer J, Rudà R, Brandsma D, Boogerd W, et al. Leptomeningeal metastasis: a Response Assessment in Neuro-Oncology critical review of Endpoints and response criteria of published randomized clinical trials. Neuro Oncol. 2014;16(9):1176-1185 https://doi.org/10.1093/neuonc/nou089.
3. Fu JB, Molinares DM, Morishita S, Silver JK, Dibaj SS, Guo Y, et al. Retrospective Analysis of Acute Rehabilitation Outcomes of Cancer Inpatients with Leptomeningeal Disease. Pm r. 2020;12(3):263-270 https://doi.org/10.1002/pmrj.12207.
4. Shrestha J, Shrestha A, Karki P, Dhakal A. Leptomeningeal Disease as an Initial Presenting Manifestation in Breast Cancer. Cureus. 2021;13(11):e19666 DOI: 10.7759/cureus.19666 .
5. Nayar G, Ejikeme T, Chongsathidkiet P, Elsamadicy AA, Blackwell KL, Clarke JM, et al. Leptomeningeal disease: current diagnostic and therapeutic strategies. Oncotarget. 2017;8(42):73312-73328 doi: 10.18632/oncotarget.20272.
6. Mack F, Baumert BG, Schäfer N, Hattingen E, Scheffler B, Herrlinger U, et al. Therapy of leptomeningeal metastasis in solid tumors. Cancer Treat Rev. 2016; 43:83-91. https://doi.org/10.1016/j.ctrv.2015.12.004.
7. Munankami S, Shrestha M, Basnet S, Rijal SS. A Rare Case of Leptomeningeal Carcinomatosis Secondary to Metastatic Non-Small Cell Lung Carcinoma. Cureus. 2022;14(5):e25436 DOI: 10.7759/cureus.25436 .
8. Lamba N, Wen PY, Aizer AA. Epidemiology of brain metastases and leptomeningeal disease. Neuro-Oncology.2021;23(9):1447-1456https://-doi.org/10.1093/neuonc/noab101.
9. Bazan F, Dobi E, Royer B, Curtit E, Mansi L, Menneveau N, et al. Systemic high-dose intravenous methotrexate in patients with central nervous system metastatic breast cancer. BMC Cancer. 2019;19(1):1029 DOI: https://doi.org/10.1186/s12885-019-6228-6.
10. Niikura N, Yamanaka T, Nomura H, Shiraishi K, Kusama H, Yamamoto M, et al. Treatment with trastuzumab deruxtecan in patients with HER2-positive breast cancer and brain metastases and/or leptomeningeal disease (ROSET-BM). npj Breast Cancer. 2023;9(1):82DOI:https://-doi.org/10.1038/s41523-023-00584-5.
11. Nicoletti GF, Umana GE, Graziano F, et al. Cauda equina syndrome caused by lumbar leptomeningeal metastases from lung adenocarcinoma mimicking a schwannoma. Surg Neurol Int. 2020; 11:225. doi:10.25259/sni_365_2020
12. Thakkar JP, Chamberlain MC. Chapter 8 - Leptomeningeal metastasis. In: Newton HB, Malkin MG, eds. Neurological Complications of Systemic Cancer and Antineoplastic Therapy (Second Edition). Academic Press; 2022:133-143.
13. Faiver L, Gutgsell O, Umemura Y. CSF and disease: brain and leptomeningeal metastases. Cerebrospinal Fluid and Subarachnoid Space. Elsevier; 2023:31-46.
14. Jesús R-MA, Iñigo VAA, Luis B-L, et al. Diagnosis and management of brain metastases: an updated review from a radiation oncology perspective. 2019.
15. Weiner M, Banovac K, Martinez-Barrizonte J. Poster 399: Cauda Equina Syndrome Due to Leptomeningeal Carcinomatosis: A Case Report and Literature Review. PM&R. 2010 Sep 1;2 (9):S175.