

Breaking Barriers: A Durable Leptomeningeal Disease Response Without Local CNS Therapy

Authors: Emily Sargent, MD[1], Aman Buzdar, MD[2], David Ramirez, MD[2], Dawid Schellingerhout, MBChB[3]

[1]Department of Internal Medicine, University of Texas Health Science Center at Houston, [2]Department of Breast Medical Oncology, MD Anderson Cancer Center [3]Departmenr of Neuroradiology, MD Anderson Cancer Center

Presentation ID: PS5-06-23

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Making Cancer History®

Introduction

Leptomeningeal disease (LMD) occurs in up to 5% of breast cancer patients and carries a poor prognosis. In a large institutional study of 233 cases, patients with HR+/HER2− disease had a median overall survival of just 3.7 months despite multimodal treatment.[1]

Standard management includes intrathecal chemotherapy and CNS radiation, though there are no consensus guidelines or randomized trials, as most LMD patients are excluded from studies. Systemic therapy can offer modest benefit, but responses are variable.[1]

We present a case of HR+/HER2− metastatic breast cancer with LMD and initially poor performance status who experienced sustained functional recovery with endocrine therapy plus a CDK4/6 inhibitor alone.

Case Presentation

A 76-year-old woman with hypertension and hyperlipidemia was diagnosed at an outside hospital with de novo metastatic invasive lobular carcinoma involving the left breast, lung, pleura, peritoneum, soft tissue, bone, and lymph nodes.

Right inguinal lymph node biopsy showed ER 99%, PR 80–90%, HER2 0, Ki-67 >50%, consistent with breast primary, and a left breast biopsy confirmed lobular carcinoma.

She later presented to MD Anderson with dyspnea and was found to be bedbound (ECOG 4) with an early sacral wound. Imaging revealed left pulmonary emboli and a large right pleural effusion; thoracentesis showed malignant cells consistent with breast adenocarcinoma.

Before starting therapy, she developed altered mental status. MRI brain demonstrated leptomeningeal disease (Figure 1), and MRI spine showed diffuse leptomeningeal involvement with cord edema. Lumbar puncture was recommended but the patient declined.

This presentation is the intellectual property of the author/presenter. Contact them at esargent@mdanderson.org for permission to reprint and/or distribute.

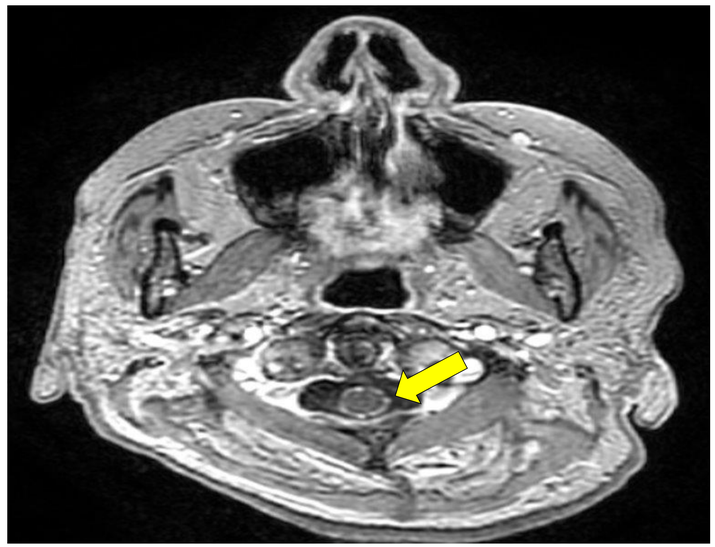


Figure 1: T1 gadolinium enhanced MR image of 8/6/2023 demonstrates abnormal surface enhancement on the medulla oblongata (yellow arrow) consistent with LMD

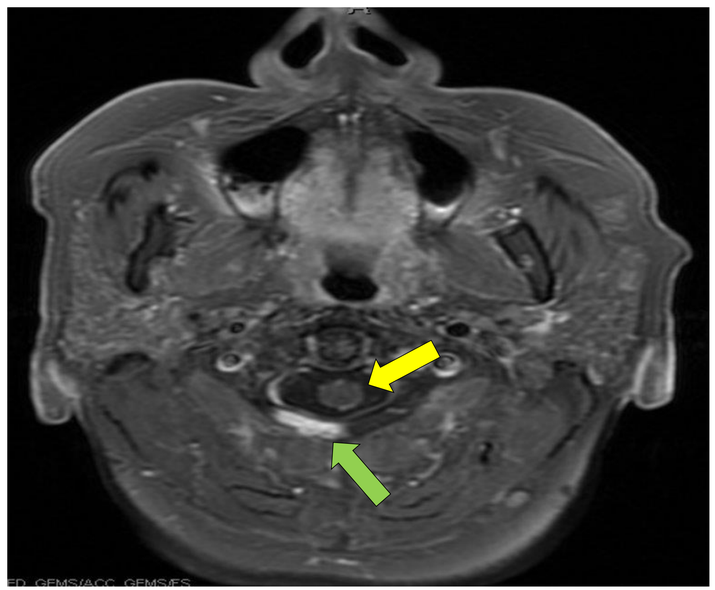


Figure 2: T1 gadolinium enhanced image demonstrates improved leptomeningeal enhancement at the time of follow-up on 9/25/2025 (yellow arrow). Also note a marrow metastasis to the C1 ring (green arrow).

Case Presentation Continued

A multidisciplinary team reviewed her case. Radiation oncology advised against CNS-directed therapy given her ECOG 4 status, and neuro-oncology confirmed radiographic LMD while determining she was not a candidate for intrathecal chemotherapy.

Following goals-of-care discussions, the patient chose systemic treatment. She began an aromatase inhibitor (AI) during hospitalization, followed by palbociclib as an outpatient, guided by PALOMA-2 data and its favorable tolerability[2]. Zoledronic acid was added for bone disease.

At 25 months, she continues first-line AI plus palbociclib with sustained benefit, including radiographic improvement in LMD (Figure 2) and a profound functional recovery to ECOG 0 with complete healing of her sacral wound. A new metastatic lesion was identified but given her otherwise stable disease and excellent clinical trajectory, she remains on the same regimen.

Discussion

This case highlights an unusual response of LMD in HR+/HER2- breast cancer to systemic therapy with an AI and CDK4/6 inhibitor. Emerging evidence suggests that CDK inhibitors may have meaningful central nervous system activity in patients with HR+/HER2− breast cancer.

In a prospective phase II trial, abemaciclib achieved CSF and brain metastasis concentrations well above the IC50 for CDK4/6 inhibition and was associated with clinical benefit in a subset of patients with brain and leptomeningeal metastases[3].

Our patient's recovery challenges the conventional guidelines regarding recommendations of intrathecal and/or radiation therapy for LMD and supports further investigation into systemic CDK4/6 inhibition for select patients, despite initial performance status.

References:

1. Abouharb S, Ensor J, Loghin ME, Katz R, Moulder SL, Esteva FJ, Smith B, Valero V, Hortobagyi GN, Melhem-Bertrandt A. Leptomeningeal disease and breast cancer: the importance of tumor subtype. Breast Cancer Res Treat. 2014 Aug;146(3):477-86. doi: 10.1007/s10549-014-3054-z. Epub 2014 Jul 20. PMID: 25038877.
2. Finn, R. S., Martin, M., Rugo, H. S., et al. (2016). Palbociclib and letrozole in advanced breast cancer. *New England Journal of Medicine, 375*(20), 1925–1936. https://doi.org/10.1056/NEJMoa1607303
3. Tolaney SM, Sahebjam S, Le Rhun E, Bachelot T, Kabos P, Awada A, Yardley D, Chan A, Conte P, Diéras V, Lin NU, Bear M, Chapman SC, Yang Z, Chen Y, Anders CK. A Phase II Study of Abemaciclib in Patients with Brain Metastases Secondary to Hormone Receptor-Positive Breast Cancer. Clin Cancer Res. 2020 Oct 15;26(20):5310-5319. doi: 10.1158/1078-0432.CCR-20-1764. Epub 2020 Jul 21. Erratum in: Clin Cancer Res. 2021 Mar 1;27(5):1582. doi: 10.1158/1078-0432.CCR-21-0193. PMID: 32694159.