Early-Stage Hormone Receptor–Positive Metaplastic Breast Cancer Treated With Chemo-Immunotherapy: A Case Report

Dali Edwards, DO[1], Cara Coleman, MD[1]; Abdur Jamil, MD[2];

1 - Hollings Cancer Center, Medical University of South Carolina, Charleston, SC; 2 – Internal Medicine Department, Samaritan Medical Center, Watertown, NY

Abstract

Metaplastic breast cancer (MpBC) is a rare and aggressive histologic subtype, accounting for fewer than 1% of breast cancer diagnoses and characterized by rapid growth, high grade, and limited responsiveness to cytotoxic chemotherapy. While most MpBCs are triple-negative, hormone receptor (HR)–positive tumors are distinctly uncommon and poorly characterized. Current NCCN guidelines recommend treating MpBC according to principles applied to invasive ductal carcinoma with similar receptor status; however, clinical outcomes remain inferior, with higher rates of chemoresistance, early recurrence, and distant metastasis.

Emerging data show PD-L1 expression in up to 95% of MpBCs, supporting investigation of immune checkpoint blockade (ICB). We present a case of early-stage, HR-positive, HER2-negative MpBC treated with neoadjuvant chemo-immunotherapy consisting of durvalumab every two weeks combined with standard of care chemotherapy.

Introduction

- HR-positive MpBCs are exceptionally rare, limiting the development of evidence-based treatment strategies.
- These tumors frequently present as large, rapidly enlarging masses.
- MpBCs consistently demonstrates poor response to standard chemotherapy.
- High PD-L1 expression in MpBC provides a rationale for ICB, though data in HR-positive disease remain very limited.

Case Presentation

- Patient: 54-year-old postmenopausal Hispanic woman, G6P5A1
- Presentation: 1-month history of painful, enlarging right breast mass; no prior mammography.
- Mammogram: 5.7 × 3.5 × 4.6 cm irregular mass, abnormal axillary nodes.
- MRI: 7.3 × 4.6 × 5.6 cm superior breast mass, additional 1.3 cm mass, 3 abnormal nodes
- CT chest, abdomen, pelvis / Bone scan: No distant metastasis.
- **Pathology**: High-grade metaplastic carcinoma with focal squamous differentiation; ER-positive 84%, PR -negative, HER2-negative (IHC 1+), Ki-67 67%, grade 3; with benign lymph node.
- **Stage: IIIA (cT3 cN0 cM0)**
- **Genetic testing**: INVITAE testing identified one pathogenic variant in MUTYH
- **Genomic risk profiling**: MammaPrint ultra–high-risk [MP2]
- **Clinical trial enrollment**: SWOG S2206 (NCT06058377), Phase 3 randomized study for patients with MammaPrint high-2-risk [MP2], stage II–III HR-positive, HER2-negative breast cancer
- **Treatment:**
  - Patient was randomized to ARM 2 (experimental)
  - Chemo-immunotherapy regimen: Paclitaxel 6 cycles, repeated every 14 days followed by Doxorubicin + Cyclophosphamide 4 cycles every 14 days; Durvalumab administered concurrently with chemotherapy every 14 days.
- **Tolerance:** Well tolerated; progressive tumor shrinkage and symptom improvement.
- **Clinical Response:**
  - Significant reduction in breast mass on serial clinical exams
  - End-of-treatment MRI confirmed marked decrease in the biopsy-proven malignancy in the superior right breast, no measurable residual enhancement, Decrease in size of three level I axillary lymph nodes.

Figures

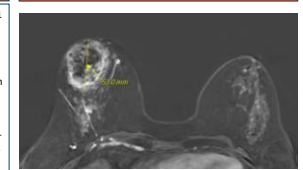


Figure 1. Magnetic resonance imaging of bilateral breasts at the time of diagnosis.

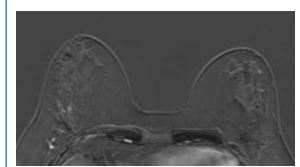


Figure 2. Magnetic resonance imaging of bilateral breasts following neoadjuvant chemo-immunotherapy.

Discussion

- This case highlights an exceptionally rare entity—ER-positive, HER2-negative MpBC—for which treatment data remain limited.
- This case demonstrated a robust response to neoadjuvant standard-of-care chemotherapy combined with durvalumab, suggesting ICB may provide meaningful clinical benefit even within this uncommon HR–positive metaplastic subtype.
- These findings add to emerging evidence that incorporating immunotherapy into treatment regimens may improve outcomes in this rare, high-risk subtype of breast cancer .
- The case highlights the urgent need for prospective trials including HR-positive MpBC and biomarker-driven research.

Conclusions

- ER-positive MpBC is a rare and understudied variant with outcomes comparable to triple-negative MpBC despite HR expression.
- Evidence supporting ICB in MpBC is derived primarily from case reports and small series in triple-negative disease, where ICB has produced encouraging responses.
- The notable clinical response in this patient underscores potential activity of ICB in HR-positive MpBC and highlights the need for broader inclusion of MpBC in clinical trials and for multi-institutional efforts to clarify the role of ICB across MpBC subtypes.

Contact:

Dali Edwards, DO
MUSC, Hollings Cancer Center
Email: edwadali@musc.edu
Fax: 843 792 1445
Phone: 843 792 9300

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