METAPLASTIC BREAST CANCER WITH MELANOCYTIC FEATURES:

Rethinking our Conventional Understanding of Breast Tumorigenesis

Simerun Singh MD, Ajay Iyer MD, Nisreen Haideri MD, Omar Hameed MD

HCA Healthcare Kansas City/Overland Park Regional Medical Center Program, Forward Pathological Solutions

INTRODUCTION

➢Metaplastic breast carcinoma (MBC) is a group of heterogeneous tumors with variable outcomes dependent on subtype and grade.[1]

➢Our case presents a patient with chemoresistant, triple negative invasive ductal carcinoma (IDC) who developed a chest wall mass shortly after treatment suggestive of melanoma. Retrospective pathologic review revealed metaplastic breast cancer with melanocytic features. Melanocytic differentiation is rare (only case reports) and portends a poor prognosis. [2]

CASE PRESENTATION

Initial Presentation

➢48-year-old female Jehovah's witness with history of lupus presented with an inflamed left breast.

➢Multiple core needle biopsies were attempted but showed only inflammatory changes. **MRI (*Figure 1*) showed a separate 3 cm mass.**

➢Core needle breast biopsy (*Figure 2*) ultimately demonstrated triple negative breast cancer with the diagnosis of **Grade III invasive ductal carcinoma (IDC) of no special type**. BRCA was negative, skin biopsy benign.

➢Neoadjuvant chemotherapy with carboplatin/paclitaxel/dose-dense adriamycin/cyclophosphamide for six months followed by bilateral mastectomy and sentinel lymph node resection **revealed 6.3 cm mass, benign lymph nodes** (T3pN0), and poor pathologic response to treatment.

➢Surgery followed by adjuvant chemotherapy with capecitabine and post-mastectomy radiation was complicated by dose-limiting cytopenia.

Six Months After Treatment

➢Patient presents to the emergency department for chest pain. CT chest shows a new chest wall mass with mediastinal lymphadenopathy. PET shows **extensive osseous, liver, and adrenal metastasis**.

➢**Chest wall biopsy (*Figure 3*) with pathology shows malignant melanoma**. Original breast biopsy pathology is asked to be reviewed.

Pathologic Reevaluation

➢Breast core biopsy, mastectomy, and chest wall specimens reviewed and IHC/staining ruled out metastatic melanoma or two distinct primary neoplasms. **Pathology showed focal area of mastectomy specimen staining positive for melanocytic markers** (HMB45/MART1) surrounded by decreased cytokeratin expression confirming diagnosis of **metaplastic carcinoma with melanocytic differentiation.**

➢Started on carboplatin/gemcitabine/pembrolizumab (triple negative IDC treatment) but could only tolerate pembrolizumab due to severe anemia. Her clinical status deteriorated acutely. She developed sepsis from pneumonia requiring intubation. Ultimately family elected for comfort care measures.

IMAGING AND HISTOLOGY

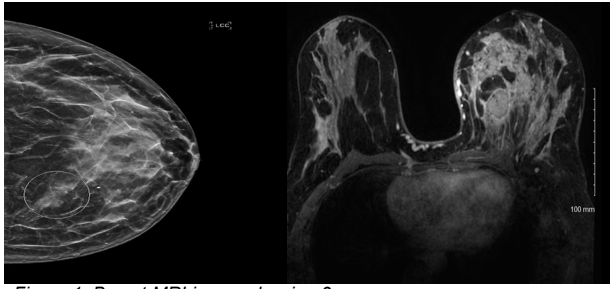

Figure 1: Breast MRI image showing 3 cm mass

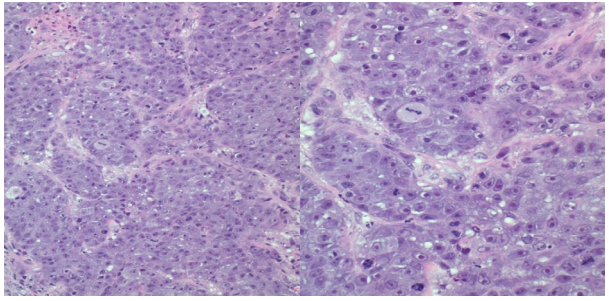

Figure 2: Core needle breast biopsy shows Grade 3 IDC.

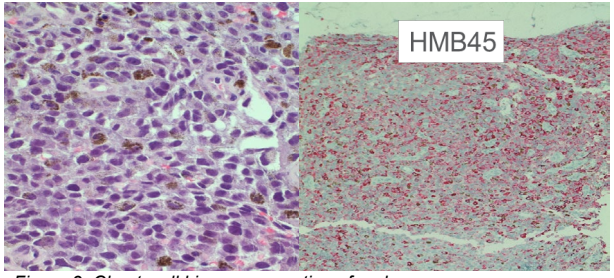

Figure 3: Chest wall biopsy suggestive of melanoma.

DISCUSSION

➢There are two hypotheses that breast metaplasia is posited to occur– the first more conventional and the second more recently described:

- Stem cell of origin within the native breast tissue (epithelial/mesenchymal) transforms based on the inherent stem cells' differentiation potential.
- Various genetic hits to the tumor at later carcinogenesis stages lead to fairly unpredictable dedifferentiation.[3]

➢MBCs tend to be aggressive, genetically heterogeneous, and harbor somatic mutations like *TPK3, PIK3CA, and PTEN.*[4]

➢MBCs are also usually chemoresistant with low nodal involvement.[2]

➢Overexpression of PD-L1 and tumor-infiltrating lymphocytes has led to a rationale for treatment with immunotherapy.[5]

➢Current research seeks to further specify the behavior of MBCs, the genetic hits and resultant mutations that may predispose tumor cells to undergo dedifferentiation/metaplasia thus revealing new potential therapeutic targets.[6]

CONCLUSION

➢ In this MBC case, staining and immunohistochemistry did not favor metastatic melanoma or collision tumor leading to further investigation. The process of metaplasia here was **represented by loss of cytokeratin expression hypothesized to be from tumor progression and profound dedifferentiation with genetic expression akin to melanocytes.**

➢ Given its chemoresistance, low nodal involvement, aggressive nature and pathologic findings; the clinicopathological diagnosis of metaplastic breast cancer with melanocytic differentiation was made.

REFERENCES

1.International Agency for Research on Cancer and the WHO Tumor Classification online via https://tumourclassification.iarc.who.int/welcome/ accessed 12/2022

2.Bendic A, Bozic M, Durdov MG. Metaplastic breast carcinoma with melanocytic differentiation. *Pathol Int*. 2009;59:676–80.

3.van Deurzen CH, Lee AH, Gill MS, Menke-Pluijmers MB, Jager A, Ellis IO, et al. Metaplastic breast carcinoma: tumour histogenesis or dedifferentiation? *J Pathol*. (2011) 224:434–7

4.Ng CKY, Piscuoglio S, Geyer FC, Burke KA, Pareja F, Eberle CA, Lim RS, Natrajan R *et al.* (2017) The landscape of somatic genetic alterations in metaplastic breast carcinomas. *Clin Cancer Res* 23, 3859–3870.

5.Adams, S. Dramatic response of metaplastic breast cancer to chemo-immunotherapy. *NPJ Breast Cancer* (2017).

6.Tse GM, Tan PH, Putti TC, et al. Metaplastic carcinoma of the breast: a clinicopathological review. J Clin Pathol 2006; 59: 1079–1083.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.