Metastatic Signet-Ring Lobular Breast Carcinoma Mimicking Gastric Adenocarcinoma: A Diagnostic Challenge

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INTRODUCTION

- Metastatic invasive lobular carcinoma (ILC) with signet ring features can closely mimic primary gastric adenocarcinoma
- We present the case of a 61- year-old woman whose initial biopsies supported a diagnosis of diffuse-type gastric adenocarcinoma with signet ring cells. Further immunohistochemical staining revealed expression of breast-specific markers
- This case underscores the critical role of immunohistochemical IHC) and next generation sequencing (NGS) in distinguishing metastatic breast carcinoma from primary gastric cancer

CASE DESCRIPTION

- A 61-year-old female presented to the emergency room for one month of dysphagia, nausea, vomiting, and weight loss
- Radiographic studies revealed abdominopelvic ascites, periportal lymphadenopathy, right adnexal enlargement containing soft tissue and cystic components, osseous lesions, and omental carcinomatosis
- An EGD was performed and a gastric biopsy revealed positive pan-cytokeratin AE1/AE3
- A subsequent omental mass biopsy stained positive for CK7 and negative for PAX8 and CDX20
- The presumptive diagnosis at this time was metastatic gastric adenocarcinoma, and treatment with oxaliplatin and capecitabine was initiated

CASE DESCRIPTION CONTINUED

- For further characterization gastric tumor specimen was submitted to outside molecular testing laboratory which revealed significant RNA expression of breast markers including cytokeratin 7, GATA3, SCGB2A2 (mammablogib) and ESR1. Immunohistochemical (IHC) staining showed expression of mammaglobin and GATA3. Pathogenic loss of function variant in CDH1 gene was detected
- Further in-house IHC staining on omental specimen showed positive for GATA-3, E-Cadherin, estrogen receptor, progesterone receptor, and rare cells positive for mammaglobin.
- An ultrasound of breast showed prominent dilated ducts in the retro-areolar area in the right breast and a right axillary lymph node with focally prominent cortex and dilated duct in the left retro-areolar region. Further MRI of the breasts did not identify a primary breast mass and there were no pathologic axillary lymph nodes

PATHOLOGY FINDINGS

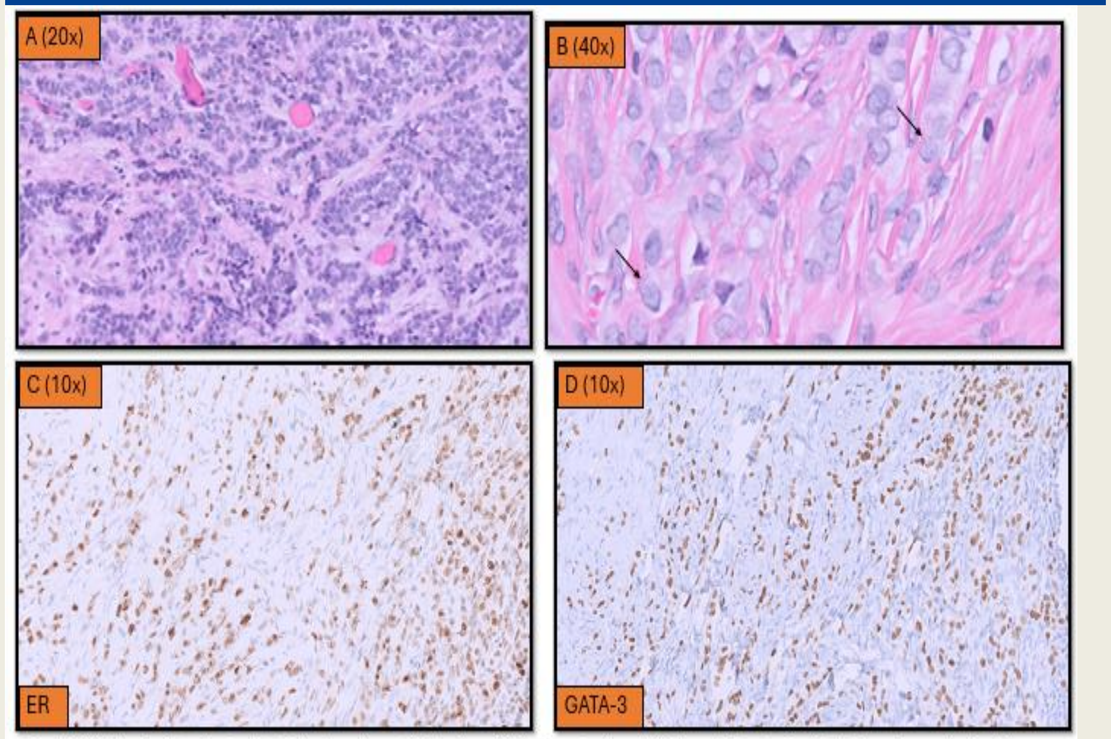


Figure # 1: A(20x) hematoxylin and eosin-stained picture shows tumor with trabecular architecture in ovarian stroma. B(40x) hematoxylin and eosin-stained picture shows neoplastic cells has cytoplasmic vacuoles (arrows). C(10x) shows neoplastic cells are positive for estrogen receptor(ER). D (10x) shows neoplastic cells are positive for GATA-3 stain.

COMMON IHC AND NGS FINDINGS

	IHC Stain	Sensitivity	Specificity
Breast origin			
	GCDFP-15	14% -78%	100%
	Mammaglobin	26% -41.7%	100%
	GATA3	86%-100%	98%
	Estrogen receptor	72%-81.8%	100%
Gastric origin			
	CK20	50%-66.7%	93.3%-100%
	CDX2	67%-72%	100%

Table 1. Sensitivity and specificity for IHC stains in diagnosing metastatic breast carcinoma and primary gastric cancer

	Mutation	Prevalence in respective malignancy
Lobular breast carcinoma		
	CDH1	63% - 65%
	PIK3CA	46%
	PTEN	2%
	AKT1	2.3%
	FOXA1	7.1% - 9%
	ERBB2 (HER2)	3.9%- 5.1%
Gastric carcinoma		
	TP53	54-61.6%
	ARID1A	23%
	CDH1	9.7%
	PIK3CA	11.7% - 12%

Table 2. Most common mutations in lobular breast carcinoma and gastric carcinoma

CONCLUSIONS

- The above case demonstrates the diagnostic difficulty of differentiating primary gastric cancer from lobular breast carcinoma that has metastasized to the stomach
- Signet ring cell carcinoma of the breast has been shown to have a poorer prognosis compared to mucinous carcinoma, highlighting the need for prompt treatment
- Integrating markers such as ER, PR, GATA3, mammaglobin, and CDH1/PIK3CA profiling into a tiered diagnostic algorithm can ultimately prevent misclassification, facilitate timely therapy, and improve patient outcomes