Estrogen and Progesterone Receptor Negativity and HER-2 Positivity in a Pure Mucinous Breast Carcinoma

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Abstract

Introduction: Mucinous carcinomas may be pure or mixed, depending on the cellularity present. They are a slow growing neoplasm, are usually low grade, with rare axillary lymph node metastases. They have a better prognosis compared with other invasive carcinomas. Immunohistochemical studies of mucinous carcinomas regularly show Estrogen Receptor (ER) and Progesterone Receptor (PR) positivity and human epidermal growth factor receptor-2 (HER-2) negativity.

Case Summary: A 54-year-old female consulted due to a gradually enlarging mass on the upper outer quadrant of her right breast. Core needle biopsy of the mass revealed an invasive carcinoma with mucinous features. The patient underwent modified radical mastectomy, where the final histopathologic diagnosis for the submitted surgical resection specimen was mucinous carcinoma with signet ring cell features, Nottingham histologic grade II. Immunohistochemical staining of the core biopsy specimen and surgical resection specimen revealed negative estrogen and progesterone receptors and positive HER2/neu receptor (3+) in 100% of the tumor cells, which is different from the typical immunohistochemistry profile of mucinous breast carcinomas.

Discussion: Pure mucinous carcinoma or colloid carcinomas accounts for not more than 2% of invasive breast carcinomas and presents with large amounts of extracellular mucin. Between pure and mixed mucinous carcinoma, prognosis is better in pure types. Modified radical mastectomy remains the gold standard of treatment for breast tumors followed by post-operative endocrine therapy, which is indicated in estrogen and progesterone responsive tumors. HER2/neu expression in breast tumors along with the absence of hormone (estrogen and progesterone) receptors is associated with an aggressive phenotype. When HER-2 is positive, treatment would be trastuzumab, although resistance for mucinous carcinomas has been reported.

Conclusion: Only few cases of pure mucinous carcinomas are positive for HER2 receptors and negative for estrogen and progesterone receptors. It is important for physicians to know that cases of mucinous carcinoma positive for HER2 and negative for estrogen and progesterone exist and to be aware of the clinical problems that they may present.

Keywords: Mucinous Carcinoma• Breast• Estrogen• Progesterone HER2-neu• Treatment• Prognosis

Objectives
1. To discuss the characteristic features of mucinous breast carcinoma.
2. To correlate the prognostic implication of this tumor with the clinical, histopathologic and immunohistochemical features of mucinous breast carcinoma.
3. To understand the role of immunohistochemistry in managing patients with breast carcinoma.

Case Summary
Presented is a case of a 54-year-old postmenopausal woman admitted for a gradually enlarging breast mass. Two years prior to admission, the patient noted a palpable mass on the upper outer quadrant of her right breast, measuring about 2 × 2 cm in size with associated tenderness. No consult was done for the said mass, until one year prior to admission when the patient consulted at the outpatient department of Baguio General Hospital and Medical Center.

Targeted right breast ultrasound revealed a circumscribed, round, high echogenic mass measuring 4.4 × 4.8 × 5.9 cm (AP × T × CC) at the upper outer quadrant of the right breast with punctuate calcifications (Figure 1).

Core needle biopsy of the right breast mass tissue was submitted revealing infiltrating tumor cells seen in solid nests accompanied by extracellular mucin pools. The tumor cells exhibit enlarged hyperchromatic nuclei, some with irregular nuclear contours, prominent nucleoli and minimal cytoplasm (Figures 2 and 3). The pathologic diagnosis of the biopsy was consistent with an invasive carcinoma with mucinous features.

A. Low power view of ER Receptor Assay with negative staining in 100% of the neoplastic cells.
B. Low power view of PR Receptor Assay with negative staining in 100% of the neoplastic cells.
C. Low power view of HER-2 neu positive staining (3+) in 100% of the neoplastic cells.

The patient then underwent Modified Radical Mastectomy of her right breast. On gross examination, the specimen submitted consisted of the right breast and right axillary tail with cut sections

Figure 1. Targeted breast ultrasound showing a large echogenic mass (arrow) with angular borders and punctuate calcifications in the right breast at 8:30 to 11 o'clock position.

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revealing a well-circumscribed mass measuring 5.5 × 4.5 cm with moist and glistening surfaces. Several axillary lymph nodes were isolated.

Microscopic examination revealed a tumor composed of multiple clusters of neoplastic cells surrounded by variable amounts of extracellular mucin (Figure 5). These cells exhibit focal tubular and cribriform patterns, displaying moderate to marked nuclear atypia, some with intracellular mucin resembling signet rings, and accompanied by few mitotic figures (Figures 6 and 7). Lymphovascular invasion was observed (Figure 8). All isolated lymph nodes were devoid of tumor. ER/PR/HER2 Testing was consistent with that of the core needle biopsy revealing ER-Negativity, PR-Negativity and HER2 Positivity (Figure 9). The final histopathologic diagnosis was Pure Mucinous Carcinoma with Signet Ring Cell Features, Nottingham Histologic Grade II. ER negative, PR negative, and HER2 positive.

Numerous studies regarding the immunohistochemistry staining of mucinous breast carcinoma show that conventionally, almost all cases are positive for estrogen and progesterone hormone receptors, especially for ER, and more than 95% of the tumors usually do not express HER2. This justifies their good behavior and prognosis, with studies demonstrating a 10-year survival rate of 90% or more among women diagnosed with the tumor [5,6]. In this case, however, there was a difference in that the ER and PR immunohistochemical staining results were negative and the HER2 staining results were strongly positive.
These cells exhibit focal tubular and cribriform patterns, of neoplastic cells surrounded by variable amounts of extracellular mucin.

Lymphovascular invasion was observed (Figure 8). All isolated neoplastic cells resembling signet rings, and accompanied by few mitotic figures (Figure 6).

Histologic Grade II. ER negative, PR negative, and HER2 positive staining (3+) in 100% of the neoplastic cells.

On the basis of intrinsic molecular subtypes, the patient is classified under HER2-enriched, associated with a more aggressive tumor and a poorer prognosis [7]. In the case presented, even if pure mucinous carcinoma is associated with an excellent prognosis, the absence of estrogen and progesterone receptors and the presence of HER2 expression may change the clinical evolution of this tumor. For the treatment, rather than using the usual tamoxifen used in mucinous breast carcinoma, trastuzumab would then be recommended (Table 1).

**Conclusion**

Only a few cases of pure mucinous carcinomas are positive for HER2 and negative for ER and PR. It is imperative for physicians to know about this entity because there are no protocols or clinical practice guidelines regarding proper treatment in positive HER2 positive mucinous carcinomas, and although few, trastuzumab resistance have been reported. The patient must also be consistently evaluated due to high risk of tumor recurrence. This also reminds practitioners the importance of immunohistochemistry in the management of patients with breast carcinomas as not all tumors behave the same way.

With continued progress in our understanding of molecular alterations and tumor biology, it has come to a realization that breast cancer is a biologically diverse disease and varies according to morphology, biology and response to therapies. Profiling of carcinomas using Immunohistochemistry (IHC) has assumed an increasingly important role as prognostic and predictive markers in providing vital information the multidisciplinary team needs, to deliver the most appropriate treatment for each individual patient.

**References**


