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## Breast Metaplastic Squamous Cell Carcinoma Diagnosed with Fine Needle and Core Biopsy: A Case Study

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Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Female • 48  
**Final Diagnosis:** Breast metaplastic squamous cell carcinoma  
**Symptoms:** Palpable mass  
**Medication:** Anthracycline  
**Clinical Procedure:** Right modified radical mastectomy  
**Specialty:** Oncopathology





**Objective:** Rare disease  
**Background:** Breast metaplastic squamous cell carcinoma (SCC) is a rare primary breast carcinoma, and overexpression of HER2 in this carcinoma is extremely uncommon.

**Case Report:** We presented a case of a 48-year-old Asian female with breast metaplastic SCC. Fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB) of the lesion were taken prior to surgical resection. FNAB smears demonstrated highly atypical squamous cells and a diagnosis positive for malignancy was rendered. CNB and a surgical resection specimen revealed invasive squamous carcinoma with keratin pearl formation and intercellular bridges. Further study demonstrated this was an unusual metaplastic SCC case with basal-HER2 (+) phenotype. HER2 has been linked to poor prognosis and response to therapy.

**Conclusions:** The pathological diagnosis of the breast metaplastic SCC was made initially by FNAB and CNB. Identification of basal-HER2 (+) phenotype was critical for selection of hormonal therapies and chemotherapy.

**MeSH Keywords:** Breast Neoplasms • Genes, erbB-2 • Mass Behavior • Metaplasia • Neoplasms, Squamous Cell

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/907254>

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## Background

Breast squamous cell carcinoma (SCC) is a rare and aggressive neoplasm, and accounts for less than 0.1% of all breast carcinomas [1]. Metaplastic SCC refers to carcinoma that shows dominant areas of non-glandular squamous differentiation; other components could include ductal cells, spindle cells, chondrocytes, osteocytes, and striated muscle cells [2]. The broad range of microscopic appearances of breast metaplastic SCCs has resulted in significant diagnostic challenges. Clinical and radiological signs of metaplastic SCC are also non-specific.

Overexpression of HER2, one of the transmembrane tyrosine kinase receptors from the epidermal growth factor receptor (EGFR) family, is uncommon in breast SCCs. Without targeted therapy, HER-2 overexpressing breast carcinomas are associated with poor prognosis. Most breast SCCs, regardless of the type of metaplastic elements, are CK5/6, CK14 positive, and according to immunohistochemistry/gene profiling classification, belong to the basal-like phenotype [3,4]. It has been assumed for a long time that HER-2 overexpression and basal-like breast carcinomas are mutually exclusive [5]. This concept has been challenged recently and the basal-HER2 (+) phenotype has been linked to poorer survival prognosis than either HER-2 overexpression or basal-like subtype [5,6]. Breast carcinomas of this phenotype benefit from anthracycline treatment and are resistant to trastuzumab or tamoxifen therapy [7,8].

In our case report, we reported a metaplastic SCC initially diagnosed by fine needle aspiration biopsy (FNAB) and core needle biopsy (CNB). Further excisional specimens showed the tumor overexpressed HER2. Thus, we reported a metaplastic SCC of extremely uncommon phenotype.

## Case Report

In March 2017, a 48-year-old female patient presented with a painless rapidly growing palpable mass of about two months, in her right breast. Physical examination found a 4×4 cm mass in the upper-outer quadrant. There was no retracted nipple or orange-peel appearance of the breast skin. Enlarged lymph nodes were palpable under the right axillary area. Ultrasound diagnostic was a solid mass with cystic region in the right breast which was classified as BI-RADS 4c.

FNAB was conducted to aspirate cystic fluid with rapid on-site evaluation prior to a surgical procedure. The FNAB cytology smears demonstrated highly atypical squamous cells scattered with large amounts of erythrocytes and necrotic tissue (Figure 1A). The tumor cells were scattered or loosely cohesive; with tadpole, irregular, or polygonal shape and rich, eosinophilic cytoplasm. Hyperchromatic, large, and pleomorphic nuclei

were identified with prominent nucleoli and coarse chromatin. Atypical mitotic figures and tumor giant cells were also observed. Some cells presented with denatured nuclei. The FNAB morphological features rendered the diagnosis as positive for malignancy and consistent with SCCs. CNB specimen revealed ductal structures with mostly benign metaplastic squamous cells; one core illustrated invasive squamous cell carcinoma with pleomorphic squamous tumor cells infiltrative to surrounding parenchyma. The moderately differentiated tumor contained regions of ribbon-like architecture with polygonal cells, eosinophilic cytoplasm, keratin pearl formation, and intercellular bridges. Furthermore, there were areas with mixed ductal and squamous epithelial cells that demonstrated the metaplastic processing (Figure 1B). The surgical resection specimen demonstrated a metaplastic SCC of 3.5×3.5×4.0 cm. Microscopically, the tumor was composed of moderate differentiated metaplastic SCC, confirming the findings of FNAB and CNB (Figure 1C). The tumor cells were located near the base of the breast. Because of palpable swollen lymph nodes, the axillary lymph node was removed. One out of 19 axillary lymph nodes were positive for metastatic carcinoma. Interestingly the metastatic carcinoma was breast ductal carcinoma in morphology (Figure 1D); the other lymph nodes were not involved. No tumor was found in the nipple nor skin.

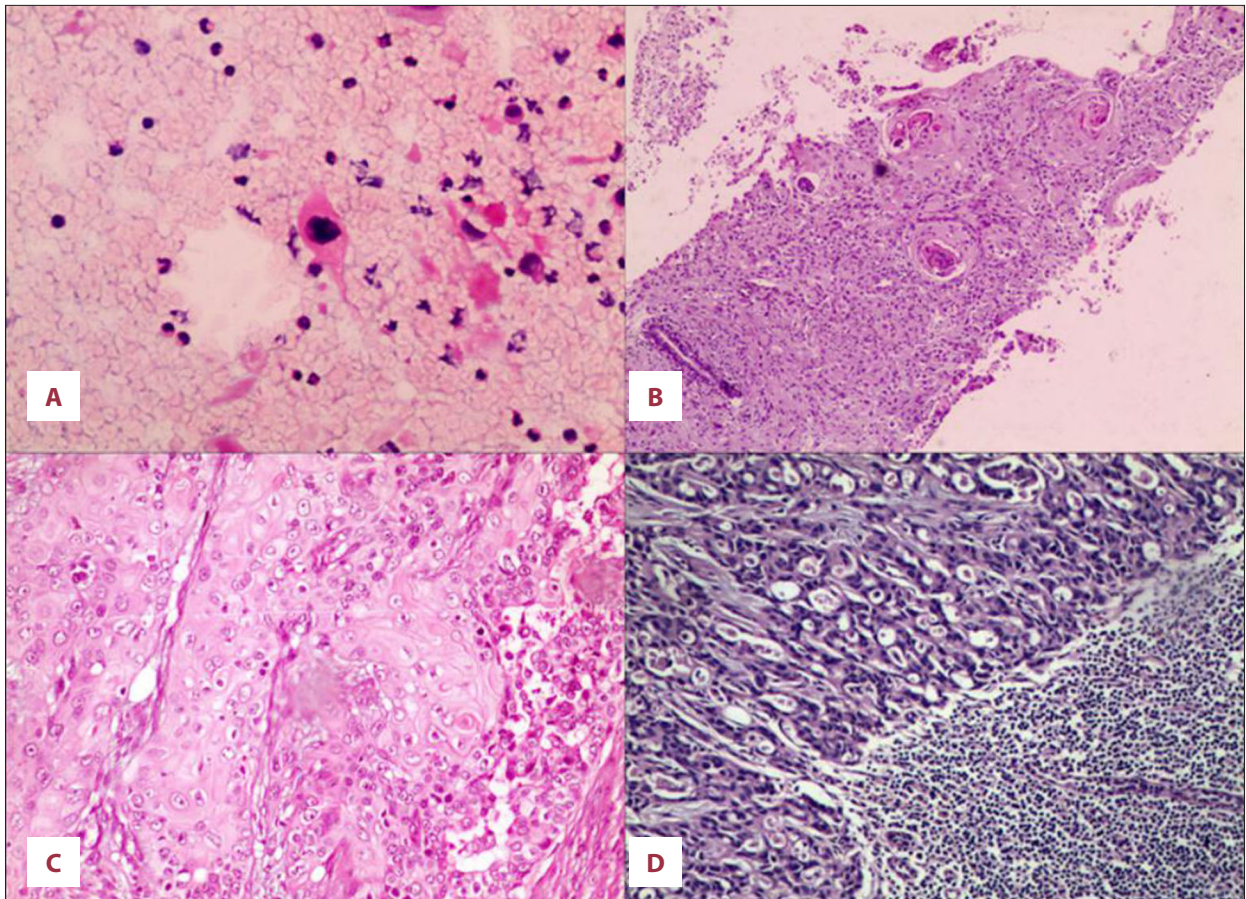
Immunohistochemistry (IHC) showed that the primary metaplastic SCC was ER negative, PR negative, HER-2 positive (3+), EGFR (1+), CK5/6 (2+), 34βE12(2+), P63 positive (the P63 positive cells were located around the cancer nest), P53 negative, SMMHC positive (1+), E-cadherin (2+), and Ki-67 was positive in 95% tumor cells. The positive IHC images of HER2, CK5/6, and EGFR are presented in Figure 2.

After right modified radical mastectomy, doxorubicin, docetaxel, and cyclophosphamide (TAC) chemotherapy was selected for our patient; in addition, radiotherapy was selected because of lymph node involvement. The patient was asymptomatic and disease-free four months after surgical resection.

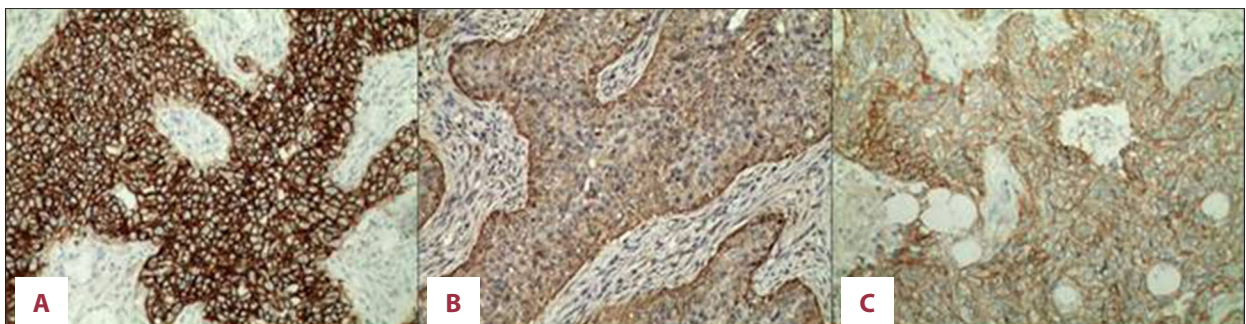
## Discussion

Primary metaplastic breast SCCs are uncommon, aggressive carcinomas and their diagnoses can only be made after exclusion of SCCs from skin and other organ systems of the body such as oral cavity or esophagus. In addition, >90% of tumor cells are usually metaplastic squamous cells [1,9]. Shuai et al. [9] reported that SSC only account for 0.1% of all invasive breast carcinoma (30 out of 25,232 cases). The current (2012) World Health Organization classification distinguishes five subtypes of metaplastic breast carcinomas [2].

Our case presented as squamous cell carcinoma. Etiology and pathogenesis of breast metaplastic SCC is uncertain [10].



**Figure 1.** Hematoxylin and eosin staining. FNAB (A): highly atypical squamous cells scattered with large amounts of erythrocytes and necrotic tissue (40×); CNB (B): ductal structures mixed with invasive squamous cell carcinoma, the moderately differentiated tumor contained regions of ribbon-like architecture with polygonal cells, eosinophilic cytoplasm, keratin pearl formation, and intercellular bridges (4×). Surgical microscopy (C): squamous carcinoma tumor cells confirmed the finding of CNB (20×); lymph node metastatic carcinoma morphology (D): breast ductal carcinoma (10×).



**Figure 2.** Immunohistochemistry staining of HER2 (A), CK5/6 (B), and EGFR (C). DAB brown positive staining and hematoxylin counter staining (10×).

Currently, most authors believe that primary breast metaplastic SCCs present with cyst/duct, and that the epithelium of the cyst/duct are metaplastic squamous carcinoma cells [11]. In our case, we identified areas with mixed ductal and squamous epithelial cells, which was highly suggestive of a metaplastic process. The metaplastic nature of the tumor was further

suggested by the fact that one of the axillary lymph nodes was positive for metastatic ductal carcinoma.

In our case study, FNAB and CNB were taken prior to the surgical excision and the diagnosis of malignancy, consistent with SCC. The FNA exfoliative cytology smear presented squamous

carcinoma cells and this finding was further confirmed by CNB. It is important to note that the role of FNAB combined with CNB as a primary diagnostic tool for breast carcinomas is not settled. This is partly because a lot of breast carcinomas are well differentiated, and it can be difficult to differentiate various atypical and metaplastic changes. In addition, it is difficult to differentiate ductal carcinoma *in situ* or lobular carcinoma *in situ* from invasive carcinomas [12–14]. However, our case report clearly demonstrated that FNAB combined with CNB was highly useful in diagnosing subgroups of breast carcinomas, including metaplastic SCCs.

Lymph node involvement of breast metaplastic cancer is typically lower than non-specific invasive breast cancer. However, Brenner et al. reported that local and/or distant metastases were observed in more than 50% of cases within five years of poor prognosis [15]. Our patient presented with one out of 19 axillary lymph nodes as metastatic and microscopically showed invasive ductal carcinoma. The components of the metastatic carcinoma matched with the surgical resection specimen, which contained mixed ductal and squamous epithelial cells and demonstrated metaplastic processing.

Only 15% to 25% of invasive breast cancers overexpressed HER2 [5]. According to CK/TN classification [16], breast carcinoma can be divided into three subtypes based on five cytokeratin markers: basal (CK5/6, CK14, CK17), luminal (CK8, CK18), and null. It has been assumed for a long time that HER-2

overexpression and basal-like breast carcinomas are mutually exclusive [5]. This concept has recently been challenged, and the HER2+ cases have been further divided into three subtypes: luminal-HER2+ (ER+, basal CK–); HER2+ (ER– and basal CK–); and basal-HER2+ (ER–, basal CK+). Each subtype was correlated with clinical pathologic features, OS, and therapies. Our patient was ER negative, HER-2 positive (3+), CK5/6(2+), and EGFR(1+), which was classified as basal-HER2(+) phenotype. This was extremely unusual (only 9% of HER2+ cases) [9]. Basal-HER2 (+) phenotype has been linked to poorer overall survival compared with two other subtypes [5,6]. Tumors of this phenotype benefit from anthracycline treatment and might be resistant to trastuzumab or tamoxifen therapy [7,8].

## Conclusions

FNAB combined with CNB are useful diagnostic approaches for breast carcinomas, and accurate diagnosis of metaplastic SCC can be rendered. Immunohistochemically markers are essential and sufficient to subtype breast metaplastic SCCs. The basal-HER2 (+) phenotype is a rare case in metaplastic SCC; identification of it is critical for selection of hormonal therapies and chemotherapy.

## Conflict of interest

None.

## References:

1. Hennessy BT, Krishnamurthy S, Giordano S et al: Squamous cell carcinoma of the breast. *J Clin Oncol*, 2005; 23: 7827–35
2. Lakhani SR, Ellise IO, Schnitt SJ (eds.): *WHO classification of Tumors of the breast*. 4<sup>th</sup> edition. Lyon, France: IARC; 2012; 85–87
3. Perou CM, Sørlie T, Eisen MB et al: Molecular portraits of human breast tumours. *Nature*, 2000;406: 747–52
4. Reis-Filho JS, Milanezi F, Steele D et al: Metaplastic breast carcinomas are basal-like tumours. *Histopathology*, 2006; 49: 10–21
5. Bagaria SP, Ray PS, Wang J et al: Prognostic value of basal phenotype in HER2-overexpressing breast cancer. *Ann Surg Oncol*, 2012; 19: 935–40
6. Liu H, Fan Q, Zhang Z et al: Basal-HER2 phenotype shows poorer survival than basal-like phenotype in hormone receptor-negative invasive breast cancers. *Hum Pathol*, 2008; 39: 167–74
7. Oliveras-Ferraro C, Vazquez-Martin A, MartinCastillo B et al: Pathway-focused proteomic signatures in HER2-overexpressing breast cancer with a basal-like phenotype: New insights into *de novo* resistance to trastuzumab (Herceptin). *Int J Oncol*, 2010; 37: 669–78
8. Karamouzis MV, Fida A, Apostolikas N, Rigatos G: A case of HER-2(+) squamous cell breast carcinoma: An unusual presentation of an unusual clinical entity. *EJSO*, 2006; 32: 1250–51
9. Shui R, Li A, Yang F et al: Primary squamous cell carcinoma of the breast with unusual basal-HER2 phenotype. *Int J Clin Exp Pathol*, 2014; 7: 5203–9
10. Flikweert ER, Hofstee M, Liem MSL: Squamous cell carcinoma of the breast: A case report. *World J Surg Oncol*, 2008; 6: 135
11. Hasleton PS, Misch KA, Vasudev KS, George D: Squamous cell carcinoma of the breast. *J Clin Pathol*, 1978; 31: 116–24
12. Mitra S, Dey P: Fine-needle aspiration and core biopsy in the diagnosis of breast lesions: A comparison and review of the literature. *Cytojournal*, 2016; 13: 18
13. Lale S, Kure S, Lingamfelter D: Challenges to diagnose metaplastic carcinoma of the breast through cytologic methods: An eight-case series. *Diagn Pathol*, 2011; 6: 7
14. Bhosale SJ, Kshirsagar AY, Deshmukh SJ et al: Squamous cell carcinoma of the breast. *Am J Case Rep*, 2013; 14: 188–90
15. Brenner RJ, Turner RR, Schiller V et al: Metaplastic carcinoma of the breast: Report of three cases. *Cancer*, 1998; 82: 1082–87
16. Steinman S, Wang J, Bourne P et al: Expression of cytokeratin markers, ER-alpha, PR, HER-2/neu, and EGFR in pure ductal carcinoma *in situ* (DCIS) and DCIS with co-existing invasive ductal carcinoma (IDC) of the breast. *Ann Clin Lab Sci Spring*, 2007; 37: 127–34