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Utility of different immunostains for diagnosis of metastatic breast carcinomas in both surgical and cytological specimens

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ABSTRACT

Objective: A panel of immunostains is usually performed to confirm a metastatic carcinoma origin. GATA3 is a transcription factor and has been proven to be a useful marker for breast carcinoma. Other immunostains including mammaglobin (MGB), gross cystic disease fluid protein 15 (GCDFP-15), estrogen receptor (ER) and progesterone receptor (PR) are also used in diagnosing metastatic breast cancer. In this study, we aimed to compare the performance of these immunostains in the work up of metastatic breast carcinoma in both surgical and cytological specimens.

Study design: This study cohort was composed of 242 metastatic breast carcinomas (142 surgical and 100 cytological specimens) during a study period from October 2013 to December 2015. Immunostain results of GATA3, CK7, MGB, GCDFP-15, ER and PR and their correlations were examined.

Results: In surgical specimens, GATA3 and CK7 were highly expressed (88% and 87%), but MGB and GCDFP-15 showed much lower positivity rates (43% and 29%). In cytological specimens, GATA3, CK7 and MGB showed similar positivity rates to those in surgical specimens; but GCDFP-15, ER and PR showed significantly lower positivity rates than those in surgical specimens. All ER-positive cases were positive for GATA3 in both surgical and cytological specimens; however, GATA3 positivity showed a significantly stronger correlation with ER positivity in surgical specimens than in cytological specimens.

Conclusions: GATA3 and CK7 performed better than other immunostains to detect metastatic breast carcinoma in both surgical and cytological specimens. GATA3 expression was positively correlated with ER expression, and the correlation was stronger in surgical specimens than in cytological specimens.

1. Introduction

Quite often, cancer first presents as a metastases without a prior history or a primary tumor. Tumors of unknown origin are clinically challenging to both clinicians and pathologists in regards to diagnosis and treatment [1]. The main goal of diagnosing metastases as a pathologist is to determine the histologic type and primary site. This is not always strait forward since morphology of different carcinomas can be similar, especially poorly differentiated ones. If the patient is a female, metastatic breast carcinoma automatically becomes one of the differentials since breast cancer is the most common malignancy in women [2].

In a clinical setting, a panel of immunostains is usually performed to confirm a metastatic carcinoma origin. Mammaglobin (MGB), GCDFP-15, ER and PR currently serve as breast-specific immunohistochemical markers in the workup of possible metastatic breast carcinoma. The rate of ER-negative metastatic breast carcinoma was reported in the range of 40–52% [3]. PR status changes from primary tumor to metastases were reported between 16% and 54.3% [4,5] and a switch from positive to negative status was common. Our previous study reported a 24% loss of PR expression in metastatic breast carcinoma [6]. The reported overall sensitivities of MGB and GCDFP-15 were 0–87% and 10–79%, respectively [7-10]. The expressions of GCDFP-15 and MGB in ER-negative breast carcinoma were only 15% and 35% [3]. These data revealed the limitations of utility of these biomarkers in the workup of tumors of unknown origin.

GATA3 (GATA binding protein 3 to DNA sequence: [A/T]GATA[A/G]) is a member of the zinc-finger transcription factor family. GATA3 plays an important role in mammary development and luminal epithelial cell differentiation as well as development of other tissues [11-14] and has been implicated in breast cancer growth, differentiation, progression, and metastasis [13,14]. GATA3 is highly expressed in luminal types of breast cancers [7,9,14,15], ER-negative breast cancers [3,8,15,16] and is tightly correlated to ER expression [17-19]. GATA3 is more sensitive than GCDFP-15 and MGB [8-10] which makes it a useful immunohistochemical marker for breast carcinoma.

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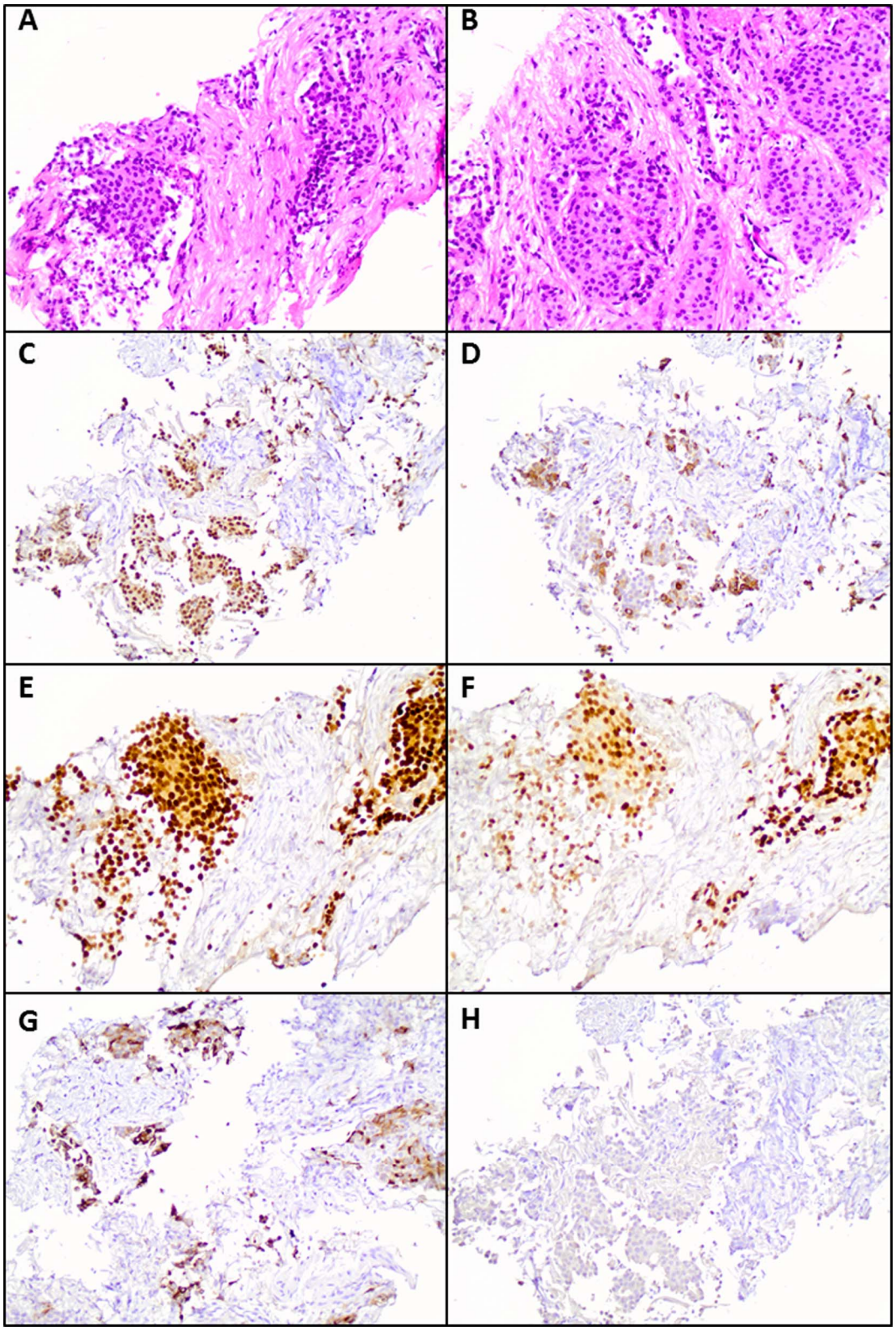

Fig. 1. One lung biopsy case with metastatic breast carcinoma. (A) H & E, 100 ×; (B) H & E, 200 ×; (C) Positive GATA3 staining, 200 ×; (D) Positive CK7 staining, 200 ×; (E) Positive ER staining, 200 ×; (F) Positive PR staining, 200 ×; (G) Positive mammaglobin staining, 200 ×; (H) Negative GCDFP-15 staining, 200 ×.

In this study, we retrospectively reviewed and compared GATA3 immunohistochemistry and other common used breast-specific biomarkers in both surgical and cytological specimens with metastatic breast carcinoma. We also correlated GATA3 expression with ER status in cases of metastatic breast carcinoma.

2. Methods and materials

2.1. Patient selection and data collection

After institutional review board approval at The Ohio State University, a pathology archive database search was performed for a