Human Pathology (2016) 57, 176–181

ELSEVIER

Human PATHOLOGY

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Original contribution

Collagen type III α1 as a useful diagnostic immunohistochemical marker for fibroepithelial lesions of the breast☆

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Received 9 May 2016; revised 15 July 2016; accepted 20 July 2016

Keywords:
Phyllodes tumor;
Fibroadenoma;
Type III collagen;
Fibroepithelial lesion;
Immunohistochemistry

Summary Phyllodes tumors (PTs) of the breast constitute an uncommon group of fibroepithelial neoplasms that are classified into benign, borderline, and malignant categories based on a constellation of histologic characteristics including cytologic atypia, mitotic count, degree of stromal cellularity, stromal overgrowth, and microscopic margins. Accurately and reproducibly differentiating these tumors is a long-standing diagnostic challenge. In addition, the distinction between benign PT from cellular fibroadenoma (FA) is especially difficult because of overlapping microscopic features. We have previously shown differential expression of various collagens, including collagen type III α1 (Col3A) in breast carcinomas. In this study, we evaluated clinicopathological characteristics of 95 cases of fibroepithelial lesions including 56 PTs and 39 FAs (25 cellular FA, 14 typical FA) and correlated them with the immunohistochemical staining pattern for Col3A. We found that stromal Col3A expression was significantly increased in PTs when compared with FAs ($P < .0001$). Among the PT groups, there was significantly increased expression from benign tumors through borderline to malignant tumors. High Col3A expression was associated with PT type, irregular margin status, and high mitotic activity. A distinct periductal cuffing pattern of Col3A staining was unique to PTs and absent in FAs. These findings suggest that Col3A can be a potential adjunct marker for both differentiating FA from PT and assessing malignant potential in PTs.

1. Introduction

Fibroepithelial lesions of the breast include fibroadenomas (FAs) and phyllodes tumors (PTs). The latter are less common, have potential to recur locally, and may metastasize. As outlined by the *World Health Organization (WHO) Classification of Tumors of the Breast*, PTs are classified into benign, borderline, and malignant grades based on a spectrum of histologic features such as stromal hypercellularity, cytologic atypia, stromal overgrowth, mitotic rate, and microscopic margins [1]. The distinction between cellular FAs and PTs can be especially difficult.

PTs present distinct challenges not only in their diagnosis, classification, and predicted behavior, but also in their clinical management. Their biologic behavior and malignant potential

☆ Competing interest: No conflict of interest to disclose from all authors.

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http://dx.doi.org/10.1016/j.humpath.2016.07.017
0046-8177/

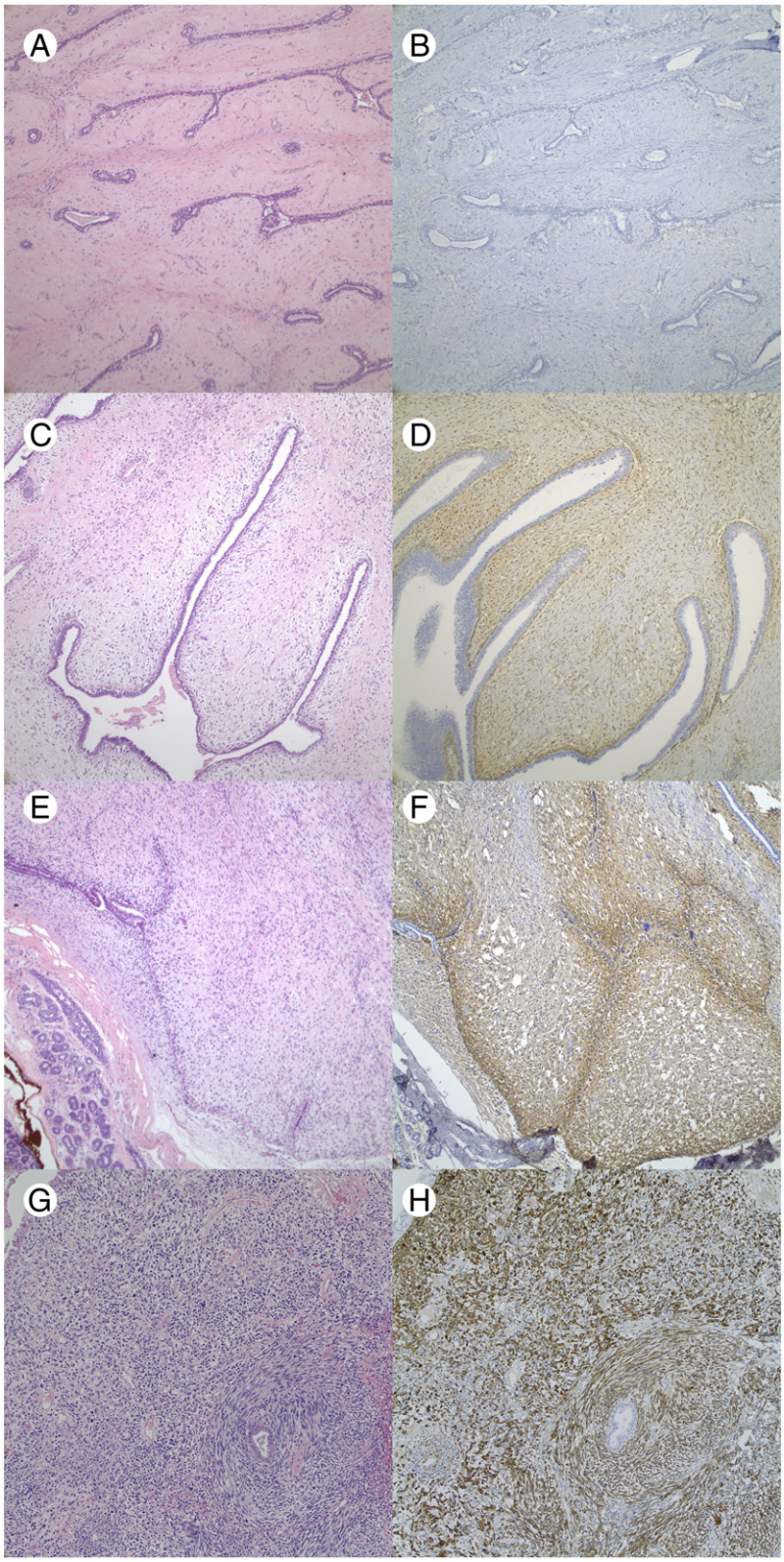

Figure Col3A staining pattern in fibroepithelial lesions and scoring. A and B, An FA with scattered faint staining of stromal cells, combined score of 1 weak (intensity score of 1, percentage score 1) without periductal cuffing. C and D, A cellular FA with combined score of 2 moderate (intensity stain 2, percentage stain >50%); this was a circumscribed mass with increased mild stromal cellularity and admixed pericanalicular and intracanalicular growth pattern. Periductal cuffing with Col3A was absent, overall score 2. E and F, A borderline PT with combined stromal score of 2 and periductal cuffing pattern present, overall score 3. G and H, A malignant PT with strong staining, combined score of 3 (intensity 3, percentage >50%) and periductal cuffing was considered present in this context. Original magnification ×400.