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Original article

Solid papillary carcinoma of the breast: A special entity needs to be distinguished from conventional invasive carcinoma avoiding over-treatment

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ABSTRACT

Introduction: Solid papillary carcinoma of the breast, a newly-defined entity, is poorly recognized, and its nature and management is still debated.
Material and methods: Eleven cases of pure solid papillary breast carcinoma in our archive and 253 cases reported in previous literature were retrospectively analyzed for their clinicopathological features and outcomes.
Results: The eleven cases occurred in elderly females. Grossly, all tumors were well-circumscribed and typically composed of solid papillary nodules. The tumor cells were bland-looking with low-grade atypia and mitoses < 5/10HPF. Immunophenotypically, all eleven cases showed positivity for ER and PR, negativity for CK5/6 and HER2, and a low proliferative index of Ki67. Five cases showed scattered positivity for myoepithelial marker p63, and four cases were positive for CK5/6 and CD10 around the nodules, whereas the other cases were completely negative for all myoepithelial markers. Five cases expressed the neuroendocrine marker synaptophysin, and six cases expressed chromogranin. In nine cases, mastectomy and axillary lymph nodes excision were performed, and only one showed micrometastasis in an axillary lymph node. There was no local recurrence or distant metastasis or breast carcinoma related-death during the follow-up periods of 50 months. Out of 253 solid papillary breast carcinomas reported in literature, the percentage of axillary lymph node metastasis was 4/136 (3%), with rare local recurrences and distant metastasis; only three patients died of breast carcinoma.
Conclusion: Solid papillary carcinoma of the breast is a rare entity with distinctive clinicopathological features and excellent prognosis and should be distinguished from conventional breast carcinoma to avoid over-treatment.

Introduction

Solid papillary carcinoma of the breast, accounting for <1% of breast carcinomas, is a new rare entity preferentially occurring in elderly women with distinctive clinicopathological features. It was first described by Maluf et al. in 1995 [1] and is classified as a special entity intraductal papillary tumor in the recent WHO classification of breast tumors, and it also co-occurs with higher-grade breast carcinoma [2]. However, because of its rarity and specificity, the nature of this tumor entity, its clinical behavior, and its optimal management still remain a matter of debate. Particularly, as solid papillary carcinoma often loses the expression of myoepithelial markers in its periphery [1,2], it is easily confused with conventional types of invasive breast carcinoma. We studied the clinicopathological features and outcomes of eleven cases of pure solid papillary breast carcinoma. In addition, we performed a retrospective analysis of 253 cases of pure solid papillary breast carcinoma reported in the literature. Our purpose is to assess the clinicopathological features and outcomes of solid papillary breast carcinoma and provide further evidence for optimal management of this distinct subtype of breast carcinoma. The results demonstrate that solid papillary breast carcinoma is a rare entity with

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excellent prognosis including a low percentage of axillary lymph node metastasis, a low level of local recurrence and distant metastasis, and a low level of breast carcinoma-related death. Because of its excellent prognosis, and the lack of association between the type of surgical intervention and clinical outcome, we think that adequate local excision with negative margins with or without hormone therapy is the optimal management instead of mastectomy and axillary lymph nodes excision. It is a key issue of solid papillary breast carcinoma to be distinguished from conventional types of invasive carcinoma and to be managed optimally.

Materials and methods

Patients materials

A retrospective search of the pathology database from 2000 to 2014 at Xi Jing Hospital using the key words solid papillary carcinoma and papillary carcinoma of the breast was done. The cases were reviewed by breast pathologists (S.P.G. and X.L.), and eleven cases of pure solid papillary breast carcinomas without coexisting conventional types of carcinoma were selected for study. The clinicopathological information including patient age, tumor size, operative model, and lymph node stage were collected. The follow-up data for ten of these patients were obtained.

Immunohistochemical staining and interpretation

The tissue was fixed in 10% buffered formalin and processed as usual for paraffin embedding. Representative tissue blocks of solid papillary carcinoma of the breast were selected by examination of the corresponding hematoxylin & eosin (H&E) stained slides and 5 μm thick sections were stained with antibodies including myoepithelial markers such as CD10, cytokeratin (CK) 5/6, P63, and neuroendocrine markers such as synaptophysin, chromogranin, and estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) and proliferative index Ki67. Immunohistochemical staining was performed using the Bond-Max automated immunostainer (Vision Biosystems, Lecia, Australia), with a polymer-based detection system. ER, PR and HER2 were scored according to the ASCO/CAP guideline [3,4].

Fluorescence in situ hybridization

One case with a HER2 protein score of 2+ by IHC was assessed for the presence of *HER2* gene amplification on 4 μm FFPE sections using a standard probe (Abbott Molecular, Des Plaines, IL). Cases were regarded as having *HER2* gene amplification if the HER2/CEP17 ratio $\geq$2.0 or the average HER2 copy number $\geq$6.0 signals/cell [4].

Statistical analysis methods

The association between the classification of solid papillary breast carcinoma and the nuclear grading of the tumor cells, the expression of neuroendocrine and myoepithelial markers, and outcome including axillary lymph node status and local recurrence were analyzed using Pearson's chi-square test. Statistical significance was defined as $P < 0.05$. Data were analyzed using the Statistical Package for the Social Science, Version 17.0.

Results

Clinical features

All eleven patients were female with a median age of 62.5 years who presented with breast masses; three patients also had a history of bloody discharge. Out of eleven patients, mastectomy and axillary lymph nodes excision were performed on nine, obtaining 113 lymph nodes. Only one axillary lymph node showed micrometastasis (1/9; 11.1%). Follow-up information was obtained in ten patients. There was no recurrence or breast carcinoma-related death during the follow-up period of a median of 50 months (range, 14–90 months). The clinicopathological information of the eleven cases was summarized in Table 1. There was no difference between the solid papillary carcinomas with or without minimal invasion in age of the patient or tumor size.

Pathologic features

Grossly, the tumors were well-circumscribed, red to gray (in the web version) with a soft texture, and of an average diameter of 2.6 cm. Eight cases showed no obvious invasion. The invasive components of the three cases with invasion had a similar morphology to the *in situ* components. The tumors were typically composed of solid papillary nodules of variable size in low power fields. There were delicate fibrous cores in solid papillary nodules, but the papillae were inconspicuous. The solid nodules in eight cases were regularly shaped with distinct borders. The stroma was mostly fibroadipose and sclerotic but without a desmoplastic reaction (Fig. 1A). In three cases, there were cysts in the solid papillary nodules containing blood or serous fluid, which was related to nipple bloody discharge. Bland-looking tumor cells were arranged around a fibrous core as solid papillary nodules forming perivascular pseudorosettes (Fig. 1B). The cellular proliferation in the tumor nodules was cohesive, usually polygonal or occasionally plasmacytoid, and lacked obvious papillae or cribriform architecture. In some cases, the cells in the lesion had a streaming and occasionally spindled appearance mimicking benign usual ductal hyperplasia. At high magnification, the tumor cells were homogenous with small nuclei and fine chromatin, and mitoses were less than 5/10HPF (Fig. 1C). All tumor cells showed low grade to moderate nuclear atypia and no case showed high grade nuclear atypia (Table 1). Extracellular mucin was present in eight cases (72.7%). Furthermore, three cases showed a geographic jigsaw pattern with more ragged and irregular margins in the background of abundant mucin, suggesting invasion. The tumor cells in the invasive component were morphologically similar to those components *in situ* with homogenous, small nuclei and fine chromatin (Fig. 1D). Papilloma and conventional-type low grade ductal carcinoma *in situ* were observed in adjacent tissues in four cases (36.4%).

Immunophenotypic features

Five of eleven (45.5%) solid papillary carcinomas of the breast expressed at least one of the myoepithelial markers including P63, CK5/6 or CD10 at the stroma/nodule interface (Table 1). However, the expression pattern was different from those of benign ductal hyperplastic lesions; only a sparse distribution of myoepithelial markers was detected in solid papillary breast carcinoma (Fig. 2A), while strong and intact myoepithelial cells were detected in the latter. Consistent with the results of immunostaining, no myoepithelial cells were observed in the peripheral nodules of solid papillary breast carcinoma in H&E-stained section. Expression of myoepithelial markers was occasionally observed around fibrovascular core within the solid papillary nodules. However, there was no expression of myoepithelial cell markers observed in three solid papillary breast carcinoma with or without infiltrative components (Fig. 2B). All eleven cases showed a luminal A immunophenotype with strong and diffuse positivity for ER (Fig. 2C) and PR, negativity for HER2, and low tumor proliferative index of Ki67