Short communication

Invasive breast papillary carcinoma with mucinous stroma

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Invasive breast papillary carcinoma is a rare type of breast cancer histologically characterized by infiltrative papillary growth without visible surrounding fibrous capsule. Here, we report the case of an invasive papillary carcinoma in which invasive papillary fronds were surrounded by abundant mucinous stroma, an occurrence that has not been described so far in this type of breast cancer.

Key words: breast cancer, invasive breast papillary carcinoma, mucinous breast carcinoma.

Invasive breast papillary carcinoma is a rare type of breast cancer composed of infiltrative fibrovascular cores covered by neoplastic epithelium, without the myoepithelial cells layer [1, 2]. In the whole group of breast papillary neoplasms, defined by the latest World Health Organization classification of breast tumors (the 5th edition), mucinous differentiation was observed only in some cases of solid papillary carcinoma [1]. Herein, we describe the case of an invasive papillary carcinoma with abundant mucinous stroma, a finding that has not yet been described in the literature.

A 69-year-old female presented with an abnormal ultrasound finding in the lower lateral quadrant of the right breast, revealing two heterogeneous hypoechogenic zones of 1.2 and 0.8 cm in close distance. A mammographic examination was without abnormalities. Core biopsy of the larger lesion was performed, with subsequent pathohistological diagnosis of grade 1 mucinous carcinoma which was hormonal receptor positive, *HER-2* negative with low Ki-67 proliferation rate (luminal A immunophenotype). The patient was presented to the breast cancer multidisciplinary team who suggested operative treatment. Mastectomy with sentinel lymph node biopsy followed, with a specimen containing two well-circumscribed, gray-white, firm nodules in close proximity, measuring 1.3 and 1 cm in the largest diameter. Histologically, the larger nodule was composed of invasive papillary fronds with central fibrovascular cores, covered by atypical carcinomatous cells (Figure 1A, B). Minor glandular component of tumour cells was present focally at the tumour periphery (Figure 1C). Papillary and glandular structures were surrounded by abundant, alcian positive mucinous stroma (Figure 1D). The smaller nodule was composed of invasive cribriform structures embedded in a fibrous stroma with focal mucinous change. Immunohistochemically, both tumors were estrogen receptor (ER) and progesterone receptor (PgR) positive, *HER-2* negative, with low Ki-67 proliferation rate (Figure 2A). The myoepithelial cells immunohistochemical markers CD10 and p63 were negative in both tumors, while the papillary tumour was immunohistochemically mammaglobin and GATA 3 positive, PAX 8, TTF-1 and CDX 2 negative (Figure 2B–D). Sentinel lymph nodes were without metastatic deposits. The pathohistological diagnosis was low-grade invasive papillary carcinoma with mucinous stroma accompanied by low-grade invasive cribriform carcinoma. The patient has received adjuvant hormonal therapy with the aromatase inhibitor with no recurrence in two years' follow-up.

Breast mucinous lesions include the spectrum of benign and malignant epithelial proliferations characterized by intracellular or extracellular mucin production, including the mucocele-like lesion, intraductal and invasive mucinous carcinoma, mucinous

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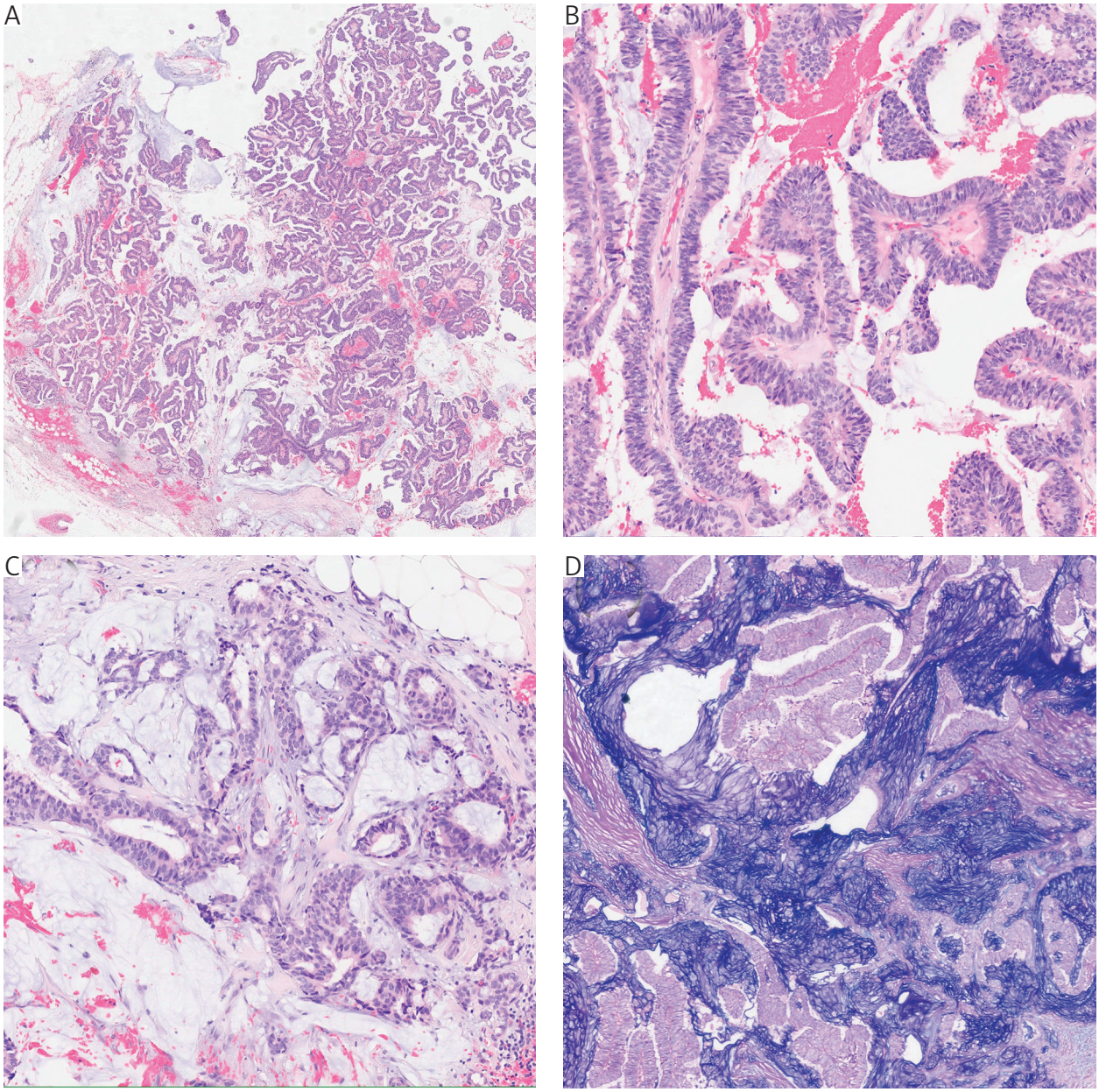

Figure 1. **A, B**) The tumor is composed of invasive papillary fronds with central fibrovascular cores, covered by atypical carcinomatous cells (HE, 40×, 100×). **C**) Minor glandular component at the tumor periphery (HE, 100×). **D**) Papillary and glandular structures are surrounded by abundant, alcian positive mucinous stroma (PAS-alcian, 100×)

micropapillary carcinoma, mucinous cystadenocarcinoma, solid papillary carcinoma, invasive lobular carcinoma with mucinous stroma, and other rare types of mucin producing carcinoma [3, 4]. Mucinous carcinoma accounts for 2% of all breast carcinomas and usually occurs in postmenopausal women, with a favorable outcome in its pure form [3–5]. Papillary invasive carcinoma is extremely rare with the incidence less than 1% among all invasive breast carcinomas [2]. Here, for the first time, we describe the case of carcinoma with invasive, true papillary fronds set in abundant mucinous stroma.

Prognostic or therapeutic implications of the mucinous stroma in invasive papillary carcinoma cannot be determined with certainty because such occurrence has not been previously reported. By analogy with other non-mucinous carcinomas containing mucinous stroma (i.e., mixed tumors), it appears that the stroma itself is not an independent favorable feature, since outcomes in such mixed tumors resemble invasive breast carcinoma of no special type rather than pure mucinous carcinoma [6]. We were unable to perform any molecular testing in our case, although it should be noted that mucinous and papillary breast carcinomas have similar molecular characteristics. Both tumors are usually luminal breast cancers with lower genomic instability and lower frequency of *PIK3CA* and *p53* mutation rates in comparison to other ER-positive

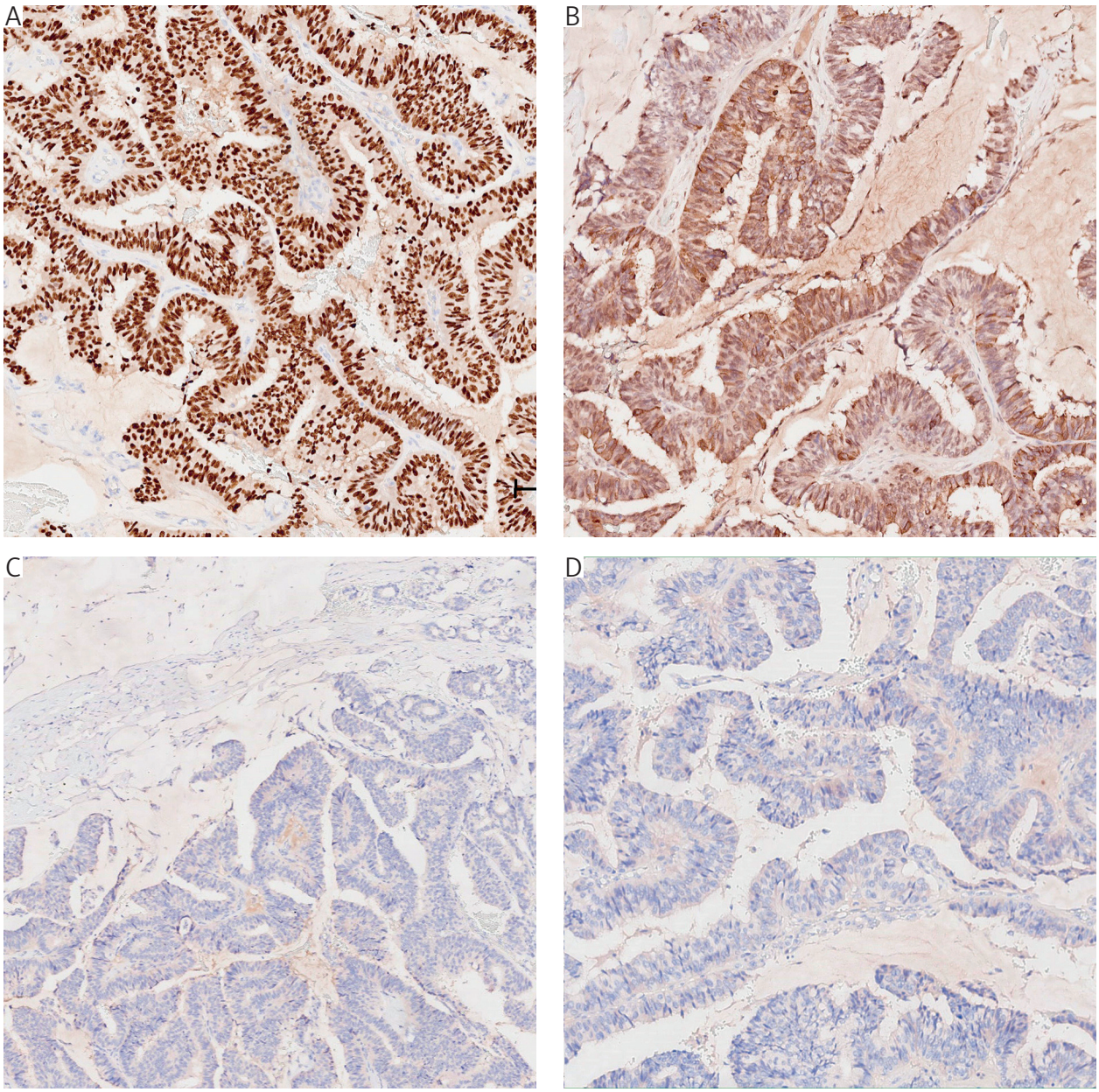

Figure 2. **A**) Estrogen receptor-positive tumor cells (IHK, 100×). **B**) Mammaglobin-positive tumor cells (IHK, 10×). **C**) PAX 8-negative tumor cells (IHK, 100×). **D**) TTF-1-negative tumor cells (IHK, 100×)

breast cancers, with the exception of the *MUC2* gene which is significantly overexpressed in mucinous breast carcinoma [2, 3, 7].

In differential diagnosis, four entities should be mentioned: mucinous carcinoma with micropapillary pattern, solid papillary carcinoma, mucinous cystadenocarcinoma and metastatic papillary carcinoma. In the presented case, the tumour was composed of true papillary stalks with clearly visible fibrovascular cores, while micropapillary mucinous carcinoma is composed of morule-like and floret-like epithelial clusters without cores, suspended in extracellular mucin [8]. Solid papillary carcinoma is without obvious papillary architecture histologically, with solid nodules of neoplastic cells and delicate fibrovascular cores in between them [3, 4]. Mucinous cystadenocarcinoma is composed of cystic spaces lined by columnar cells and filled with mucin, with intracystic complex papillary structures. Histologically, the presented case is without visible cystic spaces, with simple invasive papillary stalks set in mucinous stroma. Moreover, mucinous cystadenocarcinoma is typically hormone receptor negative, while the presented case was strongly ER and PgR positive [9]. Finally, using some of site-specific immunohistochemical markers, we excluded metastasis of some common papillary tumors like ovarian, pulmonary and thyroid carcinoma.

In conclusion, we have presented for the first time the case of an invasive breast papillary carcinoma with abundant mucinous stroma, adding another en-

tity with mucinous differentiation (along with solid papillary carcinoma) to the group of breast papillary neoplasms.

Disclosures

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2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

References

1. Mac Grogan G, Collins LC, Lerwill M, Rakha EA, Tan BY. Invasive papillary carcinoma. In: WHO Classification of Tumours Editorial Board. Breast tumours. 5th ed. IARC Press, Lyon 2019, 66-67.
2. Wang S, Zhang Q, Mao X. Invasive papillary carcinoma of the breast. Front Oncol 2024; 14: 1374091.
3. Joneja U, Palazzo J. The spectrum of mucinous lesions of the breast. Arch Pathol Lab Med 2023; 147: 19-29.
4. Ginter PS, Tang X, Shin SJ. A review of mucinous lesions of the breast. Breast J 2020; 26: 1168-1178.
5. Wen HY, Desmedt C, Reis-Filho JS, Schmitt F. Mucinous carcinoma. In: WHO Classification of Tumours Editorial Board. Breast tumours. 5th ed. IARC Press, Lyon 2019, 123-125.
6. Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, et al. Breast cancer, Version 3.2024, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2024; 22: 331-357.
7. Astashchanka A, Shroka TM, Jacobsen BM. Mucin 2 (MUC2) modulates the aggressiveness of breast cancer. Breast Cancer Res Treat 2019; 173: 289-299.
8. Barbashina V, Corben AD, Akram M, Vallejo C, Tan LK. Mucinous micropapillary carcinoma of the breast: an aggressive counterpart to conventional pure mucinous tumors. Hum Pathol 2013; 44: 1577-1585.
9. Lei T, Shi YQ, Chen TB. Mammary mucinous cystadenocarcinoma with long-term follow-up: molecular information and literature review. Diagn Pathol 2023; 18: 13.

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