A RARE ENTITY: NEUROENDOCRINE DIFFERENTIATED TRANSITIONAL CELL EPITHELIUM LINED SOLID PAPILLARY CARCINOMA OF BREAST TUMOR IN A YOUNG MALE PATIENT

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ABSTRACT

Breast carcinoma is a rare disease in males compared to females and papillary carcinoma of the breast accounts for <1% of all male breast carcinomas (1). Solid papillary carcinoma (SPC) is considered to be a variant of ductal carcinoma in situ (DCIS) and its neuroendocrine differentiation has been described in elderly women between 65-72 years of age, but in a few older male patients. Generally, affected males are older than affected females and also in more advanced stages than females (2,3). Addition of transitional cell epithelium to SPC is also a very rare entity, description of which has been limited to case reports or series with a few cases (4). We present a young male patient having SPC of the breast with neuroendocrine differentiation and transitional cell-like variant epithelium and also having early recurrence.

Case
A 28-year-old male presented with a painless mass in the left breast while under antituberculosis medications. The physical examination revealed a 4x4 cm nodular mass in the central part of the breast without palpable lymph nodes. An ultrasound (US) showed a highly vascularized 4.8x2.8 cm lobular mass with smooth margins, multiple macrocalcifications, and areas of cystic degeneration. Mammographic examination demonstrated a 5x3 cm lobular mass with smooth margins. A tru-cut biopsy of the lesion revealed a cryptiform pattern, low grade DCIS. The patient underwent mastectomy and sentinel lymph node biopsy and no axillary metastasis was reported in three sentinel lymph nodes. Pathologic examination of the specimen was interpreted as invasive papillary carcinoma with neuroendocrine differentiation and clean surgical margins. Microscopically, the tumor was characterized by cellular proliferation within multiple circumscribed nodules resembling clusters of dilated ducts. Neoplastic proliferation within the nodules typically exhibited low grade cytological features and a streaming pattern resembling florid hyperplasia, but there was significant mitotic activity and palisading.
of cells around a small, delicate hyalinized fibrovascular core. There were also papillary lesions with stratified transitional cells covering a thick fibrovascular core protruding into the dilated ducts. Myoepithelial cells were absent in these papillary lesions. Transitional-appearing epithelium is a layer of cells similar to the ‘umbrella’ cells of the bladder (Figure 1, 2). The presence of mucin has not been demonstrated either intra or extra cellularly. The invasive part of the tumor showed cells with eosinophilic granular cytoplasm, thin nuclear chromatin, and forming islands with a fibrovascular core. Immunohistochemical examination stained for estrogen, progesterone, and synoptophysin, but not smooth muscle actin, chromogranin A, or c-erb-B2. Synoptophysin strongly stained in the areas of neuroendocrine differentiated parts (Figure 3). Histopathologic and immunohistochemical examination revealed a solid papillary carcinoma with accompanying invasive neuroendocrine-like carcinoma and covering transitional cell epithelium. Patient scheduled to have chemo and radiotherapy but patient refused to take them. Regrettably, the patient developed new masses in the same breast after 1 year. The axillary examination revealed palpable, mobile lymph nodes. Ultrasonographic imaging revealed two 1x1 cm well-demarcated solid hypoechoic masses and lymph nodes in the left axillary region with an absence of hypoechoic center. FNAB of the breast lesions revealed high cellularity of the smears with groups and clusters of tumor cells, but no myoepithelium. Elaborated papillary structures were present with delicate fronds of papillae containing fine fibrovascular cores. The tumor cells had the appearance of plasmacytoid and tall columnar cells; in the background, single tumor cells with large prominent nucleoli and fine chromatin was observed (1). Ultrasonography-guided axillary lymph node biopsy revealed the same findings with the primary tumor. The patient underwent a left mastectomy and axillary lymph node dissection. The pathology findings indicated multifocal invasive solid papillary carcinoma with transitional cell epithelium and neuroendocrine differentiation (2,3). The tumor was characterized as nuclear grade 3 without lymphovascular and perineural invasion and any in situ component. The tumor had also estrogen and progesterone receptors; however, it did not have any c-erb-B2 receptors. Axillary dissection revealed two metastatic lymph nodes out of thirteen. The patient was scheduled for hormono-chemo-radiotherapy.

**Discussion**

SPC is a rare disease, first described by Maluf and Koerner and few cases of papillary carcinoma of the male breast have been reported in the literature, account for <1% of all male breast carcinomas (1,5,6). The largest series of SPC reported to date involved 1 male patient from 58 patients (7). Thus, SPC is predominantly present in females. In addition, SPC of the breast is generally a tumor of elderly patients, and rarely reported before 50 years of age. Our patient was 28 years of age and is the youngest patient
that has been reported in the literature. Otsuki et al. reported 20 patients with SPC who were between 31-80 years of age and among them, only three patients were under 50 years of age (3). Tsang and Chan and Nassar et al. reported one of 34 patients and three of 58 patients under 50 years of age, respectively (7,8). According to these findings, it can be concluded that SPC of the breast is a disease of elderly patients, but rarely occurs before 30 years of age. Maluf and Koerner described SPC as a rare type of DCIS. Papillary carcinoma of the breast exhibits many different morphologic appearances (5). We report a SPC with transitional cell epithelium closely resembling transitional cells of the urinary tract. Mooney and Tavassoli reported only five women with a solid variant of papillary carcinoma accompanying transitional cell epithelium, however, the stimulus for the development of this unusual transitional-like variant is not known (4). SPC is known to have a better prognosis than other breast carcinomas. Nassar et al. found lymph node metastasis in 20% of patients in his series (7). Biological marker analyses using immunohistochemistry, the tumor node metastasis (TNM) classification, and the Nottingham histological grade suggest an excellent prognosis for SPC patients. Whether tumors with neuroendocrine differentiation confer a better patient prognosis than tumors without neuroendocrine differentiation remains controversial (9). Collins et al. defined SPC as having an indolent clinical course, especially when there is no associated frankly invasive component; however, Nassar et al. reported local recurrence in five of 58 patients, all of whom had an invasive component (7,10). In our patient, the primary surgical margin was clear and no axillary metastasis was found in three sentinel lymph nodes, but with invasive component. After patient had first surgical treatment, we offered to patient to have chemo and radiation therapy, but patient rejected to any other medical treatment and radiation. Tumor showed an aggressive progress in our patient with multiple local recurrences and lymph node metastasis developed in one year period.

In conclusion, SPC of the breast mostly affects elderly women; however, it can also be observed in elderly males. Based on the case described herein, SPC can occur in a young male, even in the 20s. Although, it is regarded as a DCIS and has a good prognosis, our case had a poor prognosis with a local recurrence and axillary metastasis in one year. The similarity of the metastasis and local recurrence to the primary tumor morphology suggests that it is an invasive carcinoma rather than an in situ carcinoma. In addition, transitional cell epithilum may also accompany to SPC.

References