

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

Ali Aktekin<sup>1</sup>, Pembegül Güneş<sup>2</sup>, Tolga Muftuoğlu<sup>1</sup>, Pelin Demirtürk<sup>2</sup>, Fügen Aker<sup>2</sup>, Abdullah Sağlam<sup>1</sup>

<sup>1</sup>Haydarpaşa Numune Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, İstanbul, Türkiye

<sup>2</sup>Haydapaşa Numune Eğitim ve Araştırma Hastanesi, Patoloji Kliniği, İstanbul, Türkiye

GENÇ BİR ERKEK HASTADA NÖROENDOKRİN DİFFERANSİYASYON GÖSTEREN TRANSİZYONEL HÜCRE İLE DÖŞELİ MEMENİN SOLİD PAPİLLER KARSİNOMU: NADİR BİR OLGU

## ÖZET

Erkeklerde meme kanseri kadın hastalara göre daha nadir görülmele birlikte memenin papiller karsinomu tüm erkek meme kanserlerinin %1' inden azını oluşturur. Transizyonel hücre ile döşenmiş ve nöroendokrin differansiyasyon gösteren memenin solid papiller karsinomu çok nadir bir durumdur. Biz anti-tüberküloz tedavisi alan ve sol memesinde memenin solid papiller karsinomu nedeni ile ağrısız kitlesi olan 28 yaşında genç bir erkek hastayı sunduk. Tümör transizyonel hücre ve nöroendokrin differansiyasyon ile karakterize idi. Tümör cerrahi olarak eksize edildi. Memenin solid papiller karsinomu diğer meme kanserlerine göre daha iyi prognoza sahip olduğu bilinmesine rağmen, bizim hastamızda tümör hem lokal hem de aksillada bir yıl sonra nüks etti. Sonuç olarak, memenin solid papiller karsinomu transizyonel hücre ile döşenip nöroendokrin differansiyasyon gösterebilir. Bu hastalarda prognoz daha kötü seyredebilir.

**Anahtar sözcükler:** solid papiller karsinom, nöroendokrin differansiyasyon, transizyonel epitel, meme kanseri, erkek

## ABSTRACT

Breast carcinoma is a rare disease in males compared to females and papillary carcinoma of the breast is seen less than 1% of all male breast carcinomas. Solid papillary carcinoma of the breast, with transitional cell epithelium and neuroendocrine differentiation, is a rare entity. We report a 28-year-old male patient with a painless mass in the left breast due to solid papillary carcinoma while receiving anti-tuberculosis therapy. Tumor is characterized by neuroendocrine differentiation with accompanying transitional cell variant epithelium. The tumor was successfully excised. Although solid papillary carcinoma is thought to have a better prognosis than other breast carcinomas, in our patient, local and axillary recurrences were seen in one year, in contrast to reports in the literature. In conclusion, the solid papillary carcinoma with transitional cell epithelium and neuroendocrine differentiation of breast in a male is a very rare disease. Its prognosis could be worse than reported in the literature.

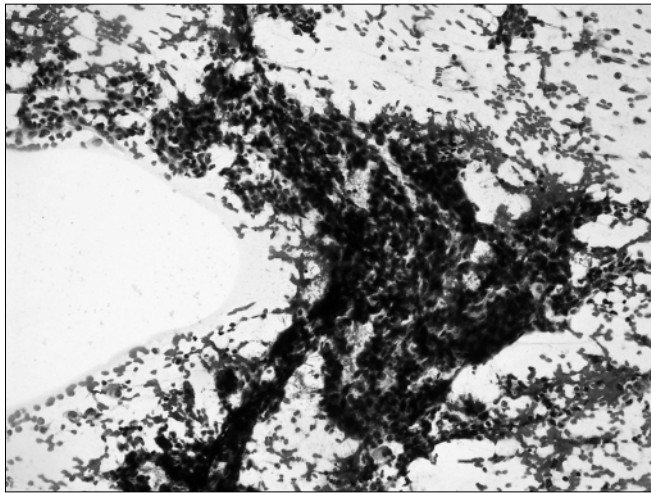
**Keywords:** solid papillary carcinoma, neuroendocrine differentiation, transitional epithelium, breast neoplasm, male

**B**reast carcinoma is a rare disease in males compared to females and also 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.

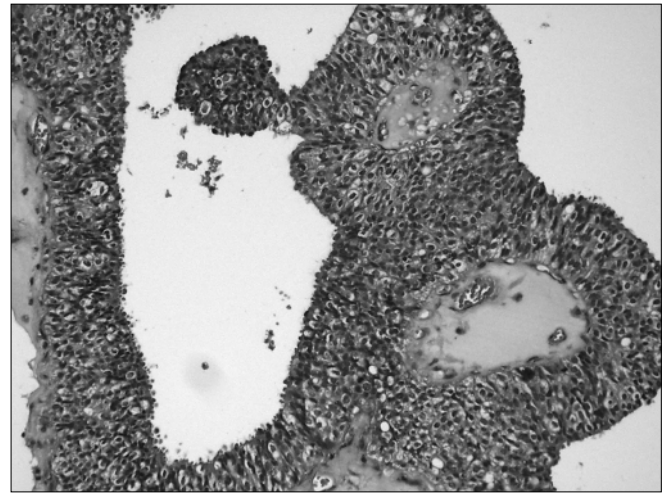
## Case

A 28-year-old male presented with a painless mass in the left breast while under antituberculosis medications. The physical

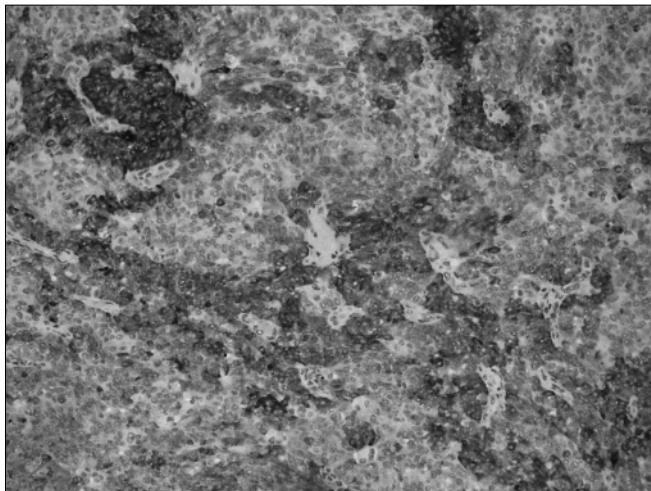
examination revealed a 4x4 cm nodular mass in the central part of the breast without palpable lymph nodes. An ultrasound (US) showed a highly vascularized 4.8x2.8 cm lobular mass with smooth margins, multiple macrocalcifications, and areas of cystic degeneration. Mammographic examination demonstrated 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



**Figure 1.** The tumor cells have appearance of plasmacytoid and tall columnar cells; in the background, single tumor cells with large prominent nucleoli and fine chromatin are observed. Tumor cells develop in three dimensional invasive groups (PAP, x100).



**Figure 2.** Papillary transitional cells are covering as an atypical umbrella cells layer overlying the solid epithelial proliferation is evident (H&E, x400).



**Figure 3.** Wide-spread intense immunohistochemical staining via synaptophysin are seen in tumor cells exhibiting neuroendocrine differentiation (synaptophysin staining, x400).

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 synaptophysin, but not smooth muscle actin, chromogranin A, or c-erb-B2. Synaptophysin 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 epithelium may also accompany to SPC.

#### References

1. Donegan WL, Redlich PN, Lang PJ, Gall MT. Carcinoma of the breast in males: a multiinstitutional survey. *Cancer* 1998; 83:498-509. ( PMID: 9690543)
2. Yamada M, Otsuki Y, Shimizu S, Tanioka F, Ogawa H, Kobayashi H. Cytological study of 20 cases of solid-papillary carcinoma of the breast. *Diagn Cytopathol* 2007; 35:417-422. ( PMID: 17580353)
3. Otsuki Y, Yamada M, Shimizu S, Suwa K, Yoshida M, Tanioka F, Ogawa H, Nasuno H, Serizawa A, Kobayashi H. Solid-papillary carcinoma of the breast: clinicopathological study of 20 cases. *Pathol Int* 2007; 57:421-429. ( PMID: 17587241)
4. Mooney EE, Tavassoli FA. Papillary transitional cell carcinoma of the breast: a report of five cases with distinction from eccrine acrospiroma. *Mod Pathol* 1999; 12:287-294. ( PMID: 10102614)
5. Maluf HM, Koerner FC. Solid papillary carcinoma of the breast. A form of intraductal carcinoma with endocrine differentiation frequently associated with mucinous carcinoma. *Am J Surg Pathol* 1995; 19:1237-1244. ( PMID: 7573685)
6. Kumar PV, Talei AR, Malekhusseini SA, Monabati A, Vasei M. Papillary carcinoma of the breast. Cytologic study of nine cases. *Acta Cytol* 1999; 43:767-770. ( PMID: 10518128)
7. Nassar H, Qureshi H, Volkanadsay N, Visscher D. Clinicopathologic analysis of solid papillary carcinoma of the breast and associated invasive carcinomas. *Am J Surg Pathol* 2006; 30:501-507. ( PMID: 16625097)
8. Tsang WY, Chan JK. Endocrine ductal carcinoma in situ (E-DCIS) of the breast: a form of low-grade DCIS with distinctive clinicopathologic and biologic characteristics. *Am J Surg Pathol* 1996; 20:921-943. ( PMID: 8712293)
9. Coady AT, Shousha S, Dawson PM, Moss M, James KR, Bull TB. Mucinous carcinoma of the breast: further characterization of its three subtypes. *Histopathology* 1989; 15:617-626. ( PMID: 2558066)
10. Collins LC, Schnitt SJ. Papillary lesions of the breast: selected diagnostic and management issues. *Histopathology* 2008; 52:20-29. ( PMID: 18171414)

#### Correspondence

Ali Aktekin  
Phone : +90 (216) 345 46 80  
E-mail : ali\_aktekin@yahoo.com.tr