Solid Papillary Carcinoma of the Breast

A Pathologically and Clinically Distinct Breast Tumor

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Solid papillary carcinomas are tumors morphologically characterized by round, well-defined nodules composed of low-grade ductal cells separated by fibrovascular cores. These tumors are rare and affect predominantly older women. Although they are considered in situ carcinomas, debate and uncertainty still exist regarding their true nature, because immunohistochemistry for myoepithelial cells has shown absence of myoepithelial cell layer along the epithelial-stromal interface of the tumor in many cases. Clinically, these tumors present as a palpable, centrally located mass or as bloody nipple discharge. Pathologically, solid papillary carcinomas exhibit low-grade features, and often the tumors display neuroendocrine and mucinous differentiation. In the majority of cases an associated invasive carcinoma is present, with colloid and neuroendocrine carcinomas being the most common. The pathologic differential diagnosis is broad and ranges from benign to malignant lesions. The treatment for solid papillary carcinomas is surgical excision. When invasive carcinoma is not present, the prognosis is excellent.

HISTOGENESIS

Solid papillary carcinomas are lesions of the ductal epithelium. Because SPCs are commonly associated with invasive mucinous carcinoma, they were originally considered precursors of colloid carcinomas. However, their association with other variants of ductal carcinomas and their frequent neuroendocrine differentiation suggest that they are probably heterogeneous tumors.

CLINICAL FEATURES

Solid papillary carcinoma is an uncommon lesion that affects primarily elderly women, with a mean age of 72 years in one series. However, occasionally this tumor can affect patients younger than 50 years. Nearly 95% of cases are unilateral, and the majority of tumors arise in the central area of the breast. There are no specific clinical features of these tumors at presentation. Most patients present with a palpable mass or a bloody nipple discharge, or with a mammographic density on a breast screening mammogram. The radiologic features of SPC have not been defined. Ultrasound with color Doppler is the most sensitive methodology for the evaluation of papillary breast lesions. Ultrasound may suggest the presence of a frondlike mass within a dilated duct, a complex intracystic lesion, or a homogeneous solid lesion. Although some radiologic features, such as posterior acoustic enhancement and associated microcalcifications, are more frequently associated with malignancy, the radiologic appearance cannot accurately predict the behavior of papillary lesions, and histologic evaluation is necessary.

PATHOLOGIC FINDINGS

Tumor size varies and ranges from less than 1 cm to 15 cm in the literature. Macroscopically, the tumors have a nodular configuration and are usually well-circumscribed, soft masses. When mucinous differentiation is present, a gelatinous appearance may be grossly appreciated. Although tumors without associated invasive carcinoma can reach a large size, in their series Nassar et al found an association between large tumor size and the presence of invasive carcinoma (mean 1.7 versus 3.2 cm).
Microscopically, these tumors appear as multiple nodules, each representing a duct filled by a neoplastic proliferation. Cells are ovoid or spindled, occasionally with a streaming appearance, similar to florid ductal hyperplasia. The cells grow in a solid pattern with intermingled fibrovascular network and no apparent papillary structures. Nuclear palisading around the stromal cores and pseudorosette formation around capillary vessels are also common features (Figure 1, A through D). Less commonly observed features are organoid pattern, microcystic spaces, foamy macrophages, and microlacinations.

Solid papillary carcinomas are composed of monotonous cells with a low to intermediate nuclear grade in the majority of cases. Cells frequently have plasmacytoid or endocrine appearance with eosinophilic, granular cytoplasm and eccentric nuclei. Sometimes spindle cells with nuclear grooves predominate. Rarely, signet ring morphology is seen. Extracellular mucin production can also be present. Glycogen-rich clear cell tumors and mucoid dermoid variants of SPC are uncommon. Mitotic figures are common; however, atypical mitoses are not present.

Cytologically, fine-needle aspiration biopsies tend to be very cellular, consisting of small to large discohesive fragments of cells. Nuclei are monotonous, small, and bland with fine chromatin and inconspicuous nucleoli. Cytologic atypia is typically mild to moderate; however, more severe atypia may be seen. Plasmacytoid cells, intracellular lumina, and low nuclear to cytoplasmic ratio can be present. Background of mucin, inflammation, capillary vessels, single or naked abnormal tumor nuclei, and rarely necrosis are present.

About half of the cases are associated with invasive carcinoma. The size of invasion varies, and invasion can be multifocal. The invasive component may have a pure or mixed colloid, neuroendocrine-like, invasive ductal, or rarely lobular or tubular pattern. In general, the invasive carcinoma component is well to moderately differentiated and is morphologically similar to the adjacent SPC.

**IMMUNOHISTOCHEMISTRY AND LABORATORY FINDINGS**

To ascertain the presence of invasion in papillary tumors, the presence or absence of myoepithelial cells at the periphery of the tumor has been routinely used by...
Nevertheless, many authors have shown that SPCs lack myoepithelial cells at their periphery in a significant number of cases. Therefore, the concept that SPCs are in situ tumors has been challenged by some, and it is still a matter of controversy. Consequently, it has been recommended by some authors that in cases with focal or complete absence of myoepithelial cells around the SPC, the tumor should be rendered as indeterminate for invasion. Frank invasion is diagnosed in papillary carcinomas when malignant cells are clearly present beyond the fibrous capsule of the lesion. Regardless of this uncertainty, SPCs are still considered noninvasive, because the absence of myoepithelial cells by immunohistochemistry around tumors that retain a smooth peripheral contour is not definitive evidence of invasion.

Solid papillary carcinomas are positive for estrogen and progesterone receptors and negative for HER2/neu. Proliferation index is low. Additionally, tumor cells are positive for neuroendocrine markers such as synaptophysin and chromogranin and are negative for cytokeratin 5/6 (Figure 2, A through D). Similarly, when invasive carcinoma is present, it is normally positive for estrogen and progesterone receptors and negative for Her-2/neu.

Mucicarmine stain is positive in those cases with mucinous differentiation.

**DIFFERENTIAL DIAGNOSIS**

The differential diagnosis ranges from benign to malignant lesions including florid ductal hyperplasia, lobular neoplasia, intracystic papillary carcinoma (IPC), and ordinary low–nuclear-grade ductal carcinoma in situ (DCIS). On low magnification, the lesion may resemble florid ductal hyperplasia with spindle or ovoid cell morphology. However, florid ductal hyperplasia does not present with fibrovascular cores, palisading of cells, or mucin production. In addition, the presence of mitotic activity is not a characteristic of florid ductal hyperplasia. Lobular neoplasia or lobular carcinoma in situ can involve papillary lesions. Additionally, the plasmacytoid appearance of SPC cells is also a feature of lobular proliferations. However, lobular neoplasia is characterized by discohesion and lack of papillary fronds. Immunohistochemistry using e-cadherin, which is positive in SPC and negative in lobular proliferations, is very helpful in difficult cases. Intracystic papillary carcinoma may come into the differential because it also presents in

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**Figure 2.** A, Immunostain for calponin, a myoepithelial cell marker, is negative along the epithelial-stromal interface of the tumor. Internal control staining surrounding small blood vessel is seen. B, Strong and diffuse staining with estrogen receptor. C, Tumor cells are focally positive for synaptophysin. D, Immunohistochemistry for basal cell-type keratin cytokeratin 5/6 is negative as seen in papillary carcinomas (hematoxylin-eosin, original magnification ×100 [A and B]; original magnifications ×630 [C] and ×100 [D]).
elderly patients, is well circumscribed, and may lack a layer of myoepithelial cells at the periphery.\(^7\) However, IPC is characterized by the presence of papillary fronds lined by cuboidal cells that often reveal higher–nuclear-grade cytology.\(^5,6\) Low–nuclear-grade DCIS might be considered in the differential diagnosis of small-size SPC, especially when limited amounts of tissue are analyzed, that is, in core needle biopsy. However, despite the cytologic similarities, DCIS does not have the monotonous morphology of SPC, or the cells with plasmacytoid or spindle cell appearance. Likewise, the presence of mucin, branching fibrovascular stroma, and ducts encompassed by fibrosis are not features of DCIS.\(^2,6\)

**PROGNOSIS AND TREATMENT**

In the absence of invasive carcinoma, SPCs have a favorable outcome. In cases associated with invasive carcinoma, the prognosis will depend upon the invasive component of the tumor.\(^1\) In these cases, distant metastasis can occur without axillary lymph node involvement.\(^16\) Maluf and Koerner\(^1\) described a case in which lung metastasis occurred without evidence of axillary lymph node involvement. Although they described a metastatic tumor morphologically indistinguishable from SPC, in this case an invasive mixed carcinoma was present. Because it has been described that invasive tumors associated with SPC are morphologically similar to the SPC,\(^1\) it is difficult to ascertain if the metastasis originated from the SPC or its invasive component. In addition, metastatic invasive carcinomas that keep a circumscribed DCIS morphology in the metastatic site can occur.\(^18\) A type of SPC with extravasated mucin has also been described. These cases are characterized by a well-circumscribed SPC with peripheral clefting and mucin deposition (without cellular component) within the cleft.\(^6,18\) These cases are difficult to differentiate from SPC with associated invasive colloid carcinoma.\(^6\) Nassar et al.\(^6\) in their series, described one such case in which distant metastasis developed 10 years after diagnosis. This finding indicates that these “gray-zone” lesions indeed have metastatic potential.

Complete excision of the lesion or total/partial mastectomy is the treatment of choice for SPC. Although sufficient data is not available to evaluate the role of sentinel lymph node biopsy in SPC,\(^18\) its use seems advisable because these tumors are frequently associated with an invasive component and therefore axillary lymph node metastasis could be present.\(^6,10\) The role of postoperative radiation and endocrine therapy in IPC and SPC remains controversial.\(^19,20\) In their series of 40 patients with pure IPC, IPC associated with DCIS, and IPC associated with invasion, Solorzano et al.\(^19\) reported that the use of radiation did not influence recurrence or survival. In a similar study, Fayanju et al.\(^19\) found that patients with IPC with associated DCIS or microinvasion more frequently undergo adjuvant radiation and endocrine therapy than patients with pure IPC. They also suggest that these treatment modalities may play a role in treatment of young patients with pure IPC.

**CONCLUSIONS**

Solid papillary carcinoma is an unusual, clinically and histologically distinct breast tumor that predominantly occurs in elderly patients. These tumors are characterized by well-circumscribed ducts, expanded by neoplastic proliferations and separated by branching fibrovascular stroma. Often, the peripheral layer of myoepithelial cells cannot be demonstrated by immunohistochemistry or electron microscopy, raising the concern of a pushing border invasive carcinoma.\(^2,12,23\) Treatment involves surgical excision. Solid papillary carcinomas have an indolent clinical course. However, they are often associated with an invasive component, in which case the prognosis will be negatively affected. Pure SPCs, without extravasated mucin or a microinvasive component, do not produce metastasis.\(^2,6\)

**References**