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Case Report

Solid Papillary Carcinoma of the Breast. Case Report of Uncommon Tumor and Review of the Literatures

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Abstract

Papillary carcinomas constitute 1-2% of breast cancers and most commonly presents in postmenopausal women. Solid papillary carcinoma represents an uncommon and rare subtype of papillary carcinomas due to their exhibition of intracellular or extracellular mucin deposition, solid papillary growth pattern, as well as neuroendocrine differentiation. Solid papillary carcinomas are mostly unilateral centrally located and is typically non-invasive unless they invade adjacent structures or have distant metastases. SPCs are diagnostically difficult to identify due to their non-specific and non-sensitive presentation on imaging as well as the rarity of the tumor. Therefore, albeit rare, SPCs should always be included within the differential diagnoses of patients with papillary lesions of the breast. By being able to identify SPCs at its early stages and performing complete excision or partial mastectomy of the mass, a more favorable prognosis is usually yielded.

Keywords: Solid papillary; Invasive; Mucinous; Neuroendocrine

ABBREVIATION

SPC: Solid papillary carcinoma, **DCIS:** Ductal carcinoma in situ, **IHC**: Immunohistochemistry

INTRODUCTION

Papillary carcinomas constitute 1-2% of breast cancers in women [1]. When the epithelium has features which are diagnostic of intraductal carcinomas, the lesion is classified as a papillary carcinoma in situ. If a cystic component is present, the tumour is defined as an intracystic papillary carcinoma. Otherwise, with presence of mucinous component and neuroendocrine differentiation, the lesion is defined as a solid papillary carcinoma (SPC) [2,5].

The solid papillary subtype is considered a rare malignant breast tumor, with an incidence ranging from 1.1% to 1.7% of all malignant breast tumors [3]. Classically, SPC is a centrally located mass on the unilateral breast [5] that mainly affects postmenopausal women; indeed, it is relatively rare for a woman to be affected before the age of 50, and the average age of diagnosis with SPC is approximately 70 years old [4].

SPC originates from expanded ducts and comprises morphologically well-circumscribed solid nodules separated by fibrovascular cores [4,7] and is regarded as a special type of ductal carcinoma in situ (DCIS) with several characteristic histopathological features, including low-grade cellular atypia, intracellular or extracellular mucin deposition, and solid papillary growth pattern, as well as neuroendocrine differentiation [3]. SPC is further divided into SPC in situ and SPC invasive based on the presence or absence of invasive component [1]. The invasion can be multifocal and may have a pattern that is neuroendocrine-like, pure or mixed colloid, tubular, or invasive ductal but is rarely lobular [7].

SPC is typically non-invasive unless they invade adjacent structures or have distant metastases [5]. This is especially concerning considering approximately 50% of cases are associated with invasive carcinoma [7]. In previous studies, invasive components have been reported in 27.2–75% of cases [4]. Unfortunately, SPC diagnosis is made more difficult as neither mammography nor ultrasound are sensitive or specific to determine malignancy [6]. The reporting of this case is to raise awareness of an uncommon and rare tumor, SPC, and its potential aggressiveness if it were to invade. A review of literature is conducted that focuses on certain differential diagnoses, characterizing histomorphology and molecular features, as well as specific treatment options for SPC.

CLINICAL PRESENTATION

A 66-year-old woman presented with right breast mass she discovered while performing self-breast exam. Her medical history is significant for controlled type-II diabetes, and her mother died from breast carcinoma at the age of 64. Physical exam showed central right breast mass measuring 7 x 5 cm. Although large in size, the clinical examination was suggestive of benign breast lesion. Mammography showed lobulated, circumscribed mass, without calcifications and ultrasonography demonstrated a hypoechoic heterogeneous solid mass. Imaging studies were not conclusive of either benign or malignant lesion and core needle biopsy of the mass was performed.

Microscopic examination revealed a solid, nested architecture punctuated by fibrovascular cores. The tumor showed various architectural features including Jigsaw-like

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pattern, irregular anastomosing islands, confluent growth, and angulated irregular contours in background of desmoplastic stroma (**Figure 1A**). The tumor was composed of homogenous population of ductal cells with intermediate nuclear grades arranged in mixed pattern of mucinous background and solid neuroendocrine-like features. Prominent nuclear palisading and pseudorosettes formation around capillary vessels was observed (**Figure 1B-1C**). Some invasive areas showed nests with more rounded shapes but their geographic confluence and expansile mass forming growth was indicative of the invasive nature of the tumor. Immunohistochemistry (IHC) was utilized for evaluation. The tumor cells were Positive for Cytokeratin AE1/AE3, chromogranin (**Figure 1D**), estrogen and progesterone receptors. The tumor cells were negative for high molecular weight cytokeratins CK5/6, and HER2/neu.2. Tumor cells were negative for P63 (**Figure 1E**) indicating absence of myoepithelial cells and confirming the invasive nature of the tumor. The histomorphology and IHC profile were diagnostic of invasive solid papillary carcinoma of the breast.

Patient tested positive for genetic mutations of BRCA1. With positive family history of breast carcinoma and positive BRCA-1, the patient elected to perform a total mastectomy. Sentinel lymph node was negative, and no axillary dissection was performed. Gross examination of the breast showed a solitary mass with nodular and soft masses with hemorrhagic and cystic components. Histomorphology confirmed the diagnosis of the core biopsy. Post-operative hormonal therapy was initiated, and patient was followed up for three years with no evidence of recurrence or metastasis after which she was lost to follow up.

DISCUSSION

Papillary breast lesions comprise a spectrum of histopathologic diagnoses ranging from benign papillomas to papillary carcinomas [19]. Solid papillary carcinoma is considered a rare papillary malignant breast tumor, with an incidence ranging from 1.1% to 1.7% of all malignant breast tumors. Histopathological examinations show that SPC originates from expanded ducts and comprises morphologically well-circumscribed solid nodules separated by fibrovascular cores [3,4,7]. In addition, nuclear palisading and pseudorosettes formation around capillary vessels are standard features [4]. Previously, studies have reported that the SPC tumor size ranges from less than 10 to 150 mm [4,12,13]. Patients can present with a benign palpable mass with or without bloody nipple discharge. They can also be asymptomatic and an abnormal mammographic density on the breast screening mammogram [8]. Macroscopically, the tumors can be solitary or multiple and are well-circumscribed, nodular, and soft masses with hemorrhagic and cystic components [4,14]. Microscopically, SPC appears as proliferative nodules, each representing a duct filled with neoplastic proliferative components, which can be either ovoid or spindle-shaped and are rarely stream-like in appearance, similar to ductal hyperplasia [4,15].

SPC exhibits a propensity to be a centrally located mass on the unilateral breast [5] that mainly affects postmenopausal women. At the time of diagnosis, approximately 90% of the cases have localized involvement, and 8% have the regional disease, with local spread to axillary lymph nodes, and less than 0.4% presents with distant metastases [8].

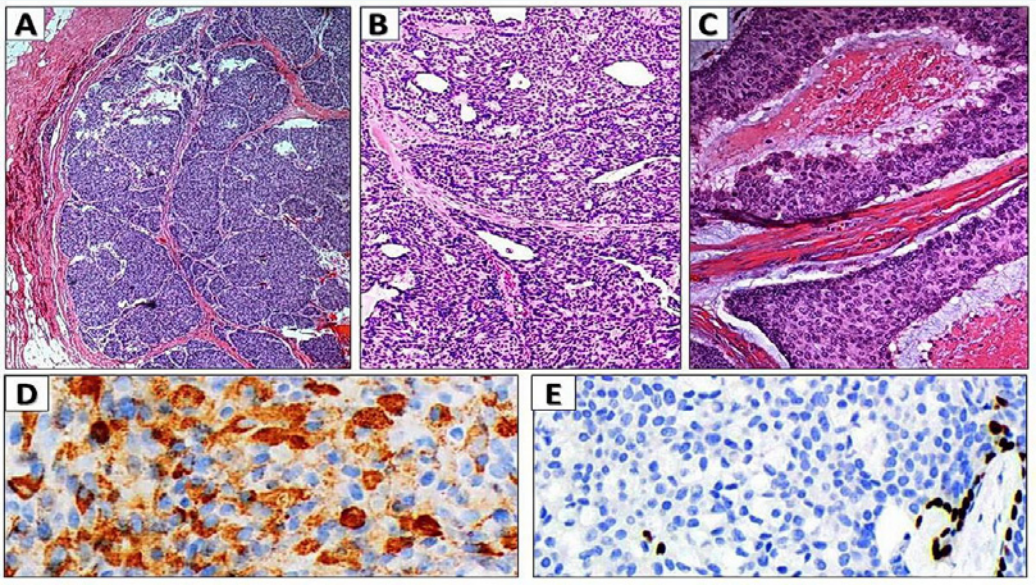

Figure 1 Pathological examination of the tumor mass, solid papillary carcinoma of the breast.
1A: Tumor showing solid nested architecture punctuated by fibrovascular cores. (H&E stain x20)
1B: The tumor showing various architectural features including Jigsaw-like pattern, irregular anastomosing islands, confluent growth, and angulated irregular contours in background of desmoplastic stroma (H&E stain x40)
1C: Mixed pattern of mucinous background and solid neuroendocrine-like features. (H&E stain x60)
1D: Tumor cells positive for chromogranin
1E: Tumor cells negative for P63

The reported risk factors include age, family history and genetic predisposition, diet, and obesity. It is known that the incidence gradually increases with age and mean age at the time of diagnosis is 63 to 67. In regard to family history, women with one or more first-degree relatives with breast cancer have increased the risk for SPC [8,9]. Genetic predisposition also plays an important role, and approximately 5-10% of SPC are associated with genetic mutations such as BRCA1, BRCA2, p53, and PTEN [2,8,9]. Dietary risk factors such as a diet low in phytoestrogens and high alcohol intake can predispose to SPC. Dietary fibers have been shown to be protective. Lastly, excessive estrogen synthesis in obesity is a major contributing factor [8]. It is recommended that SPC should be included as a differential diagnosis in palpable breast lumps as it often mimics a benign lesion clinically [10].

Several types of low-grade ductal carcinomas should be considered as differential diagnoses for SPC. In particular, papillary carcinoma is similar to SPC in many respects. However, this tumor differs from SPC by the presence of delicate papillae, a branching pattern, a cuboidal to columnar appearance of the tumor cells, and the lack of a solid growth pattern [17]. SPC can also resemble lesions like atypical ductal epithelial hyperplasia, lobular hyperplasia and DCIS [10,11]. However, careful histopathological evaluation superadded by immunohistochemistry is an effective tool to arrive at the correct pathological diagnosis to avoid untoward complications related to under diagnosis and/over diagnosis [10]. Solid papillary carcinomas are positive for estrogen and progesterone receptors and negative for HER2/*neu*.2 Proliferation index is low. Additionally, tumor cells are positive for neuroendocrine markers such as synaptophysin and chromogranin and are negative for cytokeratin 5/6 [4,16,17]. SPC may also express one of the myoepithelial markers, including P63, α-smooth muscle actin, and CD10 [4].

There are currently no evidence-based guidelines for the treatment of SPC. Whether it is in situ or invasive or intermediate grade, the management remains controversial. Hence its management is still debated [8]. However, recent studies have shown that accurate diagnosis with adequate local excision with breast-conserving surgery is the optimal treatment [5,8,16]. Therefore, currently, the ideal management of SPC varies from breast-conserving surgery to mastectomy [4].

The most common mammographic finding of SPC is usually a round, oval or lobulated density with microcalcifications [8]. The margin of the mass is usually well circumscribed, but can also be obscured or indistinct at places indicating inflammation or invasion [8,9,15]. Additionally, MRI with contrast enhancement can give detailed morphologic features. The lesions can appear as round or oval mass with well-defined margins. Other morphological features such as septations, enhancement of cyst wall, and mural nodules can also be seen [8]. However, neither mammography nor ultrasound is sensitive or specific to determine malignancy [6]. Ultrasound with color Doppler is the most sensitive methodology for the evaluation of solid papillary breast lesions. Ultrasound may reveal a hypoechoic and solid frond-like mass within a dilated duct, a complex cystic lesion, or a homogeneous solid lesion. It may also often show associated posterior acoustic enhancement and microcalcifications [8,12,14].

The literature lacks reference to specific molecular alteration in Solid papillary breast carcinoma. However, Paul Weisman and group reported particular changes in Solid-papillary carcinoma with reverse polarity (SPCRP), which is a rare subtype of breast cancer characterized by the distinct histological finding of solid-papillary architecture with a perivascular pseudorosettes-like pattern of so-called “reverse” nuclear polarity. This type of cancer is predominantly triple-negative biomarker profile and recurrent hotspot mutations in IDH2R172. The group reported for the first time (to the best of their knowledge), a pathogenic IDH1R132C mutation diagnosed in a 73-year-old female, and reported expanding the mutational spectrum for this tumor type and confirming the expected IDH1/IDH2 dichotomy seen across numerous other tumor types [18]

In the absence of invasive carcinoma, SPC in situ has an excellent overall prognosis. In patients with SPC associated with invasive carcinoma, the prognosis will depend upon the invasive component of the tumor [3,8]. In invasive SPC, the prognosis may depend on the biological tumor features of the invasive component. Distant metastasis can be found without infiltration in the axillary lymph nodes [4].

Solid papillary carcinoma should always be included in the differential diagnoses when presented with a palpable breast lesion. Though having a favorable prognosis when non-invasive, it is important to keep in mind that approximately 50% of cases are associated with invasive carcinoma [7,8]. With the added unfortunate difficulty of screening radiographically, it is crucial to include histopathological evaluation along with immunohistochemistry in order to achieve a correct diagnosis and treatment for optimal patient’s outcome.

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