Case 1

A 45 year old pre-menopausal woman applied to our clinic for breast cancer screening. Her sister had just been operated for a breast carcinoma. There was no pathological finding on breast examination but pleomorphic microcalcifications clustered in a 5mm-sized area in the upper outer quadrant of the left breast looked suspicious for malignancy on spot digital films (Figure 1). No lesion was observed by sonography. Stereotactic excision of the suspicious area was performed in March 2007. Histopathological and immunohistochemical examination of the specimen revealed in situ papillary carcinoma with multifocal low grade ductal carcinoma in situ and atypical ductal hyperplasia. In the adjacent tissue there were fibrocystic changes with papillomatosis and a focus of “carcinoma arising in a papilloma”.

**ABSTRACT**

Introduction: Papillary lesions of the breast contain a great spectrum of lesions extending from benign papillomas to frankly invasive papillary carcinomas. There are different classifications and terminologies, and most cases have coexisting lesions resulting in difficulty both in diagnosis and management. We aim to review papillary lesions of the breast by presenting three cases with different lesions. Cases: We present here an in situ papillary carcinoma, an intracystic papillary carcinoma and an invasive papillary carcinoma, all with coexisting pathologies in the surrounding tissues. Patients had to have mastectomy in all cases with evaluation of axilla either by sentinel lymph node biopsy or by axillary dissection. No metastasis was detected in axillary nodes in either case. Discussion: All papillary lesions should be excised, although benign on needle biopsy, because there may be atypia, or in situ or invasive foci around the main lesion the needle targeted. Most have an excellent prognosis if removed with an adequate free surgical margin because recurrences are usually due to skipped in situ or invasive lesions in the surrounding tissue. For invasive cases, axillary metastasis is rare, thus sentinel node biopsy has recently provided avoidance from unnecessary axillary dissection.

Keywords: breast, carcinoma, intracystic papillary carcinoma, papilloma, papillary carcinoma
surgical margin was 2 mm. We reoperated the patient performing subcutaneous mastectomy with reconstruction after sentinel lymph node biopsy. Four nodes stained with blue dye had reactive changes with no malignancy. Around the cavity of the excised tissue in the mastectomy specimen there was ductal carcinoma in situ of a low grade with micropapillary and cribriform architecture. No oncological therapy was added and the patient is at 28mo after surgery.

**Case 2**

A 62-year-old woman presented with a 4 cm-sized periareolar mass located in the right breast which caused retraction of the skin. The mass was lobular in structure with irregular margins on mammography. Sonographic examination displayed a mass looking like a complicated cyst with solid and cystic areas (Figure 2). Needle biopsy from the solid part of the mass revealed a histological grade II breast carcinoma. We performed wide local excision in May 2000. It was papillary neoplasia on frozen section examination and reexcision was performed for free margins. At the periphery of the re-excised tissue there was microinvasion in one focus. The operation was converted to mastectomy with axillary dissection. The tumor was composed of a 4 cm-sized cyst with an 8 mm-sized nodule on its wall. On microscopic examination the cyst was an intracystic papillary carcinoma with a focus of microinvasion in an area less than 1 mm in diameter (Figure 3 and 4). In the adjacent tissue, papillomatosis and focal low grade ductal carcinoma in situ of solid architecture with a diameter of less than 2mm were evident. No metastasis was found in the 14 lymph nodes removed from axilla and the tumor was positive for estrogen and progesterone receptors. The patient received hormonotherapy. Nine years have passed without disease.

**Discussion**

Prototype of the papillary lesions is a papilloma, which is named according to its location in the breast. Centrally located papillomas originate from large ducts of the breast and are usually solitary, in which case they are called either “intraductal,” “solitary,” or “central” papillomas. On the other hand, peripherally located ones are usually multiple and originate from terminal duct lobular unit (TDLU) and then the terms “papillomatosis,” “multiple papillomas,” or “peripheral papillomas” are used (4,5,6,7).

Both central and peripheral papillomas may cause nipple discharge but peripheral papillomas are most commonly occult lesions and are discovered on mammography as microcalcifications or incidentally found in biopsies performed for other reasons.

**Case 3**

A 75-year-old woman presented with a palpable mass in her left breast. On examination there was a 2x2cm-sized hard mass with regular margins in the retroareolar region. On mammography it was a round hyperdense lesion (Figure 5). The mass was hypoechoic and solid with pinpoint cystic areas inside on sonography and its size was 2.2x1.5cm. Needle biopsy from the mass revealed a papillary neoplasia. We performed modified radical mastectomy in June 2003, after getting the result of the excised mass as papillary carcinoma on frozen section examination. There was a 2cm-sized tumor of invasive papillary carcinoma, around which micropapillary ductal carcinoma in situ was evident in the adjacent tissue. Fifteen lymph nodes removed were clear from disease. Strong staining for estrogen receptors was observed and c-erb B-2 was negative. The patient received hormonotherapy after getting radiotherapy for close fascial margin. She is at her 6 years postoperatively without disease.

![Figure 1](image1.png)  
**Figure 1.** Suspicious microcalcifications on spot digital film of patient 1 with in situ papillary carcinoma and ductal carcinoma in situ.

![Figure 2](image2.png)  
**Figure 2.** Sonographic appearance of the mass in case 2 with cystic areas.
In our first and second cases, as well, papillomatosis was an incidental finding in the biopsy material around the main lesion.

Papillomas are not always innocent and when contained areas of epithelial proliferation similar to atypical ductal hyperplasia (ADH) or ductal carcinoma in situ (DCIS), the terms “atypical papilloma”, or “papilloma with atypia”, and “papilloma with DCIS” are used, respectively (1,5). Peripheral papillomas are more likely to have coexisting atypical changes, DCIS or an invasive carcinoma than central ones (5,6). In our first case papillomatosis was associated with a focus of “carcinoma arising in a papilloma” and in the second one with a focus of DCIS. Carcinoma arising in a papilloma is a term, used by Tavassoli, for those papillomas in which atypical proliferation (i.e. proliferation of monotonous ductal epithelial cells without myoepithelial proliferation) constitutes at least a third but less than 90% of the lesion and it is a step in progression from atypical papilloma to papilloma with DCIS (5). Women with atypical papilloma have an increased risk of developing invasive carcinoma and the risk is 4-7.5 times greater than that in women with papilloma without atypia (3,4,9,10).

Papillary carcinoma, on the other hand, constitutes less than 2% of breast carcinomas (3,5). It is mostly an in situ carcinoma, namely “in situ papillary carcinoma”, but in a small group stromal invasion occurs, in which case the lesion is called an “invasive papillary carcinoma” (1,5). Histologically, either invasive or noninvasive, papillary carcinoma is further classified as: “intraductal papillary carcinoma” when the duct simply expands to accommodate the proliferating lesion, “intracystic papillary carcinoma” (IPC) if it becomes cystically dilated, and “solid papillary carcinoma” when there are nodules formed by proliferated epithelial cells (1,5,8,11,12).

Intraductal papillary carcinoma is mostly detected by excision of microcalcifications observed on mammography and a mass is rare unless the tumor is invasive. In IPC, however, microcalcifications are less frequent and a palpable mass is present in 90% of the cases. On mammography there is a round well-circumscribed mass, which is a hypoechoic lesion with both cystic and solid components on sonography (11,12). Nipple discharge is the presenting symptom in at least a third of IPC cases located centrally (1,5,11). In our case 2 also, the presenting symptom was a 4cm-sized periareolar mass, which had both cystic and solid areas on sonography.

Intracystic papillary carcinoma is accepted as a borderline lesion in progression from in situ to invasive carcinoma because histologically there is scant or no MEC layer, a situation similar to invasive papillary carcinoma (12,13,14). Thus several authors concluded that at least some of these lesions might be circumscribed encapsulated nodules of invasive carcinoma and they preferred to use the term “encapsulated papillary carcinoma” for those surrounded by a fibrous capsule which do not contain a peripheral MEC layer (13,14,15). Solid papillary carcinoma, like IPC, has no MEC layer in
most cases and is also thought as a special type of low-grade carcinoma with an indolent clinical course (1,3,16).

Areas of low to intermediate grade DCIS and invasive carcinoma, mostly invasive ductal carcinoma, may be found in association with IPC (1,3,17). In our second case also, there was a focus of microinvasion in IPC and low grade DCIS was evident in a focus in the adjacent tissue.

In IPC cases without invasion, management is similar to that for DCIS. They have an excellent prognosis with local therapy alone. If there is a frankly invasive carcinoma, sentinel lymph node biopsy must be added (1,17). It is the size of the invasive focus rather than the size of IPC that determines the T stage (1,3). In difficult cases immunohistochemical staining for smooth muscle actin (SMA) and S-100 protein, which are nonspecific proteins expressed in MEC, might be useful (2,4,5,15). Recently several reagents, such as calponin, p63, and P-cadherin, have been found to be more specific for myoepithelial cells (20). In differential diagnosis of our cases we used immunohistochemical markers of SMA, S-100 protein, p63, P-cadherin and calponin, as a whole.

Prognosis for papillary carcinoma is excellent with a 10-year survival rate of 100% and a disease-free survival rate of 91% (8,21). Regional or distant metastasis is extremely rare and a conservative approach with sentinel node biopsy is recommended. Frequency of multifocality in peripheral papillary carcinomas necessitates wider excision. Presence of DCIS at the adjacent breast tissue may result in local recurrence (3). Oncological therapy for papillary carcinoma is not different from invasive ductal carcinoma. Most are hormone receptor- positive. In our case of papillary carcinoma, axillary dissection was performed but there were no metastatic lymph nodes. No chemotherapy was ordered because of patient age, but hormonotherapy was given as the tumor was stained strongly for estrogen receptors. She is alive with no recurrence at 6 years.

In conclusion, papillary breast lesions have excellent prognosis. Wide excision is recommended, even when benign on CNB, in order to examine the whole lesion. Adjacent breast tissue should be checked carefully to avoid missing other proliferative lesions which may result in recurrence.
References


