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CASE REPORT/OLGU SUNUMU

APPROACH TO PAPILLARY LESIONS OF THE BREAST (A REPORT OF THREE CASES)

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MEMENİN PAPİLLER LEZYONLARINA YAKLAŞIM (VAKA SUNUMU)

ÖZET

Giriş: Memenin papiller lezyonları, benign papillomdan invaziv papiller karsinoma kadar uzanan çok sayıda lezyonu içerir. Terminoloji ve sınıflamadaki farklılıklar ile çoğu lezyonun in situ ya da invaziv odaklarla birlikte olması, bazen tanı ve tedavide karışıklığa yol açabilir. Burada üç farklı papiller lezyon sunarak tanı ve tedavi yaklaşımlarını tartıştık. Vakalar: Bu makalede in situ papiller karsinom, intrakistik papiller karsinom ve invaziv papiller karsinomlu üç vaka sunuldu. Vakaların tümünde çevre dokuda eşlik eden patolojiler mevcuttu. Tüm vakalarda mastektomiye gidilmesi gerekti, aksillanın durumu sentinel lenf nodu biyopsisi ya da aksiller diseksiyon ile değerlendirildi. Vakaların hiç birinde aksillada lenf nodu metastazı saptanmadı. Tartışma: İğne biyopsisi sonucu benign olsa bile, memenin tüm papiller lezyonları çıkartılmalıdır, çünkü biyopsi alınan sahanın etrafında atipi, in situ ya da invaziv odaklar olabilir. Eksizyon sonrası nüksler genellikle ana lezyonun etrafındaki atlanmış in situ ya da invaziv lezyonlar nedeniyledir, yeterli bir cerrahi sınır ile çıkartıldığında çoğu vakada prognoz çok iyidir. İnvaziv vakalarda aksiller tutulum nadirdir, günümüzde sentinel lenf nodu biyopsisi ile artık gereksiz aksiller diseksiyondan kaçınmak mümkündür.

Anahtar sözcükler: meme, karsinom, intrakistik papiller karsinom, papillom, papiller karsinom

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

Introduction

Histopathologically, a breast lesion is named as papillary when there are finger-like projections with a central fibrovascular core, extending into the duct lumen (1,2,3). The term "papillary" covers a great spectrum of lesions from benign papillomas to invasive papillary carcinomas; the differentiation of which may sometimes be difficult even for an experienced pathologist. On the other hand, high frequency of coexistence of several lesions in presence of a papillary lesion and different terminologies used for the same papillary lesion sometimes make clinicians confused on decision making. Here we present a report of 3 cases with review of literature and draw attention to the excellent prognosis of most papillary lesions of the breast, when treated adequately.

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". The closest

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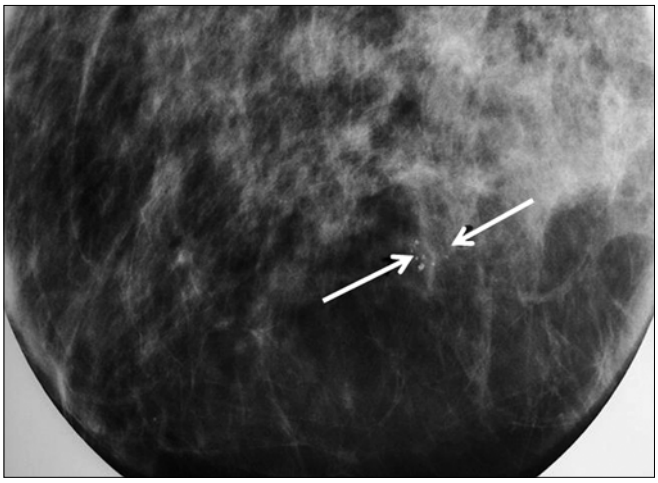

Figure 1. Suspicious microcalcifications on spot digital film of patient 1 with in situ papillary carcinoma and ductal carcinoma in situ.

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.

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

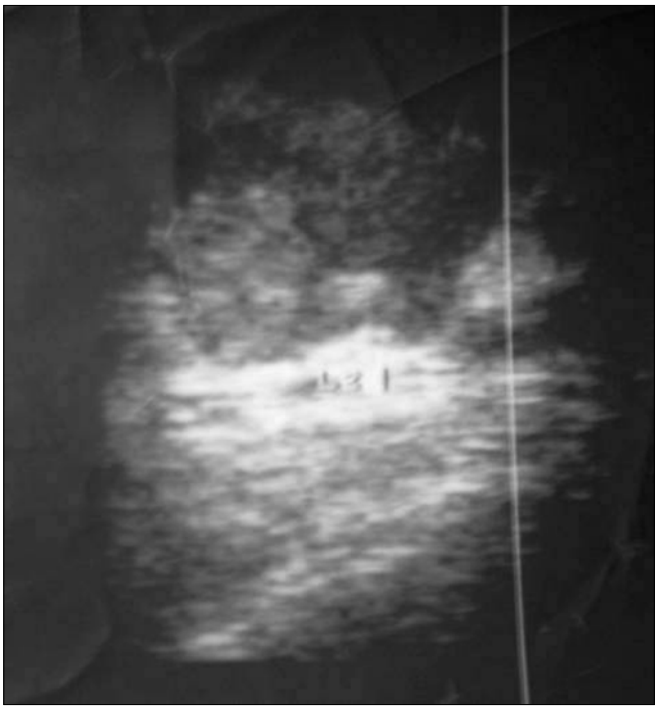

Figure 2. Sonographic appearance of the mass in case 2 with cystic areas.

it was a round hyperdense lesion (Figure 5). The mass was hypoechogenic 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.

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

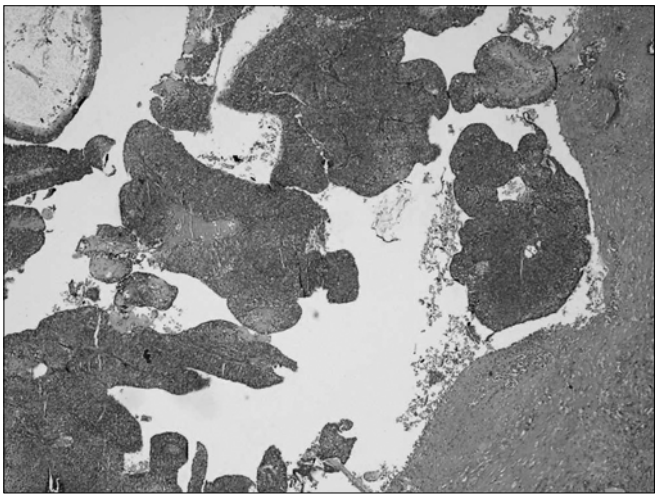

Figure 3. Intracystic papillary carcinoma: Complicated papillary structures with fibrovascular cores extending into the cyst lumen (HE X 100).

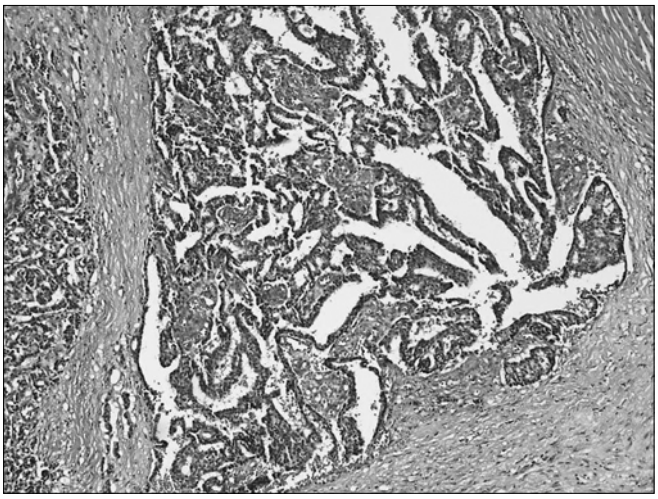

Figure 4. Desmoplastic stroma infiltrated with invasive carcinoma in case 2 with intracystic papillary carcinoma (HE& 200).

(3,8). 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).

Intraductal papilloma without atypia, however, is no longer considered premalignant. Frequency of subsequent carcinoma ranges from 0.4% to 8% depending on the presence of coexisting proliferative changes in breasts and thus carcinoma develops either in the opposite breast or elsewhere in the same breast (4,5,10). When the diagnosis of "papilloma without atypia" is made by excisional biopsy, no further therapy is required but both breasts should be followed up. However, core needle biopsy (CNB) may result in underestimation both because the tissue obtained by CNB is fragmented and because atypia may be present around the sample obtained by CNB (7). It has also been reported that in 75% of the cases with CNB- diagnosis of atypical papilloma is upgraded on excision to a more advanced lesion, such as DCIS or an invasive carcinoma (3,4). Thus wide excision of both papilloma with and without atypia and carcinoma arising in a papilloma is the recommended treatment (1).

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 expends 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

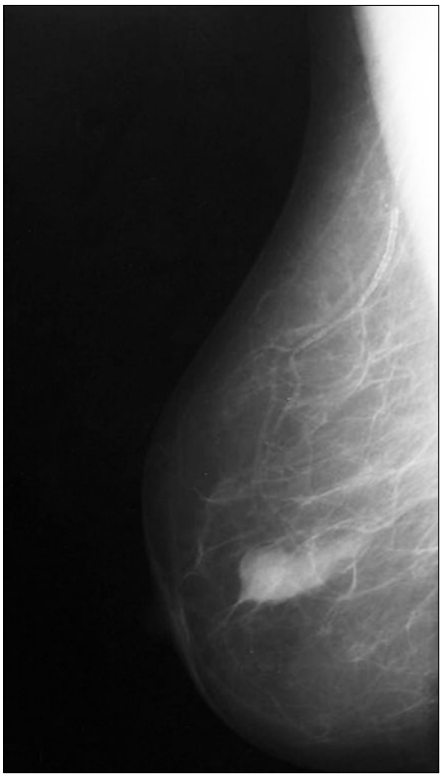

Figure 5. Mammographic appearance of case 3 with papillary carcinoma.

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). However as the size of IPC increases, metastatic potential of the tumor increases and sentinel node biopsy was suggested for lesions above 4cm in diameter (15). In our second case the size of the IPC was 4cm but there was only microinvasion. We had to perform axillary dissection in year 2000 and no lymphatic spread was found. She has been free of disease.

Majority of the patients with papillary carcinoma are in the 5th or 6th decades of life. Most cancers are solitary, palpable and centrally located. Peripherally located ones are usually multifocal and seldom palpable. In presence of nipple discharge, which occurs in about 22-34%, galactography is a sensitive test. It can demonstrate an intraductal filling defect, irregularity in the duct wall, ductal obstruction or periductal extravasation of the contrast material, but it is not specific enough to differentiate benign from malignant lesions (5,11,18). Ductoscopy, however, allows endoscopic evaluation of the duct system with tissue sampling for cytological examination (3). Ultrasonography demonstrates the cystic mass with or without septations and solid papillary projections extending into the cystic lumen (8.11). Our third case was presented with a retroareolar mass, which was visible on sonography as a lesion with solid and cystic areas and the diagnosis of papillary carcinoma was made by CNB.

Invasive focus in papillary carcinoma is usually missed by CNB because it is usually encountered at the periphery of the lesion (11). On histological basis there are several insignificant features that help to separate malignant from benign lesions, however, complete absence of MEC layer invariably identifies a papillary carcinoma (5,7,8,19). 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.

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