Chapter

Papillary Neoplasm of Breast-Changing Trends in Diagnosis and Management

Amrit Pal Singh Rana and Manjit Kaur Rana

Abstract

Papillary neoplasm of breast comprises of seven separate heterogeneous entities ranging from benign, atypical and malignancy including non-invasive and invasive carcinoma. Papillary carcinoma (PC) is seen more commonly in older postmenopausal women with favorable prognosis. PC breast typically presents with bloody nipple discharge and an abnormal mass with radiologic features of intraductal mass. Encapsulated PC and solid PC is to be treated as in situ carcinoma, but distinction of invasive PC from non invasive carcinoma is critical both at microscopic and molecular level. So, surgical excision should be the choice of definitive diagnostic technique in papillary neoplasm instead of core needle biopsy. Furthermore, treatment guidelines for invasive PC also have been framed, but incidence of recurrence and death attributable to various subtypes of carcinoma remained same. So, this is important topic to be addressed to understand the need for further management and outcome of the disease.

Keywords: papilloma, invasive carcinoma, intraductal, carcinoma in situ, solid papillary carcinoma

1. Introduction

Papillary neoplasm of the breast is a broad range of heterogeneous group of lesions that are characterized by presence of papillae supported by fibrovascular cores lined by epithelial cells with or without myoepithelial cell layer. These neoplasms may be benign, atypical or malignant and are difficult to diagnose. The main diagnostic concern is differentiating benign and malignant lesions, which can be challenging both on imaging as well as on histopathological examination [1].

2. Definition of papillary neoplasm breast

World health organization (WHO) in 2021 classified breast intraductal papillary neoplasm as intraductal papillomas (intraductal papilloma with atypical hyperplasia, intraductal papilloma with ductual carcinoma in situ (DCIS), intraductal papilloma with lobular carcinoma in situ), intraductal papillary carcinoma (solid papillary carcinoma, encapsulated carcinoma) and invasive carcinoma [1, 2].

3. Epidemiology

3.1 Age and sex

The benign conditions are commonly seen in between 30 and 50 years of age and PC commonly affects postmenopausal age group. Papillary neoplasms have sex predilection for females though intracystic papillary carcinoma (IPC) is rarely seen in males too. The clinical presentation in males and females is similar except for a higher median age in males [3, 4].

3.2 Incidence

Papillary neoplasms are less commonly seen and account for less than 3% of breast tumors and PC of the breast accounts for 0.5–1% of breast cancer [5]. The frequency of lymph node involvement in invasive papillary carcinoma, its local recurrence and distant recurrence may be 0–11%, 3–70% and 0–4%, respectively. Solid papillary carcinoma (SPC) constitutes only 1% of all the breast carcinomas, presenting as localized mass in approximately 90% of the cases, lymph node metastases in 8%, and distant metastases in less than 0.8% only. Intracystic papillary carcinoma also has localized involvement in approximately 89.6% of the cases with 0.4% distant metastases [6, 7].

4. Pathophysiology

Many researchers have analyzed the risk factors for malignant transformation in benign papilloma of breast, however the results remain inconsistent. Some investigators considered same attributable factors for carcinoma arising in papillary neoplasm as that of other carcinomas. The contributing predisposing risk factors are age, family history, genetic predilection, diet and weight gain, alcoholism, and endocrine factors [8, 9].

5. Clinical features

Papillary neoplasms may be central and peripheral in location and solitary or multiple in number. And most papillomas are centrally located with a wide age distribution and originate in the large ducts, and are typically solitary. The most common clinical presentation is serous or serosanguineous nipple discharge. The benign solitary papilloma has 1.5 to 2.0 times high risk of breast carcinoma whereas four times increased risk of malignant transformation is noted in atypical papillomas. The peripheral papillomas arise in the terminal duct lobular units and are often discovered incidentally on imaging studies and risk of carcinoma is even higher than solitary papilloma. And very rarely, benign papillomas of breast presenting with local or distant metastases have been reported [10–18]. However, behavior and management of papillary carcinoma whether in situ or invasive remain a matter of debate. The lymph node involvement, local recurrence and distant recurrence may be seen. Solid papillary carcinoma are localized lesions and may involve lymph node however distant metastasis is rare [6, 7]. Common clinical features include nipple discharge and palpable masses in some cases, however papillary lesions may be diagnosed in asymptomatic women or on screening [19].

6. Diagnosis

Treatment of benign papillary neoplasms require careful evaluation as the presence of papillary architecture is known to be associated with a higher risk of carcinoma breast [20]. The precise diagnosis of papillary neoplasm of the breast is difficult on cytomorphological charaterstics alone. A benign diagnosis on fine needle aspiration or core needle biopsy may not completely exclude malignancy especially if it manifests as focal carcinoma in-situ or abruption of the myoepithelial layer. Microcalcification is an important factor in the management of breast intraductal papillomas diagnosed on core biopsy [21–24]. The benign papillary lesions can be diagnosed with sonographically guided 14-gauge core needle biopsy. The sensitivity for detecting papillary lesions is greater by ultrasound than mammography. The USG findings of papillary neoplasm are found to be correlated with pathologic findings [13, 25]. Recently, automated breast ultrasound scanners have been developed, and the ultrasound volume data set of the whole breast can be acquired in a standard manner [26]. MRI features including a mass size exceeding 10 mm may indicate a papilloma with high-risk or malignant lesions [27].

However, histopathological examination is the gold standard tool for the diagnosis. Nevertheless, the morphology is more important than the immunostaining pattern, and diagnosis of neoplastic proliferation should not be made on the immunostaining pattern alone. For intraductal papillary neoplasm CK5/6 is good marker to differentiate between intraductal hyperplasia (CK5/6 positive) and intraductal proliferation resembling DCIS or ADH (CK5/6 negative). Immunohistochemical examination with CK5/6 and a panel of two myoepithelial markers (p63, SMA, CD10, calponin) acts as useful tool in assessing papillary neoplasms of the breast [28, 29].

7. Treatment and prognosis

The treatment of benign and atypical papilloma is being evolved. The surgical excision of all papillary lesions is recommended for definitive diagnosis and standard management for malignant papillary lesions [24, 30]. Li X et al. suggested the vacuum assisted excision is applicable for complete excision of small papillomas, even papillomas with atypical hyperplasia [31]. Bianchi et al. also emphasized that, in addition to surgery, vacuum assisted excision of beingn intraductal papilloma may be done [32]. However, some authors have recommended that benign papillary lesions diagnosed by core needle biopsy (CNB) might not require immediate excision, but may be safely managed with imaging follow-up for at least 5 years rather than with surgical excision [33, 34]. Accurate results and coordination between a trained radiologist and pathology are of utmost importance in the decision making between follow-up or surgery [35]. However, Fatima K et al. have observed no reliable clinical or imaging features that can pre-surgically predict atypical upgradation or malignant potential [30]. Tokiniwa H and fellows detected surgical excision advantageous for papillary lesions especially for the lesions located far from the nipple [36]. The atypical papillary lesions should be excised surgically (**Figure 1**) [37].

Intraductal carcinomas like encapsulated papillary carcinoma (EPC) with presence of myoepithelial cells at the periphery should be treated as DCIS and with lack of myoepithelial cells may behave in an indolent invasive pattern with reported lymphnode metastasis and lymphovascular invasion. The present harmony is to manage EPC as in situ disease, though recurrence may be seen associated with aggressive behavior (**Figure 2**).

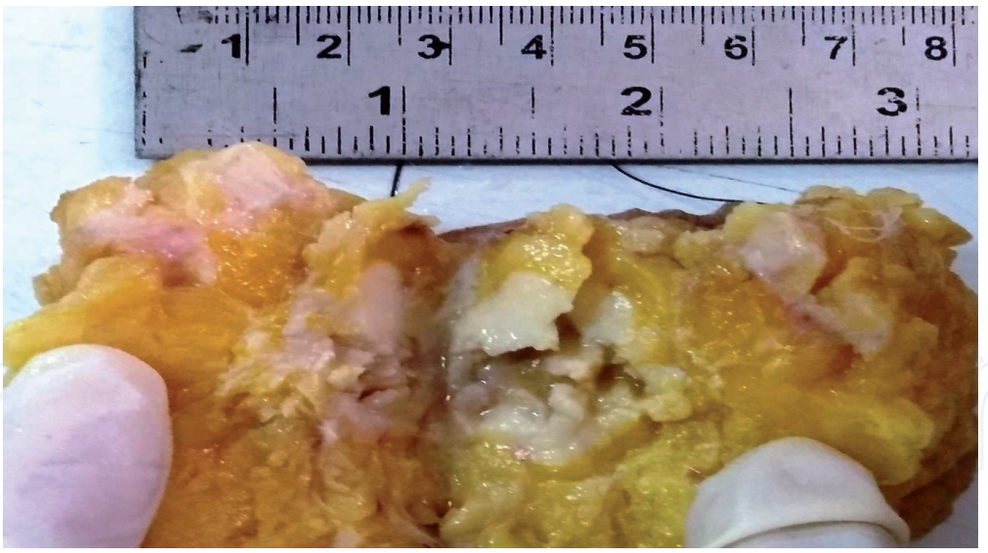

Figure 1.
Surgically excised specimen of papillary neoplasm.

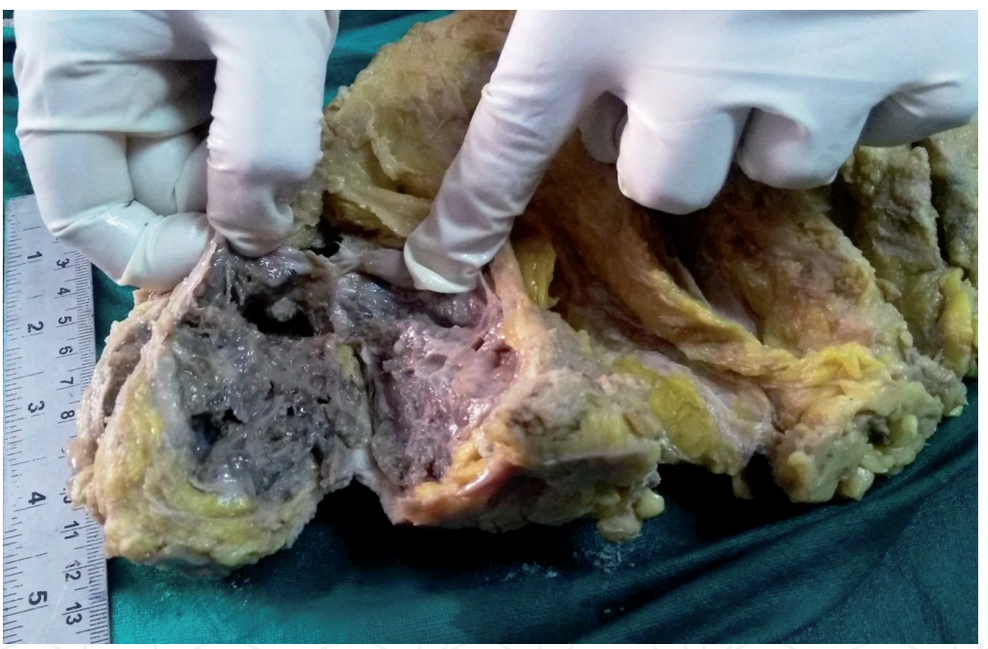

Figure 2.
Surgically excised specimen of EPC.

Due to lack of evidence of behavior and criterion of diagnosis, SPC is difficult to categorize as benign or malignant and current consensus is to consider it as an in-situ disease. Consensus is to treat these types of neoplasms for local control without axillary node sampling or systemic therapy. Inspite of very low risk of metastatic potential, evidence does not support use of conventional forms of adjuvant systemic therapy. IPC is known to have benign behavior with 100% disease-specific survival rate so to be treated with similar way to other types of carcinoma breast except in cases with moderate nuclear atypia [7, 38].

8. Conclusion

Papillary neoplasm is difficult to detect and diagnose, if diagnosed, surgical excision is the treatment of choice. Encysted and solid papillary carcinoma should

be treated as DCIS, irrespective of nuclear grading. Amongst imaging studies ultrasoography is better than mammography. In difficult cases immunohistochemical markers (CK 5/6 and minimum two myeloepithelial markers provide the support. Invasive papillary carcinoma may be treated as per guidelines of invasive carcinoma breast and shows good prognosis.

Author details

Amrit Pal Singh Rana[1*] and Manjit Kaur Rana[2]

1 Department of Surgery, Baba Farid University of Health Sciences, Faridkot, Punjab, India

2 Department of Pathology/Lab Medicine, All India Institute of Medical Sciences, Bathinda, Punjab, India

*Address all correspondence to: dramritpalsingh@gmail.com

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