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Papillary lesions of the breast diagnosed using core needle biopsies

HIDEAKI TOKINIWA[1], JUN HORIGUCHI[1], DAISUKE TAKATA[1], MAMI KIKUCHI[1], NANA ROKUTANDA[1], RIN NAGAOKA[1], AYAKO SATO[1], HIROKI ODAWARA[1], KATSUNORI TOZUKA[1], TETSUNARI OYAMA[2] and IZUMI TAKEYOSHI[1]

Departments of [1]Thoracic and Visceral Organ Surgery, and [2]Diagnostic Pathology, Gunma University Graduate School of Medicine, Gunma 371-8511, Japan

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Abstract. Papillary lesions of the breast include a broad spectrum of lesions, from benign papillomas to papillary carcinomas. It is difficult to determine whether a lesion is benign or malignant based on the fragmented material of a core needle biopsy (CNB). This study evaluated patients with papillary lesions examined using CNB. We retrospectively reviewed 31 papillary lesions diagnosed using CNB between 2004 and 2007. The clinical findings of benign and malignant papillary lesions were compared. The average patient age was 48.9 years. Twelve patients presented with a discharge and 10 patients presented with a lump. Eight patients were asymptomatic. The initial diagnoses by CNB of the 31 lesions were 25 intraductal papillomas, 4 intracystic papillomas and 2 adenomas. After CNB, excisional biopsies were performed in 23 patients and biopsies with a Mammotome® in 2 patients. Seven patients underwent regular follow-up. Five (16%) of the 31 patients with papillary lesions were ultimately diagnosed with breast cancer. The average distance from the nipple to a tumor diagnosed as malignant was 2.46 cm, which was longer than for a tumor diagnosed as benign. Ultimately, 5 papillary lesions (16%) were diagnosed as breast cancer. To avoid overlooking a malignancy, surgical excision is advantageous for papillary lesions, particularly those located far from the nipple.

Introduction

Core needle biopsy (CNB) has become widely used in diagnosing breast disease (1,2). CNB is a uncomplicated examination, which is easier for patients to accept than excisional biopsy. Papillary lesions are a heterogeneous group of breast lesions and include papilloma, papillomatosis, atypical papilloma, non-invasive ductal carcinoma and invasive ductal carcinoma. Sometimes, distinguishing malignant from benign papillary lesions using CNB can be difficult since only a small portion of the lesion is examined. This study evaluated the follow-up methods and results of excisional biopsies for patients with papillary lesions initially diagnosed using CNB.

Correspondence to: Dr Hideaki Tokiniwa, Department of Thoracic and Visceral Organ Surgery, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan
E-mail: tokiniwa@med.gunma-u.ac.jp

Key words: papillary lesion of the breast, core needle biopsy, breast cancer

Patients and methods

We retrospectively reviewed 31 papillary lesions of the breast diagnosed using CNB between 2004 and 2007. All cases were reviewed regarding the follow-up methods, distance from the nipple to the tumor and final pathological diagnosis.

Patient background. The median patient age was 48.9 years (range 22-81). Twelve patients came to our hospital due to nipple discharge, 10 patients presented with a lump, 8 patients had an abnormal check-up and 1 patient presented with another complaint. Ultimately, 14 patients developed nipple discharges: 8 were bloody and 6 were serous.

Percutaneous biopsy method. Ultrasonographically guided procedures were performed with the patient in the supine or supine oblique position. Imaging was performed with a high-resolution 8-12 MHz linear array transducer (Acuson Sequoia 512; Siemens®). The biopsy was performed using a freehand technique with a 14-gauge needle and spring-loaded biopsy gun (Bard Magnum®). The distance from the nipple to the tumor was measured using ultrasonography at the time of CNB (Fig. 1). The biopsy specimen was evaluated by an experienced breast pathologist.

Results

The initial diagnosis was intraductal papilloma in 25 patients (80%), intracystic papilloma in 4 (13%) and adenoma in 2 (7%). After CNB, excisional biopsies were performed in 23 patients and Mammotome® biopsies in 2 patients. The CNB was repeated in 2 patients. Four patients did not undergo any further biopsy, but were followed up with ultrasonog-

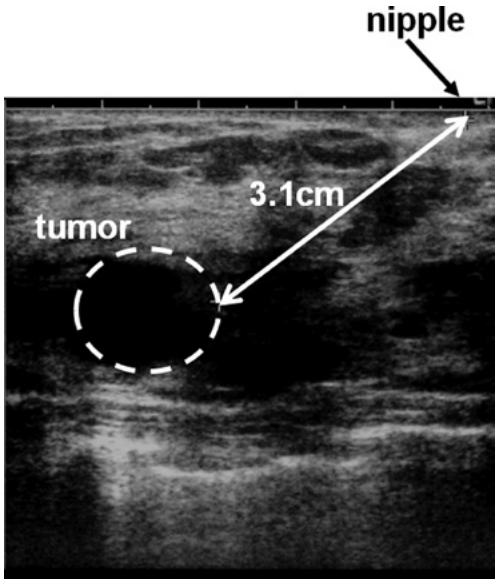

Figure 1. Distance from the nipple to the nearest tumor edge was measured using ultrasonography. In this case, the distance from the nipple to the nearest tumor edge was 3.1 cm.

raphy alone at the' request of the patients. Five (16%) of the 31 patients with papillary lesions were ultimately diagnosed with breast cancer.

Five malignant cases. The mean patient age was 48.8 years (range 37-72). All cases were diagnosed as intraductal papilloma initially. Two patients presented with a lump, 2 with abnormal check-up results and only 1 with a bloody nipple discharge. The average distance from the nipple to the tumor was 2.46 cm. To obtain the final diagnosis, 4 patients underwent excisional biopsies and 1 a repeat CNB. The final diagnosis was invasive ductal carcinoma in 4 cases and non-invasive ductal carcinoma in the others. After the final diagnosis, 4 patients underwent breast-conserving surgery and 1 underwent a total mastectomy. Sentinel lymph node biopsies were performed at the time of surgery in all cases, and there was no cases of lymph node metastasis (Table I).

Discussion

We examined the difference between the initial diagnosis, based on CNB, and the final diagnosis, based on excisional biopsy, for papillary lesions. Comparing the distance from the nipple to the tumor, it was 2.46 cm (range 0.5-4.0) for those diagnosed as malignant and 1.76 cm (range 0.5-4.5) for those diagnosed as benign. Malignant lesions were located farther from the nipple than benign lesions (Table II), although the difference was not statistically significant. There was no significant difference in the age of the patients with benign and malignant lesions (Table III). Distinguishing malignant from benign papillary lesions can be problematic. The presence or absence of a myoepithelial cell layer in the papillary component of the lesion is the most important feature for differentiating a benign papilloma from a papillary carcinoma.

We reviewed 21 studies (including ours); 10 studies supported the need for surgical excision and 10 did not (Table IV) (3-22). There were 643 cases in these studies; 424 cases (65.9%) underwent excisional biopsies: 334 cases (78.8%) were diagnosed as benign; 27 were diagnosed as atypical ductal hyperplasia; 21 were non-invasive ductal carcinoma; and 27 were invasive ductal carcinoma. Ultimately, an excisional biopsy was required in 75 cases (11.7%). Ten studies stated that an excisional biopsy was necessary to diagnose papillary lesions, while the other 10 studies concluded that it was not necessary.

It remains controversial whether papillary lesions of the breast diagnosed using CNB need a further excisional biopsy. An excisional biopsy has some merits. The pathologist can diagnose the papillary lesion as benign or malignant from the entire lesion, the nipple discharge will stop after an excisional biopsy and no repeat CNB is necessary. Conversely, there are certain disadvantages to an excisional biopsy. Local anesthesia

Table I. Five malignant cases.

Case	Age (years)	Initial diagnosis	Clinical presentation	Discharge	TND (cm)	Follow-up	Final diagnosis	Op
1	72	Intraductal papilloma	Discharge	Bloody	0.50	CNB	IDC	Bt
2	44	Intraductal papilloma	Lump	No	4.00	Excisional biopsy	IDC	Bp
3	37	Intraductal papilloma	Lump	No	3.20	Excisional biopsy	IDC	Bp
4	41	Intraductal papilloma	Asymptomatic	No	1.10	Excisional biopsy	DCIS	Bp
5	50	Intraductal papilloma	Asymptomatic	No	3.50	Excisional biopsy	IDC	Bp
Average	48.8				2.46			

TND, distance from the nipple to the tumor; Op, operation; CNB, core needle biopsy; IDC, invasive ductal carcinoma; DCIS, non-invasive ductal carcinoma; Bp, wide excision; Bt, total mastectomy.

Table II. TND of malignant lesions and benign lesions.

Lesion	TND mean (range)
Benign	1.76 (0.5-4.5)
Malignant	2.46 (0.5-4.0)

TND, distance in cm from the nipple to the tumor. p=0.13.

Table III. Age of the patients with malignant and benign lesions.

Lesion	Age, in years mean (range)
Benign	48.4 (22-78)
Malignant	48.8 (37-72)

p=N.S.

Table IV. Papillary lesions of the breast diagnosed with core biopsy; summary of the literature.

Author/(Refs.)	Year	No. of cases	No. of excisions	Benign	ADH	DCIS	IDC	Other	Conclusions
Ioffe *et al* (3)	2000	28	8	8					No excision
Philpotts *et al* (4)	2000	16	6	4				2	No excision
Liberman (5)	2000	7	4	4					No excision
Mercado *et al* (6)	2001	12	6	5			1		Excise
Rosen *et al* (7)	2002	44	14	11	2	1			No excision
Irfan and Brem (8)	2002	6	3	1	1			1	-
Ivan *et al* (9)	2004	30	6	6					No excision
Puglisi *et al* (10)	2003	31	31	29			2		Excise
Agoff and Lawton (11)	2004	25	11	11					No excision
Renshaw *et al* (12)	2004	8	8	8					No excision
Gendler *et al* (13)	2004	13	13	9	2		2		Excise
Carder *et al* (14)	2005	2	1	1					No excision
Liberman *et al* (15)	2006	50	25	20		4	1		Excise
Mercado *et al* (16)	2006	43	36	14	8	2		12	Excise
Valdes *et al* (17)	2006	36	36	30			6		Excise
Plantade *et al* (18)	2006	86	37	32		5			No excision
Skandarajah *et al* (19)	2007	80	80	54	11	8	7		Excise
Arora *et al* (20)	2007	18	18	18					Excise
Sydnor *et al* (21)	2007	38	38	37			1		No excision
Askenazi *et al* (22)	2007	39	20	13	3		4		Excise
Present study		31	23	19		1	3		Excise
Total		643	424	334	27	21	27	15	Ten studies recommend excision

ADH, atypical ductal hyperplasia; DCIS, non-invasive ductal carcinoma; IDC, invasive ductal carcinoma.

(e.g., allergy and toxicity) and surgery convey various risks, an excisional biopsy may alter the breast shape and an accurate sentinel lymph node biopsy may be impossible as the lymphatic flow is altered. Several reports supporting CNB alone for distinguishing benign and malignant papillary lesions are based on immunohistochemical studies, which suggest that different cell surface markers help differentiate the two. Saddik and Lai proposed that CD44 is a marker for benign papillary lesions (23). Recently, high-molecular-weight cytokeratins, particularly CK5 and 6, have been studied as markers (24). Shah *et al* added CK5 and 6 to calponin and p63 and investigated their effect on the accuracy of CNB (25). The overall accuracy increased from 84.5 to 92.8%. Moreover, Moriya *et al* suggested that certain immunohistochemical markers are quite useful in diagnosing various breast lesions, particularly for separating benign lesions and malignant neoplasms; however, the situations in which these markers are valuable are not universal, and their application and methods for evaluation are limited (26).

Ultimately, 5 papillary lesions (16%) initially diagnosed as benign papillary lesions were diagnosed as a breast cancer. The average distance from the nipple to the tumors diagnosed as malignant was longer than that for those diagnosed as benign. For papillary lesions, including intraductal papilloma, located far from the nipple, it is also necessary to consider a carci-

noma which may be hidden near them. To avoid overlooking a malignancy, surgical excision is advantageous for papillary lesions, particularly those located far from the nipple.

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