Int Surg 2017;**102:**119–124
DOI: 10.9738/INTSURG-D-15-00107.1

Case Report

Diagnosis of Intracystic Papillary Carcinoma of the Breast by Preoperative Core Needle Biopsy: A Case Report

Keiichi Takahashi

Department of Surgery, Takahashi Breast and Gastroenterology Clinic, Osaka, Japan

Intracystic papillary carcinoma (ICPC) of the breast is rare. It is categorized as noninfiltrating papillary ductal carcinoma in situ (DCIS). It protrudes and grows into the inner cavity in a papillary form, usually unaccompanied by severe infiltration in the surrounding interstitium. ICPC is often a noninfiltrating carcinoma and differentiating it from benign intracystic papilloma is difficult using preoperative imaging alone. Therefore, deciding on a treatment policy is often difficult. For correct diagnosis, it is vital to perform fine needle aspiration (FNA) or core needle biopsy (CNB) of the intracystic solid part accurately and under ultrasound guidance. However, the rate of accurate diagnosis by FNA cytology is low, and diagnosis by CNB is reported to be more effective than cytology. CNB of the solid part of a cyst for preoperative diagnosis is difficult and has a sensitivity of 60%. There is also a report stating that preoperative diagnosis could not be obtained in 40% of patients with ICPC. Therefore, biopsy by resection should be considered in patients who cannot be diagnosed by either FNA or CNB. However, DCIS had better be preoperatively diagnosed because not only axillary lymph node dissection but also sentinel lymph node biopsy might be omitted. The patient was a 42-year-old woman. She found a tumor mass in the left inner breast 10 weeks before her initial visit to the author's clinic. It was difficult to differentiate between the benignity or malignancy of the tumor from images, but a diagnosis of ICPC was made using preoperative CNB.

Key words: Intracystic papillary carcinoma of the breast – Cyst – Fine needle aspiration – Core needle biopsy – Ductal carcinoma in situ – Atypical ductal hyperplasia – Cytokeratin – Sentinel lymph node biopsy

Corresponding author: Keiichi Takahashi, Takahashi Breast and Gastroenterology Clinic, Yamazaki Seiren Bldg. 2F, 6-2-22, Uehonmachi, Tennoji-Ku, Osaka City, Osaka 543-0001, Japan.
Tel.: +81 6 6767 0621; Fax: +81 6 6767 0623; E-mail:takahashi-nyusen@dolphin.ocn.ne.jp

Intracystic papillary carcinoma (ICPC) of the breast is a rare disease, accounting for 0.5% to 1% of all breast cancer cases.[1–3] It is categorized as noninfiltrating papillary ductal carcinoma in situ (DCIS). It protrudes and grows into the inner cavity, which is surrounded by fibrotic walls in a papillary form, while the surrounding interstitium is usually not severely infiltrated.[2] It is preferable to diagnose DCIS for ICPC preoperatively on the ground that not only axillary lymph node dissection, but also sentinel lymph node biopsy (SLNB) might be avoidable. For all papillary lesions of the breast, FNA cytology is unreliable to get the pathologic diagnosis of DCIS, also initial surgical excision before FNA and CNB to exclude DCIS or invasive carcinoma is not recommended proactively. This report differs from the others in emphasizing the importance of CNB for initial way of diagnosis for papillary lesions of the breast. A case of noninfiltrating ICPC that could be diagnosed by preoperative CNB, after differentiation between benignity and malignancy based on imaging proved difficult, is reported herein.

Case Report

The patient was a 42-year-old Asian Japanese woman whose general condition was good. Her medical history was unremarkable, but a review of her family history revealed that her grandmother had gastric cancer. She found a tumor mass in the left inner breast 10 weeks before her initial visit to the Takahashi Breast and Gastroenterology Clinic, Osaka, Japan.

Mammography showed several mostly homogeneous tumor shadows with smooth margins in the left breast region. No calcification was observed (Fig. 1a, 1b). Ultrasonography showed cysts of 15.5 × 21.0 × 15.6 mm and 11.2 × 11.7 × 10.1 mm, accompanied by posterior echo enhancement and a papillary tumor of 15 × 10 × 10 mm, which protruded into the inner cavity. The tumors were accompanied by a lateral shadow and enhancement of posterior echo (Fig. 2a). Color Doppler of ultrasonography showed a surrounding vascular pattern (Fig. 2b).

The CNB needle was seen as a linear diagonal shadow from the right side to just before the tumor (Fig. 2c). The CNB needle was securely inserted into the solid tumor without being disturbed in the cyst (Fig. 2d).

CNB of the left tumor resulted in the diagnosis of intraductal (intracystic) carcinoma. Long cylindrical neoplastic cells, with elliptical cores stained with chromatin, showed papillary proliferation accompanied by interstitium and fine fibers in the cystic cavity. The core was atypical and mildly polymorphic. The resected segment showed no interstitial or vascular infiltration (Fig. 3a, 3b).

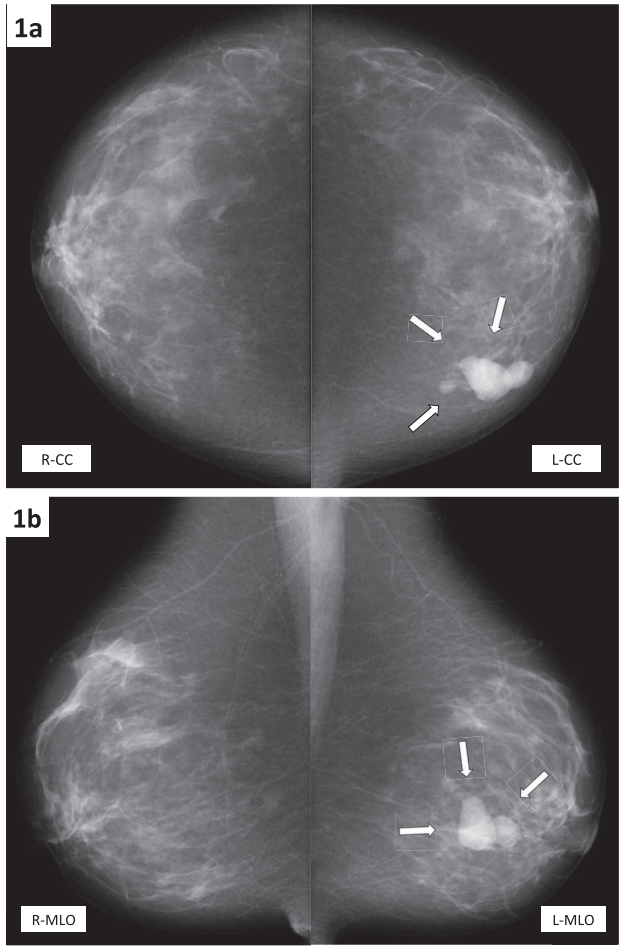

Fig. 1 Mammography (a, b). Mammography showed several mostly homogeneous tumor shadows with smooth margins in the left breast region. No calcification was observed.

The patient was diagnosed with left breast cancer and underwent partial resection of the left breast. The histopathologic findings of the resected specimen were DCIS, intracystic carcinoma, estrogen receptor 80%, progesterone receptor 80%, MIB-1 (antibody) labeling index ≤2%, nuclear grade 1, and human epidermal growth factor receptor (EGFR)-2 score of 0.

Discussion

ICPC is a breast cancer that protrudes and proliferates into the inner cavity of a cyst in a papillary

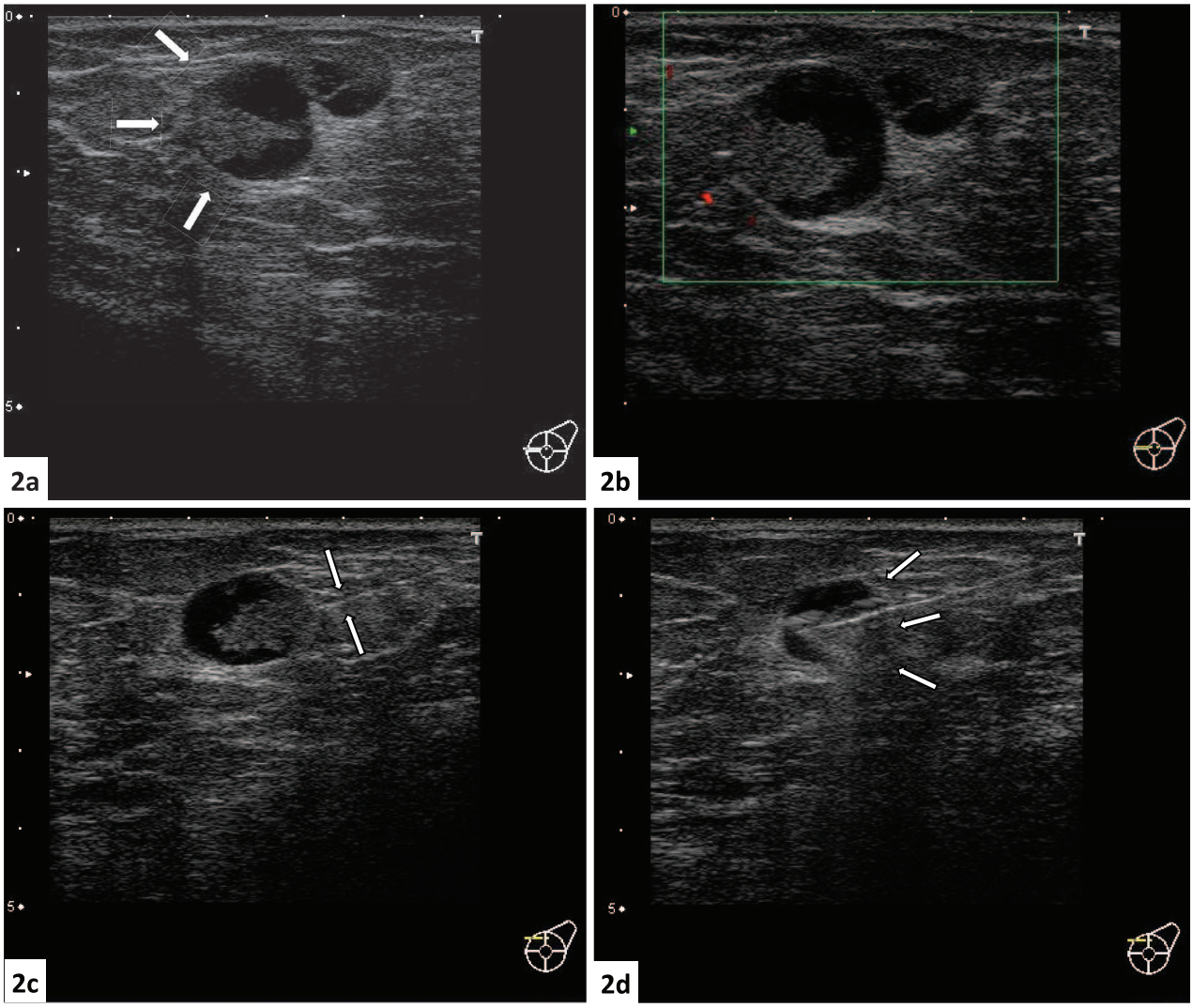

Fig. 2 Breast ultrasonography (a) Ultrasonography showed cysts of 15.5 × 21.0 × 15.6 mm and 11.2 × 11.7 × 10.1 mm, accompanied by posterior echo enhancement and a papillary tumor of 15 × 10 × 10 mm, which protruded into the inner cavity. The tumors were accompanied by a lateral shadow and enhancement of posterior echo. (b) Color Doppler of ultrasonography showed a surrounding vascular pattern. (c) The CNB needle was seen as a linear diagonal shadow from the right side to the anterior side of the tumor. (d) The CNB needle was securely inserted into the solid tumor without touching the cyst.

form, and which reportedly accounts for 0.5% to 1% of all breast cancer cases.[1–3] A common symptom is recognition of a gradually enlarging breast tumor,[4] and bloody nipple discharge is found in 22% to 34% of all cases.[5–7] It is generally classified as DCIS and rarely accompanied by infiltration. According to the latest version of the general rules for clinical and pathologic recording of breast cancer, it is defined as a state where a lesion is localized in a cyst, presenting as noninfiltrating intracystic carcinoma. However, there are reports of cases with infiltration outside the cyst, broad intraductal extension,[8] or simultaneous liver metastasis.[9] Differentiation from benign intracystic papilloma is considered difficult.

The patient's age is an important factor in predicting whether intracystic papilloma is benign or malignant. The mean age of patients with ICPC is 69.5 years, older than that of patients with ordinary breast cancer,[6] whereas the mean age of patients with benign intracystic papilloma is 40.7 to 47 years.[10] In this case, the age of the patient was 42 years, which was younger than that of mean ICPC. According to reports, breast cancer was found in 81% of patients 60 years or older who were

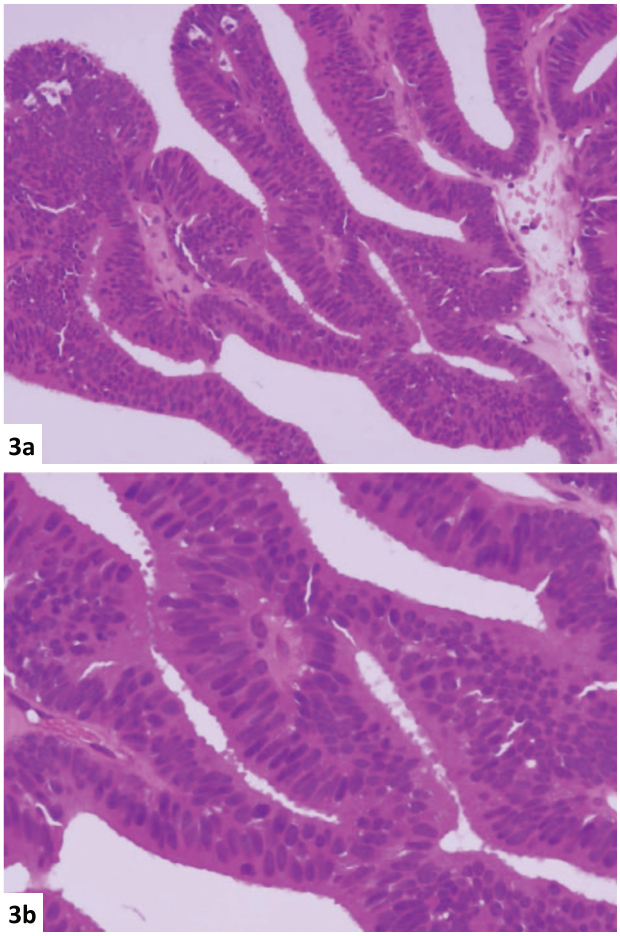

Fig. 3 Pathologic analysis. (a, b) CNB of the left tumor resulted in the diagnosis of intraductal (intracystic) carcinoma. Long cylindrical neoplastic cells, with elliptical cores stained with chromatin, showed papillary proliferation accompanied by interstitium and fine fibers in the cystic cavity. The core was atypical and mildly polymorphic. The resected segment showed no interstitial or vascular infiltration. (a) Hematoxylin and eosin stain, ×50. (b) Hematoxylin and eosin stain, ×100.

diagnosed with an intracystic tumor.[2,10–15] In addition, mean diameters of tumors including cysts are reportedly 2.6 cm for ICPC and 1.9 cm for intracystic papilloma.[13] Larger tumor diameters generally indicate malignancy rather than benignity. However, the diagnostic value of tumor size for differentiation between benignity and malignancy is considered low.[13,14] Ultrasonography often shows irregular margins for both benign and malignant intracystic tumors, and therefore, is ineffective for differential diagnosis.[14,15]

For diagnosis, it is essential to securely perform fine needle aspiration (FNA) or CNB of the intracystic solid part under ultrasound guidance. Moreover, many ICPCs are low grade and the determination of benignity or malignancy by cellular atypia alone is considered difficult. The rate of accurate diagnosis using FNA cytology is low, while diagnosis by CNB is believed to be more effective than cytology.[16] CNB of the solid part of a cyst for preoperative diagnosis is difficult and has a sensitivity of 60%, whereas reportedly, preoperative diagnosis was not possible in 40% of ICPC patients.[10] Therefore, biopsy by resection should be proactively considered in patients who cannot be diagnosed by FNA or CNB.[16–18] Papillary lesions of the breast pathology remain a challenging subject in diagnostic breast pathology, and it is still problematic about whether CNB is sufficiently accurate in the diagnosis of benign pathology to avoid surgical biopsy. Radiologic imaging, while it is helpful, cannot reliably distinguish between benign and potentially malignant papillary lesions revealed by CNB. All the more mammography is not reliable for distinction between benign and atypical papillary lesions. It is initially reported that all papillary lesions revealed on CNB required follow-up surgical excision to exclude DCIS or invasive carcinoma.[19,20] However, more recent data have suggested that benign papillary lesions can be diagnosed comfortably by means of CNB using particularly larger core needle to enable more samples and only ADH revealed by CNB need surgical excision[21] because a significant proportion of these lesions contain DCIS or invasive carcinoma. By contrast, frozen section obtained from surgical excision is less reliable than permanent section, and it is often difficult to distinguish DCIS from ductal hyperplasia on frozen section because the tissue structure is not completely preserved. In the diagnosis of surgical margins on frozen section, it is reported that a diagnostic accuracy is 86%, sensitivity is 83%, and specificity is 86%.[22]

Cytokeratins (CKs) are generally thought to be the very important markers of epithelial differentiation because the specific composition of CKs in epithelial cells reflects not only cell type but also differentiation status. The use of CKs in the distinction of benign epithelial proliferations from DCIS has been previously investigated. It is reported that immunohistochemical expression of the 2 cytokeratins which are CK5/CK6 and CK14 can aid in evaluating papillary breast lesions to differentiate the benign papilloma from the malignant in situ papillary carcinoma.[23] Further study of CKs for papillary breast lesions might be expected well.

As for lymph node, generally DCIS cannot give axillary lymph node metastasis by definition. Therefore, axillary dissection is not indicated. Moreover, the role of the SLNB in the management of DCIS has not yet been established. SLNB should be considered in the case of DCIS where there exists a strong doubt of invasion at the definitive histology, such as large solid tumors or diffuse or pluricentric microcalcifications undergoing mastectomy. If the SLN is micrometastatic, complete axillary lymph node dissection is not essential.[24] Consequently, it is preferable to diagnose DCIS for ICPC preoperatively on the ground that not only axillary lymph node dissection but also SLNB might be avoidable.

According to the literature about the whole ICPC including DCIS and invasive carcinoma, the mean percentages for nuclear atypia in ICPC were 26% for grade 1, 51% for grade 2, and 23% for grade 3 tumors.[25] Furthermore, research suggests that ICPC is highly hormone-sensitive; 90% of patients with ICPC were shown to be estrogen receptor–positive, 100% were negative for human EGFR-2, and 10% were negative for these markers.[26]

Although bloody intracystic fluid is seen in 88.9% of ICPC cases,[27] bloody fluid is also observed in 76% of intracystic papillomas,[12] making differential diagnosis difficult. With regard to prognosis, the 5-year relative survival rate is reportedly 97.3% and the 10-year relative survival rate is 95.6%, with little difference between the noninfiltrating and infiltrating types.[6] However, tumors with diameters of $\geq$4 cm have metastatic potential.[28] The frequency of lymph node metastases of ICPC ranges from 0% to 25%, which is lower than in ordinary breast cancer.[14,15] According to previous reports, infiltrating cancer is not rare. Intraductal progression of a tumor ($\geq$2 cm) from the cystic wall in the mammary duct has been reported.[12] Importantly, infiltrating cancer can be treated with the same modalities as those used to treat DCIS.

Conclusion

Intracystic papillary tumor of the breast is difficult to differentiate malignancy or benignity by imaging, so pathologic examination is necessary to diagnose it.

It is very important that DCIS for intracystic papillary tumor of the breast is preoperatively diagnosed because not only axillary lymph node dissection but also SLNB might be omitted.

FNA cytology is not effective to get the pathological diagnosis of DCIS for intracystic papillary tumor of the breast and also initial surgical excision prior to FNA and CNB is not recommended proactively.

This report suggests that the initial choice of CNB might be better recommended than both FNA and surgical resection to get the diagnosis of DCIS for ICPC on the first way of diagnosis.

A case of noninfiltrating ICPC was diagnosed based on a preoperative CNB, thus avoiding not only a biopsy by surgical resection and but also axillary lymph node dissection and SLNB.

Acknowledgments

Conflict of interest statement: Keiichi Takahashi who is the author declares that he has no conflict of interest. Keiichi Takahashi declares he has no source of support in the form of grants, equipment, drugs, or all of these.

References

1. Carter D, Orr SL, Merino MJ. Intracystic papillary carcinoma of the breast. After mastectomy, radiotherapy or excisional biopsy alone. *Cancer* 1983;**52**(1):14–19
2. Czernobilsky B. Intracystic carcinoma of the female breast. *Surg Gynecol Obstet* 1967;**124**(1):93–98
3. Gatchell FG, Dockerty MB, Clagett OT. Intracystic carcinoma of the breast. *Surg Gynecol Obstet* 1958;**106**(3):347–352
4. Wilkes AN, Feig SA, Palazzo JP. Breast imaging case of the day: intracystic papillary carcinoma of the breast. *Radiographics* 1998;**18**(5):1310–1313
5. Dogan BE, Whitman GJ, Middleton LP, Phelps M. Intracystic papillary carcinoma of the breast. *AJR Am J Roentgenol* 2003; **181**(1):186
6. Grabowski J, Salzstein SL, Sadler GR, Blair S. Intracystic papillary carcinoma. A review of 917 cases. *Cancer* 2006;**113**(5): 916–920
7. Soo MS, Williford ME, Walsh R, Bentley RC, Kornguth PJ. Papillary carcinoma of the breast: imaging findings. *AJR Am J Roentgenol* 1995;**164**(2):321–326
8. Hashimoto K, Nio Y, Koike M, Itakura M, Yano S. Four cases of intracystic breast cancer. SURGERY 2006;**68**(3):365–370
9. Okita R, Ohsumi S, Takashima S, Saeki T, Aogi K, Nishimura R. Synchronous liver metastases of intracystic papillary carcinoma with invasion of the breast. *Breast Cancer* 2005; **12**(4):327–330
10. Akagi T, Kinoshita T, Shien T, Hojo T, Akashi-Tanaka S, Murata Y. Clinical and pathological features of intracystic papillary carcinoma of the breast. *Surg Today* 2009;**39**(1):5–8
11. McKittrick JE, Doane WA, Failing RM. Intracystic papillary carcinoma of the breast. *Am Surg* 1969;**35**(3):195–202

12. Yamashita A, Yoshimoto Y, Iwase T, Watanabe S, Kasumi F. Clinicopathological images of intracystic breast carcinoma. *J Jpn Surg Assoc* 1994;**55**(11): 2726–2731
13. Hayashi T, Nishida M, Sato K, Yamasaki T, Tamaki K, Hiraide H *et al*. Study of intracystic tumors lesions of the breast experienced at the department. *J Jpn Surg Assoc* 1996;57(10): 2355–2359
14. Inayoshi A, Ogi S, Sawada T, Muramoto K, Moriyasu M, Arita T *et al*. Evaluation of ultrasonography and needle aspiration cytology for intracystic tumors of the breast. *J Jpn Surg Assoc* 1999;**60**(4):893–897
15. Saikawa Y, Kosaka A. Eight cases of intracystic cancer of the breast. *J Jpn Surg Assoc* 1991;**52**(12):2887–2890
16. Mugler K, Marshal C, Hardesty L, Finlayson C, Singh M. Intracystic papillary carcinoma of the breast: differential diagnosis and management. *Oncology (Williston Park)* 2007; **21**(7):871–876
17. Al-Kaisi N. The spectrum of the 'grayzone' in breast cytology. A review of 186 cases of atypical and suspicious cytology. *Acta Cytol* 1994;**38**(6):898–908
18. Solorzano CC, Middleton LP, Hunt KK, Mirza N, Meric F, Kuerer HM *et al*. Treatment and outcome of patients with intraductal papillary carcinoma of the breast. *Am J Surg* 2002; **184**(4):364–368
19. Puglisi F, Zuiani C, Bazzocchi M, Valent F, Aprile G, Pertoldi B *et al*. Role of mammography, ultrasound and large core biopsy in the diagnostic evaluation of papillary breast lesions. *Oncology* 2003;**65**(4):311–315
20. Jacobs TW, Connolly JL, Schnitt SJ. Nonmalignant lesions in breast core needle biopsies: to excise or not to excise? *Am J Surg Pathol* 2002;**26**(9):1095–1110
21. Ivan D, Selinko V, Sahin AA, Sneige N, Middleton LP. Accuracy of core needle biopsy diagnosis in assessing papillary breast lesions: histologic predictors of malignancy. *Mod Pathol* 2004;**17**(2):165–171
22. Noguchi M, Minami M, Earashi M, Taniya T, Miyazaki I, Mizukami Y *et al*. Pathologic assessment of surgical margins on frozen and permanent sections in breast conserving surgery. *Breast Cancer* 1995;**2**(1):27–33
23. Tan PH, Aw MY, Yip G, Bay BH, Sii LH, Murugaya S *et al*. Cytokeratins in papillary lesions of the breast. Is there a role in distinguishing intraductal papilloma from papillary ductal carcinoma in situ? *Am J Pathol* 2005;**29**(5):625–632
24. Veronesi P, Intra M, Vento AR, Naninato P, Caldarella P, Paganelli G *et al*. Sentinel lymph node biopsy for localised ductal carcinoma in situ? *Breast* 2005;**14**(6):520–522
25. Lefkowitz M, Lefkowitz W, Wargotz ES. Intraductal (intracystic) papillary carcinoma of the breast and its variants: a clinicopathological study of 77 cases. *Hum Pathol* 1994;**25**(8): 802–809
26. Calderaro J, Espie M, Duclos J, Giachetti S, Wehrer D, Sandid W *et al*. Breast intracystic papillary carcinoma: an update. *Breast J* 2009;**15**(6):639–644
27. Ikeda G, Suzaki M, Sakai H, Machishi H, Umeda K. A case of male intracystic carcinoma of the breast–review of the domestic cases of this disease. *J Jpn Surg Assoc* 1994;**55**(10): 2537–2541
28. Mulligan AM, O'Malley FP. Metastatic potential encapsulated (intracystic) papillary carcinoma of the breast: A report of 2 cases with axillary lymph node micrometastases. *Int J Surg Pathol* 2007;**15**(2):143–147