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● Original Contribution

CORRELATION BETWEEN ULTRASOUND APPEARANCE OF SMALL BREAST CANCER AND AXILLARY LYMPH NODE METASTASIS

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Abstract—To study the correlation of ultrasonographic signs of small breast cancer (maximum diameter ≤ 2.0 cm) with axillary lymph node metastasis, pre-operative ultrasonographic images of 153 small breast malignant neoplasms in 143 breast cancer patients were analyzed according to their pathologic features. Of the small breast tumors included, 47 showed axillary lymph node metastasis. Diagnosis of all patients was obtained with radical axillary surgery or a sentinel lymph node biopsy procedure. Ultrasonographic signs included irregular shape, microlobulated contour, spiculation, microcalcification, posterior echo attenuation, blood-flow grade, perforating vessels, changes in fascia or Cooper's ligament and maximum cortical thickness of lymph nodes. The relationship between ultrasonographic features and axillary lymph node metastasis was analyzed using a chi-square test for univariate distributions and logistic regression for multivariate analysis. A logistic regression model was established by taking the pathologic diagnosis of lymph node metastasis as the dependent variable and the ultrasonographic signs of each small breast cancer as independent variables. In small breast cancer, characteristics such as perforating vessels and maximum cortical thickness of lymph nodes >3.0 mm correlated well with axillary lymph node metastasis as determined by univariate analysis ($\chi^2 = 13.945, 51.276$, respectively, $p < 0.05$) and multivariate analysis (OR = 48.783, 46.754, respectively, $p < 0.05$). (E-mail:) © 2017 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: Breast neoplasm, Logistic model, Metastasis, Ultrasound, Ultrasonographic pattern.

INTRODUCTION

Santamaría et al. (2005) analyzed 97 masses in 95 breast cancer patients and found that large primary breast tumors were associated with early metastasis and recurrence. The rate of axillary lymph node metastasis in large breast tumors was 30%–35% (Chan et al. 2005; Santamaría et al. 2005), indicating that prognosis was relatively poor. Studies on small breast cancer (maximum diameter <2.0 cm) (Fornage et al. 2004) and small breast cancer with axillary lymph node metastasis are limited (Zhou et al. 2015), and typical ultrasonographic indicators of breast cancer, such as irregular shape, microlobulated contour, spiculated margin, microcalcification, posterior echo attenuation and hyperechoic halo, are often not obvious (Del Frate et al. 2006; Jiang and Li 2007). In this study, ultrasonographic images of 153 small breast cancers were classified by

ultrasonographic indications based on pathologic features. A logistic regression model was established to assess the correlation between the ultrasonographic indications and axillary lymph node metastasis.

MATERIALS AND METHODS

General design and image database

This retrospective study was approved by the institutional review board at People's Hospital of Xinjiang Uygur Autonomous Region (Urumqi, China). All patients provided written informed consent for the breast sonography.

During the period December 2010–January 2015, 183 patients with 201 small breast neoplasms of suspected malignancy (as detected by conventional ultrasound analysis) were enrolled in the study. The management plan for patients included radical axillary surgery or a sentinel lymph node biopsy procedure after the examination. The inclusion criteria included a maximum diameter <2.0 cm. A total of 40 patients with 48 neoplasms were excluded from the

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study because they had no pathologic diagnosis. A total of 153 small breast neoplasms detected in 143 patients were included in the study: 2 found in each of 8 patients, 3 found in 1 patient and 1 found in each of the remaining 134 patients. Therefore, we created a database containing clinical data and digital ultrasound images from a total of 143 patients.

Included in this study were 143 patients age 29–79 y (average age 50.3 ± 10.1 y). Among them, 47 patients were diagnosed with breast cancer with ipsilateral axillary lymph node metastasis. The maximum diameter of the tumor mass was 0.5–2.0 cm, with an average length of 1.5 ± 0.5 cm. Of the 153 small breast neoplasms, 52 were located in the outer upper quadrant of the breast, 18 in the outer lower quadrant, 33 in the inner upper quadrant, 7 in the inner lower quadrant and 43 in the central zone. Surgical resection pathology confirmed that the maximum diameter of each breast tumor was <2.0 cm. Therefore, these cases were considered as small breast cancer.

Equipment and methods

A linear array transducer (5.0–15.0 MHz, LOGIQ E9, GE Medical Systems, Milwaukee, WI, USA) was used at a standard frequency of 12.0 MHz. Breast ultrasonography was performed by three physicians with many years of experience in assessment of breast ultrasounds. A regular breast ultrasonic scan was performed to obtain 2-D ultrasonographic images of the tumor and axillary lymph nodes, determine blood signals surrounding and inside the tumor, measure maximum velocity of blood flow (V_{max}) and resistance index (RI) and observe the spectrum shape of the tumor.

Image analysis

The anonymized image database was analyzed by X.Y., an experienced ultrasonographic deputy director with 10 y of experience in analyzing breast ultrasounds. X.Y. was blinded to the patients' clinical characteristics and histologic results. She evaluated the 153 neoplasms according to the American College of Radiology BI-RADS-US classification system (Mendelson et al. 2002) and the recommendations of the DEGUM definition (Del Frate et al. 2006; Madjar et al. 2006; Nori et al. 2007). The sonographic criteria that were considered suspicious for malignancy included: an irregular shape, microlobulated margin, spiculation, heterogeneous, microcalcification, posterior echo attenuation, the ratio between length diameter and width diameter of neoplasms (length-to-width ratio) > 0.71 , blood flow grade II–III, internal perforating vessel branches, maximum velocity of blood flow (V_{max}) > 15 cm/s, resistance index (RI) > 0.7 , steep rising and declining blood flow spectrum, hyperechoic halo, changes in superficial fascia, changes in deep fascia, changes in Cooper's ligaments, the ratio between long arm

and short arm of lymph nodes (long/short arm ratio) < 2 , maximum cortical thickness of lymph node ≥ 3 mm, the ratio between cortex diameter and medulla diameter of lymph nodes (cortex/medulla ratio) > 1 and blood flow type of peripheral or mixed. Small breast neoplasms containing one or more suspicious malignancy ultrasound appearances were included in the study. A combination of criteria was necessary for diagnosing breast neoplasms as malignant and lymph node metastasis. When a tumor was found positive for one or two suspicious ultrasound signs for malignancy, it was considered suspicious malignant. When a tumor was found positive for three or more suspicious ultrasound signs for malignancy, it was considered malignant. When diagnostic indicators, such as perforating vessel branches, $V_{max} > 15$ cm/s, RI > 0.7 and a steep rising and declining blood flow spectrum shape, were analyzed, a total of 19 small breast neoplasms were excluded because of the absence of blood flow. These neoplasms included four cases of axillary lymph node metastasis; whereas in the other 15 cases not metastasis was found.

The blood flow inside the tumor mass was graded according to the criteria described by Adler et al. (1990). Criteria used are: Grade 0: no blood signal; Grade I: a small amount of blood flow, 1–2 blood spots; Grade II: a medium amount of blood flow, a major bloodstream that is longer than the radius of the lesion or several small vessels; Grade III: adequate blood flow, 4 or more blood vessels, or the presence of blood vessel network.

The most suspicious malignant lymph nodes were analyzed. Lymphadenectasis and metastasis were identified as maximum cortical thickness of axillary lymph nodes > 3.0 mm, long/short arm ratio < 2.0 and cortex/medulla ratio > 1.0 (Deurloo et al. 2003; Duchesne et al. 2005). The type of lymph node blood flow distribution was defined according to criteria described by Yang et al. (2000). No blood flow: no blood signal was detected inside or around the lymph nodes. Hilar type blood flow: blood flowed into the cortex through the lymph node hili and presented a radial distribution. Peripheral type blood flow: blood vessels and perforating branches were detected at the periphery of lymph nodes. Mixed-type blood flow: the presence of both hilar and peripheral types. Peripheral and mixed type blood flow were deemed suspicious malignant.

The 153 resected breast tumors were pathologically categorized according to the histologic and diagnostic criteria of breast tumor by the World Health Organization (Tavassoli and Devilee 2003), which include infiltrating ductal carcinoma, infiltrating lobular carcinoma, ductal carcinoma *in situ*, lobular carcinoma *in situ* and intra-ductal papillary carcinoma. A total of 153 breast tumors in 143 patients were removed by surgical resection or a sentinel lymph node biopsy procedure. Subsequent pathologic screening identified 105 cases of infiltrating ductal carcinoma, 12 cases of infiltrating lobular carcinoma, 18 cases

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