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Breast cancer in very young women (<30 years): Correlation of imaging features with clinicopathological features and immunohistochemical subtypes

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ABSTRACT

Objective: Early diagnosis of breast cancer in very young women (<30 years) is challenging and the characteristic imaging findings are not yet fully understood. We evaluated the imaging findings of breast cancer in very young women (<30 years) and to correlate them with clinicopathological features.
Material and Methods: A total of 50 surgically confirmed breast cancers were included in our retrospective study. The medical records were reviewed and the radiological features were analyzed according to the new 5th edition of the ACR BI-RADS lexicon.
Results: The breast cancers in our study population most commonly presented as a self-detected mass (74%), T2-3 stage (58%), histological grade III (52.3%) and ER-positive (80%) subtype. The most common finding was an irregular (87.5%) hyperdense (66.7%) mass with indistinct margins (50%) on mammography and an irregular (75.6%) indistinct (57.8%) hypoechoic/heterogeneous (77.8%) mass without a posterior acoustic feature (60%) on ultrasonography. MRI revealed an irregular shape (63.3%), irregular margins (43.3%), and heterogeneous enhancement (60%) with washout kinetics (69.4%). Mammographically, microcalcifications were correlated with the HER2-enriched type, and mass-type lesions were correlated with triple-negative cancer ($p = 0.04$). An oval/round mass on ultrasound ($p = 0.005$), rim enhancement ($p = 0.004$) and intralesional T2 high signal intensity ($p = 0.04$) on MRI were associated with the triple-negative type.
Conclusions: On all imaging modalities, breast cancer in very young women usually presented as an irregular mass, and certain radiological features could be used for predicting the specific tumor type.

1. Introduction

Breast cancer is rare in very young women. Women less than 30 years of age account for approximately 0.65 % of all breast cancers in Western countries [1–3] but for more than 3.1 % of cancers diagnosed in Asian countries [4]. Although the diagnosis of breast cancer in very young women (<30 years) is uncommon, it can have a greater impact than in older counterparts. Breast cancer occurring at a young age tends to present at a later stage, be more aggressive and have a poorer prognosis [2,4–8]. Previously published studies have also shown that tumors in younger women are more frequently poorly differentiated and estrogen receptor-negative and that they have a higher proliferating fraction and more lymphovascular invasion [6,9,10]. However, early diagnosis of breast cancer in very young women is challenging because they are excluded by standard screening program guidelines. Moreover, the accuracy of both physical examination and mammography is lower in this age group due to denser breast tissue compared with older women [11–15]. Additionally, the characteristic imaging features in very young women (<30 years) are not yet fully understood.

In 2013, the 5th edition of the American College of Radiology (ACR) Breast Imaging Reporting and Data System (ACR BI-RADS,

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5th edition) was updated to provide further clarification of image interpretation and to standardize lesion terminology and reporting. The revised BI-RADS provides uniform terminology in the lexicon across all three imaging modalities: mammography, ultrasound (US), and magnetic resonance imaging (MRI) [16]. There have been several reports on the radiological features of breast cancer in young women with different age cut-offs [17–19], but most studies did not use the revised BI-RADS.

Therefore, the aim of our study was to evaluate the characteristic imaging features of breast cancer in very young women (<30 years) using the updated BI-RADS. A further aim was to correlate the clinical and imaging features with tumor molecular subtype in this age group.

2. Materials and methods

2.1. Patients

Our institutional review board approved this study, and the requirement for informed consent was waived. Of the 1382 consecutive patients who underwent surgery to treat breast cancer in our institution from March 2009 through September 2012, a total of 50 women under 30 years of age were included in our study. The patients ranged in age from 14 to 30 years, with a mean age of 27.3 years. Clinically evaluated data included age, indication (screening or diagnostic) and clinical manifestation (palpable mass, nipple discharge and others), family history (first-degree relatives or no relatives), and personal history (underlying conditions such as hematologic malignancy or pregnancy).

2.2. Radiological evaluation and interpretation

Mammograms were available for 41 patients, US for 47 and MRI for 36. For the mammograms, standard craniocaudal and mediolateral oblique views were obtained using a Mammomat 3000 unit (Siemens Medical Solutions, Solna, Sweden) and a Lorad M3 mammography unit (Hologic, Inc., Boston, MA). In our institution, mammography is not routinely performed in women under 40 years of age, and US is used as the initial imaging modality in young women. If a sonographically suspicious finding is detected and the biopsy result is malignant, mammography is recommended for the detection of additional malignant foci. The US images were acquired using a 7–15 MHz linear probe (iU22 Ultrasound System, Phillips Ultrasound; Bothel, WA, USA) and a 6–14 MHz linear probe (EUB-8500 scanner, Hitachi Medical, Tokyo, Japan). The MRI scans were acquired with the patient in the prone position in a 3.0T scanner (Magnetom Verio; Siemens Medical Solutions, Erlangen, Germany) equipped with a breast coil. The MR images with the Verio scanner were acquired using the following sequences: an axial, turbo spin-echo T2-weighted imaging sequence (TR/TE 4530/93 ms, flip angle 80°, 34 slices with FOV 320 mm, matrix 576 × 403, 1 NEX, 4 mm slice thickness, acquisition time 2 min 28 s) and a pre- and post-contrast axial T1-weighted flash three-dimensional VIBE sequence (TR/TE 4.4/1.7, flip angle 10°, 1.2 mm slice thickness with no gap, acquisition time 60 s) obtained before and at 7, 67, 127, 187, 247, and 367 s after a bolus injection of 0.1 mmol/kg Gd-DPTA. All mammography, US, and MRI findings were retrospectively interpreted by two breast radiologists with 5 and 13 years of experience without knowledge of the image findings of other modalities. All lesions were interpreted using the morphological criteria described for mammography, US, and MRI in the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) lexicon, fifth edition [16].

2.3. Pathological analysis

The pathological reports were reviewed to determine the tumor size, histological grade, the presence of axillary lymph node metastasis, perineural invasion, vascular invasion and lymphatic invasion. Each patient's ER, PR and HER2 status was determined by immunohistochemical analysis. The Allred score was used to determine the ER and PR status. The results were classified as positive when the total score, expressed as the sum of the proportion and immunointensity scores, was 3 or more. With regard to the HER2 evaluation, tumors with a 3+ score were classified as HER2-positive, and tumors with a 0 or 1+ score were classified as negative. In tumors with a 2+ score, gene amplification using FISH analysis was used to confirm the HER2 status. Ki-67 of more than 15% was considered positive expression. By immunohistochemical definition, breast cancer tumors are clinically categorized into one of three major subtypes to facilitate targeted therapy – ER-positive (luminal type, A or B), HER2-enriched or triple-negative. We categorized the breast cancers into one of the following three major subtypes—ER positive, HER2 positive or triple-negative breast cancer (TNBC)—using three standard immunohistochemical markers.

2.4. Statistical analysis

The data were processed using SAS version 9.2 (SAS institute, Cary, NC, USA). Student's unpaired *t*-test or one-way ANOVA was used to examine differences in continuous variables, and the Chi-square test or Fisher's exact test was used for categorical variables. Significance was assumed for p-values < 0.05.

3. Results

3.1. Clinical data

The clinicopathological characteristics of the 50 cases are shown in Table 1. Three patients were pregnant at the time of diagnosis. Family histories of breast cancer in first- or second-degree relatives were noted for three patients. The results from testing for BRCA mutations were available for two patients but none had the mutations. In our study, 39 out of 50 tumors (78%) were detected by clinical symptoms, and 11 out of 50 tumors (22%) were asymptomatic. These 11 asymptomatic patients were planning a pregnancy and US examinations were performed at the patients' own request (Fig. 1). Tumor sizes ranged from 0.8 to 9.8 cm (mean 3.4 cm), and T2-3 tumors accounted for 58% of all cases. The mean size of tumors in symptomatic patients was 3.8 cm (range: 0.8–9.8 cm), whereas it was 1.8 cm (range: 0.8–3.3 cm) for tumors detected by screening. The rate of breast-conserving surgery with axillary dissection (76%) was higher than the mastectomy rate (24%). The axillary lymph nodes were positive in 42% of patients. Invasive ductal carcinoma (IDC) was the most common breast cancer type (72%), followed by DCIS (12%). Of the invasive ductal carcinomas, 52.3% were high-grade tumors (grade III). The most frequent tumor subtype by immunohistochemistry was ER-positive (luminal A 60%, luminal B 20%), followed by triple-negative (12%) and HER2-enriched (8%).

3.2. Imaging

3.2.1. Mammography

Mammography was available in 41 patients, and the mammographic findings of the 41 cases are shown in Table 2. In 9 out of 11 asymptomatic patients, diagnostic mammographic examinations were additionally performed after suspicious lesions were detected on US screening and were confirmed to be malignant by core