The Breast 20 (2011) 495–500

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

Clustered microcalcifications of intermediate concern detected on digital mammography: Ultrasound assessment

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ARTICLE INFO

Article history:
Received 4 December 2010
Received in revised form
3 May 2011
Accepted 8 May 2011

Keywords:
Digital mammography
Microcalcifications
Cluster
Microcalcifications
Amorphous
Coarse heterogeneous
Ultrasound

ABSTRACT

To report our experience with targeted-ultrasound in assessing 142 cases with clustered microcalcifications of intermediate concern detected on digital mammography. All cases had histopathologically-proven microcalcifications within the biopsied or surgical specimens. There were 30%[43/142] breast cancers and 70%[99/142] benign lesions. Only 26%[37/142] of clustered microcalcifications were identified on targeted-ultrasound and other findings including negative study ($n = 33$), anechoic ducts or cysts ($n = 70$), dilated ducts with echogenic content ($n = 13$) and hypoechoic nodules ($n = 26$). There was no statistical difference of the frequency of negative ultrasound between benign and malignant microcalcifications ($P = 0.071$). However, only 7.1%[5/70] cases with anechoic ducts or cysts were proven to be breast cancer. The frequencies of depiction of dilated ducts with echogenic foci or hypoechoic nodules were significantly higher for malignant microcalcifications ($P < 0.001$). Ultrasound was significantly more sensitive for the identification of malignant cases but biopsy of clustered microcalcifications is still warranted when targeted-ultrasound revealed negative findings.

Introduction

Screening mammography has been advocated as an effective tool for reduction of the death rate from breast cancer among women >40 years of age.[1,2] The reduction is higher among women >50–69 years (16–35% reduction) than women <40–49 years of age (15–20% reduction).[1–3] The smaller reduction of death rate in women <50 years of age is probably due to the presence of more rapidly growing tumors and radiographically dense breasts which may reduce the sensitivity of mammography.[4,5] Digital mammography can improve the degree of contrast and thus enhance the detection of early breast cancer and microcalcifications, even in dense breasts.[1,6] The Breast Imaging Reporting and Data System (BI-RADS) has standardized the description and management of findings seen on mammograms.[7,8] The microcalcification descriptors "pleomorphic" and "fine-linear" indicate a high probability (50–80%) of malignancy and thus biopsy or appropriate action should be taken. In contrast, the descriptors "coarse heterogeneous" and "amorphous" are of intermediate concern with only a relatively low probability (6–20%) of malignancy, leading to a high rate of negative imaging-guided biopsy.[7–9] As with microcalcifications in a ductal distribution (segmental or linear) highly suggestive of ductal carcinoma in situ, clustered distribution also represents an intermediate risk of malignancy.[8,9] With wider adoption of digital mammography for breast cancer screening, a higher rate of detection of microcalcifications than the conventional screen-film method can be expected. Recent studies have shown that ultrasound (US) is useful in identifying malignant microcalcifications for US-guided procedure as an alternative to the time-consuming stereotactic method.[10–16] However, the significance of US features in patients with clustered coarse heterogeneous or amorphous microcalcifications has not been well addressed. We report our experience with targeted-US in the assessment of clustered microcalcifications of intermediate concern without other abnormalities detected on digital mammography.

Materials and methods

Patients

We searched the digital mammography data bank of our department from January, 2005 to December, 2009 and reviewed

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doi:10.1016/j.breast.2011.05.003

the medical records and mammograms of patients with morphologic microcalcification descriptors such as "coarse heterogeneous" and "amorphous" (i.e. breast microcalcifications of intermediate concern) as well as the distribution descriptor, "cluster". The inclusion criteria were (1) mammographically detected clustered coarse heterogeneous or amorphous microcalcifications without any other abnormalities such as associated masses or architectural distortions, (2) preoperative mammographically-directed targeted-US for evaluation of the site of microcalcifications, (3) subsequent biopsy (US-guided or stereotactic mammographically-guided core biopsy) or surgery (US-guided or stereotactic hookwire localization with immediate mammographic follow-up) and (4) specimen radiography and/or histopathological proof of the presence of microcalcifications. This retrospective study was approved by the institutional review board of our hospital and informed consent was waived due to the retrospective and anonymous nature of the analysis.

Digital mammographic and US procedures

Digital mammography (Selenia; Hologic, Danbury, CT) was performed with standard mediolateral oblique and craniocaudal images of the breasts in each patient; additional spot compression magnification images of areas of microcalcification were also obtained in all except five patients. All mammographic images were evaluated on a high-resolution monitor (Barco View, MGD 521MK II, Kortrijk, Belgium) via a picture archiving and communication system (PACS) (Centricity Workstation, version 2.0, General Electric Healthcare, Milwaukee, WI, USA). The mammographic report was done using the descriptors and classification described in the 4th edition of the Breast Imaging Reporting and Data System (BI-RADS) published by the American College of Radiology. Of note, the morphologic descriptor "coarse heterogeneous microcalcifications" indicates the presence of coarse irregular, conspicuous calcifications (>0.5 mm) which tend to coalesce with a somewhat coral-like appearance. The morphologic descriptor "amorphous microcalcifications" indicates the presence of tiny, hazy indistinct calcifications sufficiently small that a more specific morphologic classification cannot be assigned. The distribution descriptor "clustered" indicates >5 microcalcifications per cm^3.[7–9]

US examinations were performed by one of two radiologists who had 10–17 years experience with breast imaging. A Sequoia 512 scanner (Acuson, Mountain View, CA) with a 15 MHz linear transducer (with maximal setting at 14 MHz) was used. For the patients with large breasts, additional evaluation of the deep part of the breast with an 8- or 10-MHz transducer was also done. All US evaluations were performed with the patient lying supine and with both arms raised above the head. Routine scanning of the entire breast and axillary regions were performed. Afterward, US evaluation was targeted to the suspected site seen on the mammograms with thorough scanning in the sagittal and transverse directions to assess the lesion, if present, in three dimensions. This was followed by evaluation in the planes radial and antiradial to the nipple to detect subtle abnormalities extending toward the nipple along the ductal system. All detected lesions were labeled on US images using a traditional quasigrid pattern by viewing the breast as a clock face. The distance of the lesion from the nipple and the depth of the lesion were also recorded. All US images then were sent to the PACS for review.

Core biopsies were performed with a multi-pass automated gun and a 14- or 16-gauge needle (Bard, Covington, GA, USA). In the presence of hyperechoic spots suggestive of microcalcifications on targeted-US, US-guided biopsy of the suspected lesions using a Sequoia 512 scanner and follow-up specimens mammograms were performed. For microcalcifications seen on mammography alone, stereotactic biopsy was performed using a prone table (LORAD Multicare Platinum, Hologic, Beford, MA). For patients with suspicious malignant lesions without visible microcalcifications seen on targeted-US and the patients who requested for surgical removal of the lesions, US-guided or stereotactic mammographically-guided hookwire localization for open surgical excision were performed. Post-procedure craniocaudal and true lateral mammograms were followed after hookwire insertion to confirm appropriate localization of the microcalcifications and to provide the surgeon with reference images. Specimen radiography was obtained after core biopsy or surgical excision to confirm the presence of microcalcifications in the specimen. Histopathologic results from each core biopsy and surgical excision were reviewed. For patients undergoing core biopsy of the microcalcifications followed by surgical excision, the final surgical pathology results were used to avoid underestimation of the disease process.

Data and statistical analyses

The percentages of US detection of clustered coarsen heterogeneous and amorphous microcalcifications demonstrated on digital mammography among benign and malignant lesions were calculated. US findings were categorized into 4 patterns: negative findings, anechoic ducts or cysts, dilated ducts with echogenic content and presence of nodule. The shape, contour and presence of posterior acoustic shadowing were also recorded. The chi-square test was used to compare differences between the frequencies of benign and malignant lesions in each US group. Findings with a p value <0.05 were considered statistically significant.

Results

Out of 15507 mammographic studies, there were 252 patients with clustered coarse heterogeneous or amorphous microcalcifications for an overall prevalence of 1.6%. Among these patients, 84 whose mammograms demonstrated masses or parenchymal traction associated with clustered microcalcifications were excluded. Twenty patients (35%[7/20] with coarse heterogeneous and 65%[13/20] with amorphous microcalcifications) were excluded because no pre-procedure US was available since the surgeons requested for direct hookwire localization (85%[17/20]) for open surgical biopsy or stereotactic mammographically-guided biopsy (15%[3/20]). Among these 20 cases, the percentage (35%[7/20]) of cases with coarse heterogeneous microcalcifications, which were more likely to be detected on US, was higher than that of 142 cases (29.60%[42/142], indicating that there was no selection bias to include more US detectable microcalcifications in the present study. Two patients in whom the clustered coarse heterogeneous microcalcifications could not be found on US and stereotactic localization was not successful were also excluded for the patients refused further intervention and the microcalcifications appeared stable on annual mammographic follow-up for two and three years respectively. Four patients refused further management and were lost to follow-up. A total of 142 patients (age range, 27–77 years; mean, 49 years) with clustered coarse heterogeneous (29.6%[42/142]) and amorphous (70.4%[100/142])) microcalcifications fulfilled the inclusion criteria and constituted our study population. There were 43 (30%) breast cancers and 99 (70%) benign lesions and all patients had specimen radiographs and/or histopathological proof of microcalcifications.

The visibility of microcalcifications on targeted-US among the various benign and malignant pathologies is summarized in Table 1. Of the 142 clustered microcalcifications, 26%[37/142] of cases with hyperechoic spots suggestive of microcalcifications were identified within the lesions on targeted-US including: (a) anechoic ducts or