ORIGINAL ARTICLE

MAMMOGRAPHIC PARENCHYMAL PATTERNS IN SOLID BREAST TUMORS

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ABSTRACT

OBJECTIVE: To determine the frequency of various breast parenchymal patterns on mammography and an association of the presence of a solid tumor with any pattern. **STUDY DESIGN:** Analytical descriptive study **DURATION AND SETTING:** January 2009 to September 2010, at Radiology department, Dow Medical College/ Civil Hospital (DUHS), Karachi. **METHODS:** Adult females diagnosed with single solid breast lesion placed in BIRADS category II-VI on mammography and ultrasound, were included. The parenchymal pattern of breast was classified into predominantly fatty (N1), < 25% glandular (P1), > 25% glandular (P2) and very dense glandular tissue (DY) according to Wolffe's classification. Those with multiple lumps, ductal dilatation, chemo or radiation therapy to breast, or recent hormonal or contraceptive use were excluded. The overall data was described as measures of central tendency and dispersion. Significance of association was determined using chi square test at P<0.05. **RESULTS:** There were a total of 76 patients with mean age of 47.6 ± 10.45 years; 74 (97.4%) were married with average parity of 4.5 ± 2.8 and 64 (84.2%) had lactated. Lesions included 65 (82.2%) carcinomas, 10 (10.5%) fibro adenomas and 01 (1.3%) lipoma. The distribution of parenchymal patterns was found to be 22.4% N1, 44.7% P1, 26.3% P2 and 6.6% DY patterns. There was a strong association of P1 and P2 patterns with solid breast lesions (p=0.024). The overall association of carcinoma with P1 and DY patterns was also significant (p= 0.041). **CONCLUSION:** Scattered fibro glandular and heterogeneously dense mammographic parenchyma had a strong association with presence of solid malignant lesion in breast. These findings are incongruous with the reported patterns from the West and may represent inherent oncogenic characteristic in Pakistani ladies.

Key words: Mammography, breast parenchyma, parenchymal pattern, solid lesion, carcinoma, Wolffe's classification

Introduction

Breast cancer (ca) is leading cause of death in females.[1] One million cases are reported annually worldwide, 42% of whom occur in developing countries.[1] In Pakistan, it is the commonest cancer of females accounting for one fourth of all malignancies.[2] Early diagnosis of breast cancer is made possible by mammography which is a specific type of imaging in which low dose radiation are used for examination of breast.[3] It is a proven sensitive screening tool for early detection of Ca breast,[4] with sensitivity ranging from 65-91%.[4]

The mammographic image of the breast density is a combination of radio dense areas formed of epithelial and stromal tissues and radiolucent zones which represent fat or adipose tissues.[5] The relative fibro glandular and fatty content in an individual changes the breast tissue density,[5] and therefore affects the sensitivity and accuracy of cancer detection.[5] As the density of breast parenchymal increases, sensitivity of mammography decreases.[3] Apart from that, breast

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density *per se* is considered an independent risk factor for the development of breast cancer.[6] The breast density is affected by age, parity, lactation, and hormonal therapy.[6]

In 1976, Wolfe was the first to describe the mammographic appearance of breast parenchymal patterns as an index of risk for developing breast cancer.[7] He placed mammographic densities according to parenchymal patterns into four groups; N1 being predominantly fatty density , P1 being < 25% heterogeneously dense scattered fibro glandular tissue, P2 being > 25% heterogeneously dense fibro glandular tissue, and DY predominantly very dense glandular tissue.[7] Sickles later on validated these patterns and found these to be an accurate predictor of the possible risk of breast cancer, with N1 having the lowest and DY having the highest risk of breast cancer.[8]

The rationale of this study was to evaluate the breast parenchymal patterns of local population with particular reference to the presence of solid breast tumors. This in the context of its unique socio-cultural setup where early pregnancies and breast feedings are a norm and breast density is expected to be different with the Western women. No published data on breast parenchymal patterns is yet available from Pakistan; the result of this study will identify the suspicious breast parenchymal patterns that are associated with the presence of solid breast tumors, and should be more closely followed up. It is the first study to identify the breast parenchymal patterns in Pakistani women.

The precise objective of this study was to determine the proportion of various parenchymal patterns of breast parenchyma in adult females seen on x-ray mammogram and determine their association with presence of solid breast tumors at

Methods

This analytical study was conducted by a retrospective review of records of patients undergoing mammography from January 2009 to September 2010, at Radiology department, Dow Medical College/Civil Hospital (DUHS), Karachi. It included all those adult female patients who presented with breast lumps, underwent x-ray mammography and ultrasound and were found to have a solid breast tumor (either benign such as fibroadenoma and lipoma or a carcinoma) later confirmed with histopathology. Solid breast tumor was defined as a space occupying lesion in breast visible on mammography and ultrasound as having a solid, non-liquefied appearance.[3] Those found to have a cystic component or necrosis involving more than a quarter of the size in three dimensions, intracystic carcinoma and those with incomplete records were excluded. BI- RADS categories 2, 4, 5 and 6 were included. Those with BI-RADS 1 (needing additional imaging) or BIRADS 3 (needing follow up) were excluded. Those with history of hormonal therapy or contraceptives in the last one year were also excluded.

The sample size was 76 patients based on 95% (Confidence interval), p=0.12% (expected population proportion for solid tumors),[3] and 0.05 (margin of error).

Verbal/ written consent was taken from every patient at the time of mammography for the procedure and later use in research study on the condition of anonymity. Institutional ethical approval was not requested this being a retrospective, non- interventional research. Data was collected on a purposive structured Performa. After history taking and breast examination, mammography was performed on Planned Sophie classic RFH 40822. Standard mediolateral oblique (MLO) and cranio-caudal (CC) projections were obtained along with additional views (cone compression, magnification) if and when required. The patients were then subjected to high frequency ultrasound of breast to confirm the solid nature of tumor. Studied variables included age, parity, and family history of breast cancer, menstrual/ marital/obstetrical history, and presence of lump, parenchymal patterns, mammography findings and ultrasound findings. Mammography and ultrasound were reported and confirmed by the consultant radiologist (FCPS with women imaging training and experience in mammography) for evaluation of abnormalities and the breast parenchymal patterns. The diagnosis of lesion seen on mammography was made by the consultant Radiologist and confirmed on follow up with the referring clinician.

The statistical analysis was performed by using SPSS Version 17. Frequencies and percentages were calculated for categorical variables like marital status, use of oral contraceptive pills, and frequency of parenchymal patterns. Mean and standard deviation were

calculated for quantitative variable like age and parity. Association of parenchymal patterns with presence of breast tumor was determined by comparing proportions using chi-square test with significance at $p<0.05$.

Results

There were a total of 76 patients with mean age of 47.6 ± 10.45 years ranging from 30-75 years; 74 (97.4%) were married with average parity of 4.5 ± 2.8 (range = 0-12, mode = 5 in 15 i.e. 19.7%); and 64 (84.2%) had lactated. Only one lady (1.9%) had a positive history family history of breast cancer. Three patients (3.9%) had used oral contraceptive pills in the past.

The clinical diagnosis on the referral sheet was malignant mass in 65 cases (85.5%) and benign lump in 10 (13.2%) cases. One sheet only stated palpable axillary nodes. The overall distribution of parenchymal patterns was predominantly fatty (N1) in 17(22.4%), fatty with scattered fibro glandular (P1) in 34 (44.7%), heterogeneously dense (P2) in 20 (26.3%) and dense (DY) in 05(6.6%). Mammographic lesions included 65 (82.2%) carcinomas, 10 (10.5%) fibro adenomas and 01 (1.3%) lipoma. Distribution of parenchymal patterns in different BIRADS categories is given in (Tab. 1), and in benign and malignant lesions overall is given in (Tab. 2).

There was a strong association of P1 and DY patterns with solid breast lesions (p=0.024). The overall association of carcinoma with P1 and DY patterns was also significant (p= 0.041).

Variable	BI-RADS 2	BI-RADS 4	BI-RADS 5	BI-RADS 6	Total
Predominantly fatty (N1)	0	14 (27.5%)	3 (20%)	0	17 (24%)
Fatty with scattered fibroglandular pattern (P1)	3 (33.3%)	22 (43.1%)	9 (60%)	0	34 (44.7%)
Heterogeneously dense (P2)	3 (33.3%)	14 (27.5%)	2 (13.3%)	1 (100%)	20 (26.3%)
Predominantly dense (DY)	3 (33.3%)	1 (2%)	1 (6.7%)	0	5 (6.6%)
	9 (100%)	51 (100%)	15 (100%)	1 (100%)	76 (100%)

Table 1: Distribution of parenchymal patterns in BIRADS categories assigning a definite category (N= 76)

Variable	Benign	Malignant	Total
Predominantly fatty (N1)	0	17	17
Fatty with scattered fibroglandular pattern (P1)	3	31	34
Heterogeneously dense (P2)	3	17	20
Predominantly dense (DY)	3	2	5
	9	65	76

Table 2: Distribution of parenchymal patterns in benign and malignant lesions

Discussion

Previous local studies on dense breast imaging found a small proportion of malignancy. This study evaluated the mamographically dense breast in another perspective and found the results incongruous with the west as well the previous local studies.

Despite the multiparity and lactation, majority of the ladies with a solid breast had a rather dense glandular breast parenchymal pattern occupying more than 2 quarters of the breast. This translates to the presence of greater amount of glandular tissue that is said to be a risk factor in the causation of breast malignancy. While the American College of Radiology (ACR) recommends breast density grades, and automated computer based percent density measurements and parenchymal segmentation are available,[9] A recent study comparing the percent density and parenchymal patterns and coarseness on mammography concluded that high-risk and low-risk women have different mammographic parenchymal patterns with significantly higher difference in the parenchymal patterns than the breast percent density alone.[10]

Till now, this was the first study conducted in Pakistani women with solid breast to evaluate their association with the mammography based breast parenchymal patterns. The previous local studies have only concentrated on determining whether any additional pathology could be determined by ultrasound in dense breasts;[11,12] They found a rather low percentage of malignancy in the denser breast. Ghaffar et al. found only 2 malignancies in a 100 ladies with BI-RADS grade 3 and 4 (higher grades) density.[11] Masroor et al. found only one malignancy in 76 patients with dense breasts.[12] So the authors decided to evaluate

a different approach that was to study the breast parenchymal patterns in Pakistani ladies having solid breast lumps which was not studied previously. This has important implications as Pakistan has a high breast cancer incidence. Pakistani immigrants to other regions may carry this tendency abroad where screening mammography is diligently practiced so that relevant data must be available.

It was found that majority of these ladies had a heterogeneous dense breast. This was despite excluding those on recent or current hormonal therapy whether for replacement or contraception, to control the confounding effect of hormones on breast texture. The majority had more than 4 children and had breast fed them. This theoretically has the effect of reducing the breast density as the proportion of breast adiposity increases in parous, post-lactation females with a consequent decrease in breast density, which was not seen in the studied group of patients. This certainly raises further questions for future research on this aspect.

Most of these ladies had a P1 and P2 patterns. This is certainly different from all the available literature that states that P2 and DY are the patterns at risk.[7,8,13] It may well represent an epidemiological variation inherent to Pakistani women and again strengthens the need to look for unknown genetic factors which might be at play.

Gosh et al. followed the lobular involution and breast patterns in women diagnosed with benign breast disease for an average of 13 years and concluded that those with P1 were at 1.23 times, those with extremely dense breast (DY) at 1.6 time and those with P2 at 1.96 times increased risk of developing cancer.[14]

The main limitation of this study is that it is a single-center, retrospective study. The BI-RADS density grading was not applied as the authors were more interested in determining the hitherto undetermined parenchymal patterns in the adult Pakistani ladies, rather than the density grades which have been extensively studied particularly in the context of mammography and ultrasound. This in fact is one of the unique and novel features of this research that it has determined these patterns for the first time in Pakistan.

Another limitation of the study is visual evaluation of the parenchymal pattern instead of computer aided detection. The latter has come up as a strong and sensitive tool,[9] however it is costly and subject to technical variations. In a recent published study comparing raw and processed digital mammograms (DM), it was concluded that features of processed versus raw DM depended highly on the DM vendor, and image acquisition settings.[15] The mammograms studied in this study were all digital mammograms processed at standard settings.

Another limitation is that the authors had applied the Wolffe system of classification in the current study. A more recent classification is that of Tabár I-V MPP classification system.[15] This was not applied due to non-familiarity with that classification system. However population based studies have shown a wide distribution of parenchymal patterns that may affect the cancer risk even with this latter system.[16]

Conclusion

Scattered fibro glandular and heterogeneously dense mammographic parenchyma had a strong association with presence of solid malignant lesion in breast. These findings are incongruous with the reported patterns from the West and may represent inherent oncogenic characteristic in Pakistani ladies.

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