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Imaging and Pathological Correlation in Spectrum of Fibrocystic Breast Disease and its Mimics – our Experience

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ABSTRACT

Background: Fibrocystic change (FCC) of the breast is one of the most common benign breast diseases commonly observed between 20-50 years, with a peak in the perimenopausal age group. Patients present with various symptoms such as lump in the breast, mastalgia (commonly related to the menstrual cycles) or nipple discharge.

Materials and Methods: In our retrospective study, which included 172 patients, the imaging findings were observed by ultrasound and X-ray mammogram. Based on the Breast Imaging Reporting and Data System (BI-RADS) guidelines given by the American College of Radiology (ACR), our imaging findings were classified as BI-RADS 2 in benign lesions, and complicated cysts were classified as probably benign - BI-RADS 3. Indeterminate findings were classified as suspicious lesions and BI-RADS 4a/b/c. Imaging and histopathological correlation was performed.

Results: Ultrasound findings revealed diffuse/bilateral abnormalities with the most common finding being simple cysts followed in descending order by complicated cysts, clustered cysts, complex solid cystic masses, solid lesions, duct ectasia, and intraductal lesions. Mammogram showed dense (type C or D) fibro glandular pattern obscuring the lesions, followed by well-defined/partly obscured opacities. Simple cysts and complicated cysts showed predominant features of cyst formation on HPE. Atypical hyperplasia was seen in ductal and complex solid cystic mass lesions.

Conclusion: It is essential for radiologists to be familiar with imaging and pathological findings of fibrocystic disease of the breast for further workup and management.

INTRODUCTION

Fibrocystic change (FCC) of the breast is a benign alteration in the terminal ductal lobular unit of the breast. It is one of the common diseases encountered in day-to-day practice. FCCs are commonly observed among women of the reproductive age group, between 20 and 50 years, with a peak in the peri-menopausal age group.[1-3] Cole *et al.* observed that the age standardized incidence rate for fibrocystic diseases was 89.4 per 100,000 woman years.[1]

FCCs commonly have diffuse, multifocal abnormalities affecting both breasts. Clinical presentation is usually mastalgia, lump in the breast, or nipple discharge. The lesions arise from the terminal ductal lobular unit (TDLU) due to aberrations in the TDLU resulting in various imaging and pathological manifestations. Evaluation is done using imaging modalities like ultrasound, X-ray mammogram and MRI. BIRADS assessment is done using American College of Radiology (ACR)

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guidelines and suspicious lesions need further pathological analysis. In this study, we evaluated the various imaging manifestations of FCC on ultrasound and X-ray mammogram with further histopathological correlation.

This study was carried out to evaluate the radiological presentation of FCC and to correlate them with histopathological examination. We consider this topic on the spectrum of fibrocystic changes (FCC) and its mimics as FCC is one of the most common benign diseases. Although it commonly presents as benign appearing cysts, it can sometimes appear as suspicious lesions. Hence, an effort was made to review the various imaging appearances of FCC along with histopathological correlation for better understanding of the different imaging appearances of fibrocystic disease spectrum.

MATERIALS AND METHODS

Study setting and participants

This retrospective study was carried out among all the patients with pathological/radiological diagnosis of fibrocystic disease in our tertiary teaching institution for a period of 16 months. Data of 172 women were entered and analyzed in this study.

Selection criteria

Patients with either radiological or pathological diagnosis of fibrocystic disease were included. The radiological diagnosis was made in line with the 5th edition of ACR BI-RADS. The pathological criteria included features of adenosis, fibrosis and cyst formation. Features like apocrine metaplasia or columnar cell metaplasia in the biopsy/excision specimens were also considered. Other parameters included sclerosing adenosis, intraductal papilloma and ductal hyperplasia with or without atypia.

Patients with breast malignancy diagnosed by either radiology or histopathology were excluded.

Data collection

Participants under 40 years of age underwent breast ultrasound and participants over 40 years underwent X-ray mammogram with ultrasound correlation. In participants who were symptomatic and had dense glandular parenchyma, ultrasound screening was performed in addition to X-ray mammography.

Computed radiography (CR) mammogram was performed using GE Alpha ST® machine (Exposure parameters -35kV, 100mA). Digital X-ray mammography (automated exposure) was performed using Fujifilm AMULET Innovality® machine. Ultrasound breast and guidance for interventions was done using Toshiba Aplio® 500 ultrasound machine using linear high frequency probe (6-10 MHz). Depending on the imaging findings, the appropriate BI-RADS category was assigned based on the recent American College of Radiology (ACR) BI-RADS guidelines (5th edition).[4]

Ultrasound guided intervention was performed in all the lesions categorized under BIRADS4a/b/c. BI-RADS 3 lesions were either followed up or intervention was performed for symptomatic relief to reduce the patients' anxiety in cases of strong family history of breast cancer. BI-RADS 2 lesions were termed as benign and intervention was performed if the cyst was large and causing discomfort to the patient.

Ultrasound guided fine needle aspiration (FNA) was done using 24 Gauge needle and slides were prepared and sent for cytological analysis. Ultrasound guided core biopsy was done using 14 gauge, 10cm length needle and the tissue samples obtained were sent for histopathological correlation. The pathology results and the imaging findings were retrospectively analyzed.

Overall, 62% of the lesions were identified on ultrasound and most of the lesions (62%) were assigned to BI-RADS 2 category. Simple cysts were the most common pathology (65.7%) identified followed by complicated cysts (50 %) and clustered cysts (45%) being the next commonly identified lesions in the FCC spectrum.

Pathologically simple cyst formation (45%) was the most commonly identified finding and ducts with apocrine metaplasia epithelial hyperplasia without atypia were the second most common finding (24%).

RESULTS

The age distribution of the study population was from 21 to 80 years, with a mean age of 43 years. Ultrasound was performed on 110 patients. X-ray mammogram with ultrasound correlation was performed on 62 patients. Among 172 patients, BI-RADS 2 was assigned to 67 patients (39%), BI-RADS 3 to 59 patients (34.3%), BI RADS 4a to 28 patients (16.2%), BI-RADS 4b and 4c to 16 (9.3%) and 2 (1.1%) patients, respectively (Table 1).

Focal abnormality (single focus of clustered cysts/solid lesion/dilated duct, located either unilaterally or bilaterally) was seen in 10 patients (5.8%). Diffuse abnormalities (scattered throughout the breast, either unilaterally or bilaterally) were seen in the rest of the 162 (94.2%) the patients. Most of the findings were bilateral (163 patients, 94.8%), with a few cases (9 patients, 5.2%) having a unilateral distribution.

The most common ultrasound imaging finding was simple cysts (113 patients), followed in order by complicated cysts (50 patients), clustered cysts (45 patients), complex solid cystic masse (26

patients), solid lesions (26 patients), duct ectasia (26 patients) and intraductal lesions (12).

Table 1. Background profile of the specimens

Characteristics	Frequency (N=172)	Percentage (%)
Ultra sound	110	64
X-ray Mammogram	62	36
Focal abnormality		
Clustered cysts/ Solid lesion/dilated duct,located either unilaterally or bilaterally	10	5.8
Diffuse abnormalities	162	94.2
Bilateral	163	94.8
Unilateral	9	5.2
BIRADS		
BIRADS 2	67	39
BI-RADS 3	59	34.3
BI-RADS 4	28	16.3
BI-RADS 4b	16	9.3
BI-RADS 4c	2	1.1

Common findings on X-ray mammogram were dense fibro-glandular pattern (42 patients), followed in order by equal density lesions (20 patients), calcifications (15 patients) and asymmetry (4 patients) (Table 2).

Table 2. Radiological findings among the participants

Characteristics	Frequency N(172)	Percentage (%)
Ultra sound imaging finding*		
Simple cysts	113	65.7
Complicated cysts	50	29.1
Clustered cysts	45	26.5
Complex solid cystic masses	26	15.1
Solid lesions	26	15.1
Duct ectasia	26	15.1
Intraducal lesions	12	7.0
X- ray mammogram*		
Fibroglandular pattern	42	24.4
Equal density lesions	20	11.6
Calcifications	15	8.7
Asymmetry	4	2.3

*Total percentage will not tally for 100

Among 172 patients, 81 patients underwent ultrasound-guided interventions (either FNAC/ Biopsy). Pathological findings revealed simple cyst formation in 45 patients, ducts with apocrine metaplasia in 24 patients, epithelial hyperplasia without atypia in 24 patients, sclerosing adenosis in 18 patients, intraductal papillomas in 2 patients, and atypical ductal hyperplasia in 2 patients (Table 3).

Table 3. Findings of ultrasound guided intervention among the participants

Characteristics	Frequency N(172)	Percentage (%)
Simple cyst formation	45	26.2
Ducts with apocrine metaplasia	24	14.0
Epithelial hyperplasia without atypia	24	14.0
Sclerosing adenosis	18	10.5
Intraductual papillomas	2	1.2
Ductal hyperplasia	2	1.2

As for the correlation of imaging and pathological findings, simple and complicated cysts revealed cyst formation in 95% of the cases and epithelial hyperplasia in 5% of the cases. Complex solid cystic masses revealed cyst formation in 88% of the cases, with 10% showing epithelial hyperplasia and 2% showing atypical ductal hyperplasia. Simple duct ectasia lesions revealed dilated ducts with epithelial hyperplasia without atypia in all cases (100%). Ducts with internal echoes and clustered cysts showed apocrine metaplasia in 75% of the cases and epithelial hyperplasia without atypia in 25% of the cases. Dilated ducts with solid components showed intraductal papilloma in 75% of the cases and atypical ductal hyperplasia in 25% of the cases (Table 4).

Table 4: Histopathological correlation among the isolates

Characteristics	**Percentage (%)**
Imaging and pathological findings	
Simple and complicated cyst formation	95
Epithelial hyperplasia	5
Complex solid cystic masses	
Cyst formation	88
Epithelial hyperplasia	2
Atypical ductal	10
Epithelial hyperplasia without atypia	100
Clustered cysts	
Apocrine metaplasia	75
Epithelial hyperplasia without atypia	25
Dilated ducts with solid components	
Intraductal papilloma	75
Atypical ductal hyperplasia	25

DISCUSSION

The basic functional unit in the breast is the terminal ductal lobular unit (TDLU).[5,6] TDLU is the most important component as all the major diseases pertaining to the breast originate from the functional unit. The development of fibrocystic disease is linked to the hormonal status, as studies have shown a positive link between estrogen and fibrocystic disease. The fibrocystic disease is a consequence of aberration in the normal process of development and involution (ANDI) with associated hormonal irregularities. There is a high prevalence of FCC among patients with polycystic ovarian disease (PCOD) and those on hormone replacement therapy.[7,8] ANDI results in apocrine metaplasia, clear cell changes, eosinophilic change and microcystic involution. These epithelial changes result in epithelial hyperplasia, and accumulation of secretions causing dilatation of ducts, which in turn result in cyst formation, causing calcifications on mammography. Histologically, the normal breast tissue may also show aberrations, many of which are not detected clinically or on imaging.[9]

On ultrasound, the lesions were commonly bilateral. Focal abnormalities were less common compared to diffuse widespread abnormalities. Simple cysts (Figure 1a) were the most common imaging finding in FCC on ultrasound.[10] They were usually multiple and bilateral, either single or clustered together. These groups of lesions were categorized as BI-RADS 2 as per ACR guidelines.[11,12] Complicated cysts (by infection/inspissated secretions) showing internal echoes within (Figure 1b) were another feature on ultrasound which was categorized as BI-RADS 3. The two above categories were commonly followed up. Intervention was performed either for symptomatic relief or to allay the patients' anxiety.

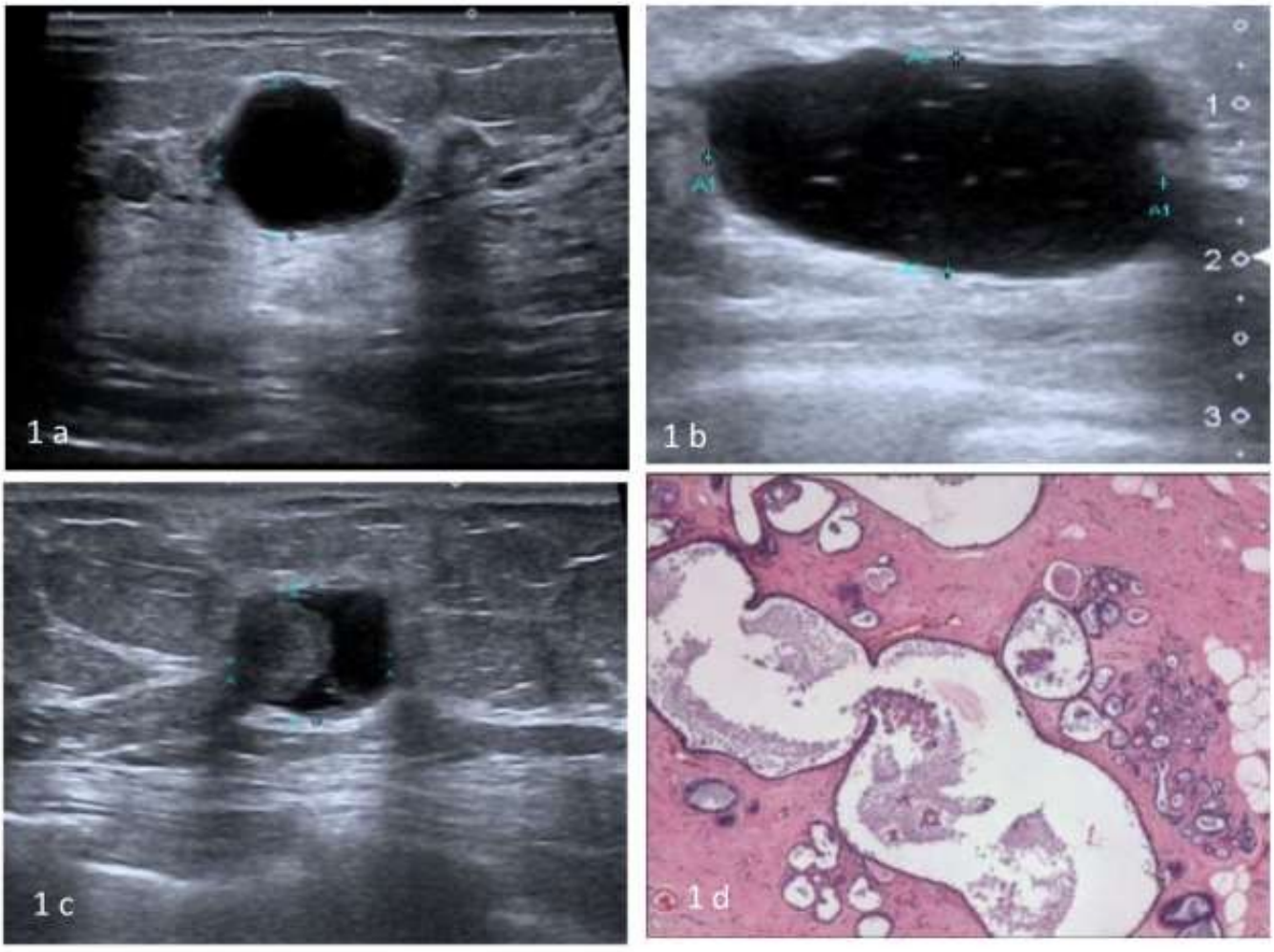

Figure 1. 1a: Ultrasound showing clear cyst with posterior acoustic enhancement. 1b: Ultrasound showing complicated cyst with internal echoes and posterior acoustic enhancement. 1c: Ultrasound showing a complex solid cystic mass with eccentric solid component and septation. 1d: Light microscopy showing breast tissue with cystically dilated ducts, filled with secretions (H&Ex40)

Solid lesions were also seen, with most of them appearing as hypoechoic (Figure 2a) or isoechoic focal lesions and a few of them showing cystic areas within (Figure 2b). The lesions were

either well circumscribed or showed partly obscured borders (Figure 2c), with the former classified as BI-RADS 3 and the latter as BI-RADS 4a/4b. On color Doppler imaging, lesions showing increased vascularity were classified as either 4b or 4c. They generally presented as solid lesions with a few mimicking malignancy.[13,14] On light microscopy, most of the solid lesions showed compressed ducts surrounded by dense stroma and a few cystically dilated ducts (Figure 2d).

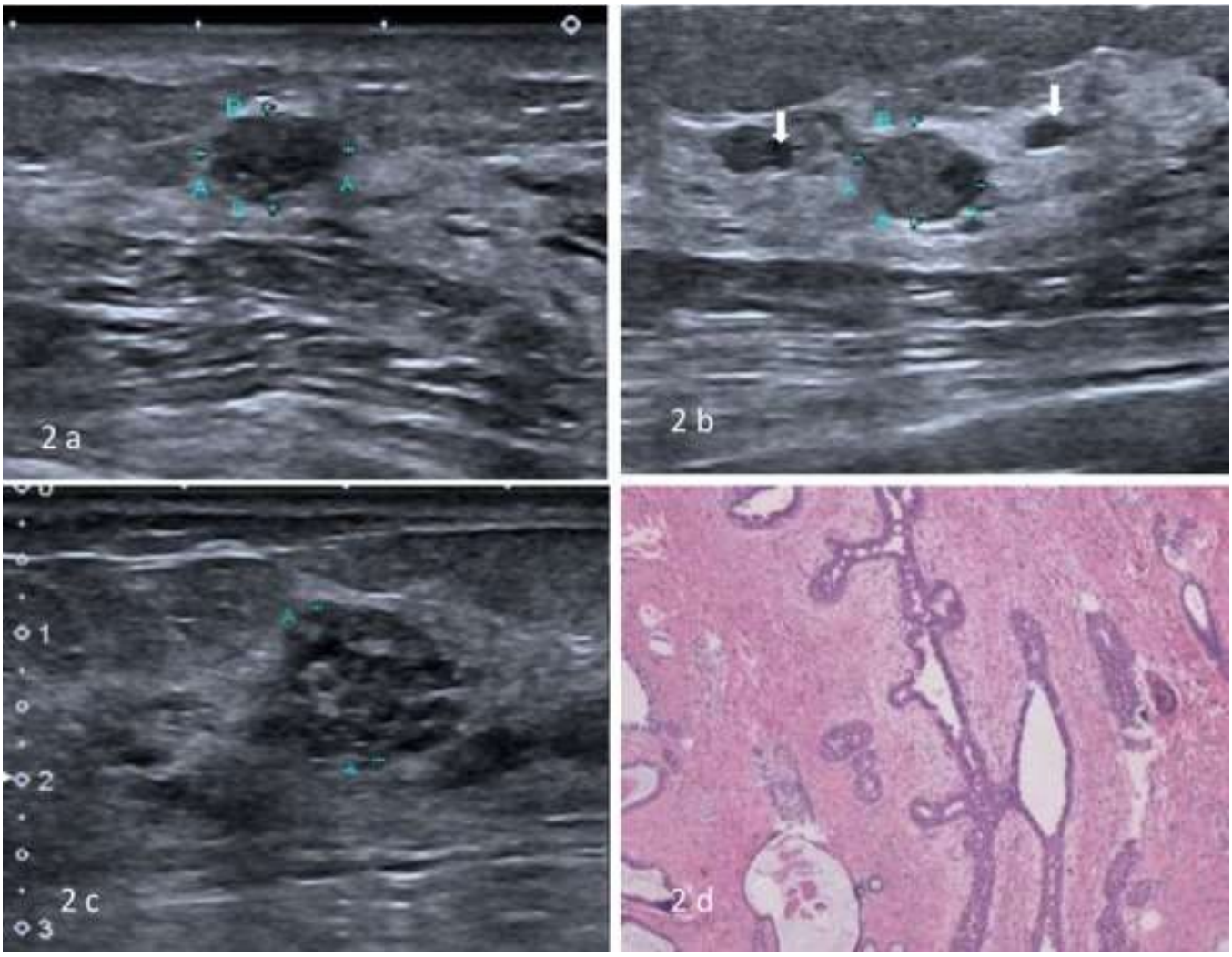

Figure 2. 2a: Ultrasound showing well circumscribed hypoechoic solid lesion in the breast. 2b: Ultrasound showing solid lesions with tiny cystic areas (arrow) 2c: Ultrasound showing Solid lesion with a few tiny cystic areas and partly obscured margins. 2d: Light microscopy showing compressed ducts surrounded by dense stroma and a few cystically dilated ducts (H&Ex200).

The most common ductal abnormality was simple duct ectasia commonly encountered in the central sub areolar region and seen more often bilaterally (Figure 3a). These lesions were categorized as BI-RADS 2. Sometimes the ducts show internal echoes / debris with no internal vascularity/mild wall thickening (Figure 3b). These lesions were categorized as BI-RADS 3. Light microscopy of the lesions indicated dilated ducts showing apocrine change (Figure 3c). Breast tissue showing group of ducts was surrounded by sclerosis (Figure 3d). Features of duct ectasia that should raise suspicion for an underlying malignancy include a peripherally dilated duct (one well away from the retro areolar region), overall irregularity of the duct margin, focal wall thickening, and adjacent hypoechoic tissue.

The most common abnormality on X-ray mammography was dense fibro-glandular pattern (type C or type D). The problem of dense fibro-glandular parenchyma generally obscures the underlying mass lesions (Figure 5a and 5b). The other common abnormality includes opacities caused due to cysts and solid lesions (Figure 5c and 5d), clearly seen on ACR type A breasts.

Benign micro-calcifications were commonly associated with fibrocystic disease. Lobular patterns of rounded calcifications were the most

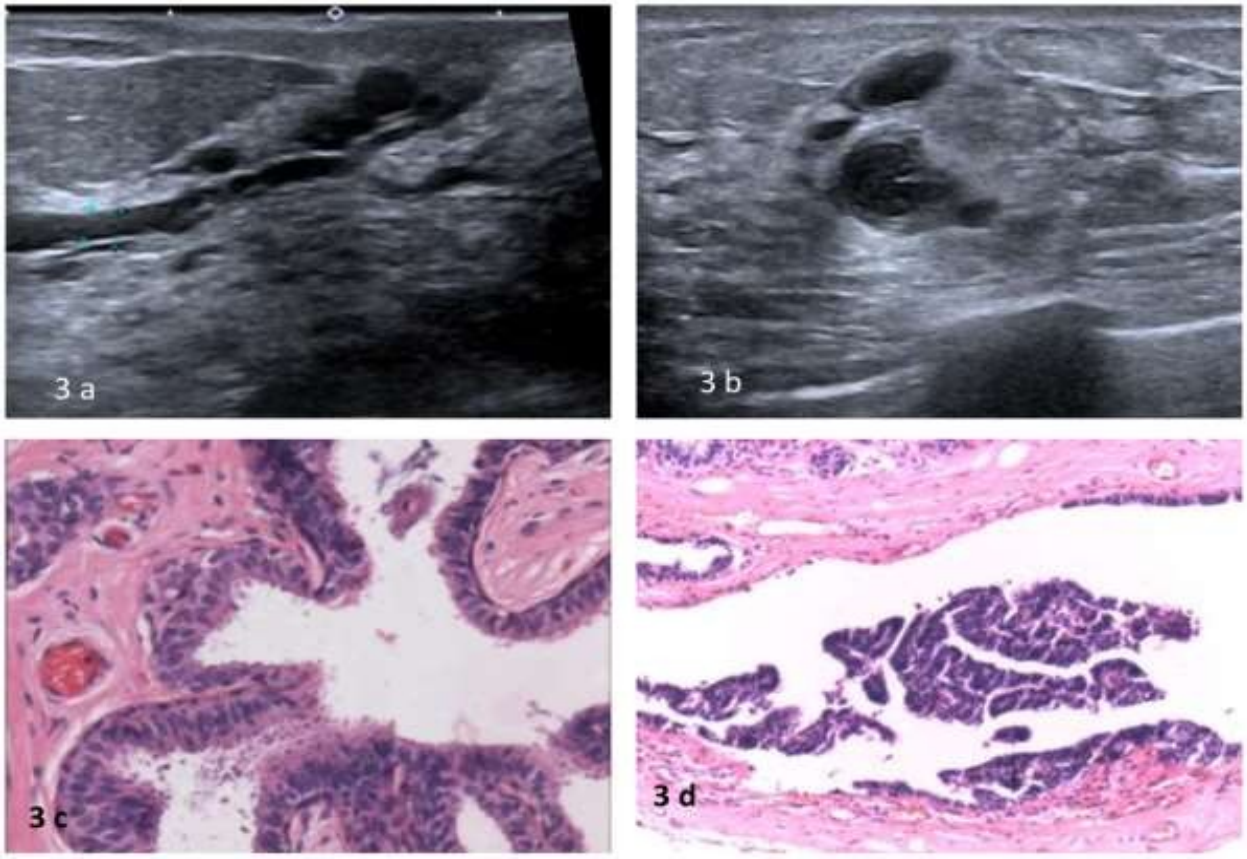

Figure 3. 3a Ultrasound showing dilated duct (>2mm or ampullary portion >3mm) with no internal echoes/solid components centrally located and not associated with mass lesion. 3b Ultrasound showing dilated ducts which reveal internal echoes/debris and mild wall thickening. 3c Light microscopy reveal dilated duct showing apocrine change (H&Ex200). 3d Light microscopy showing group of ducts surrounded by sclerosis (H&Ex40)

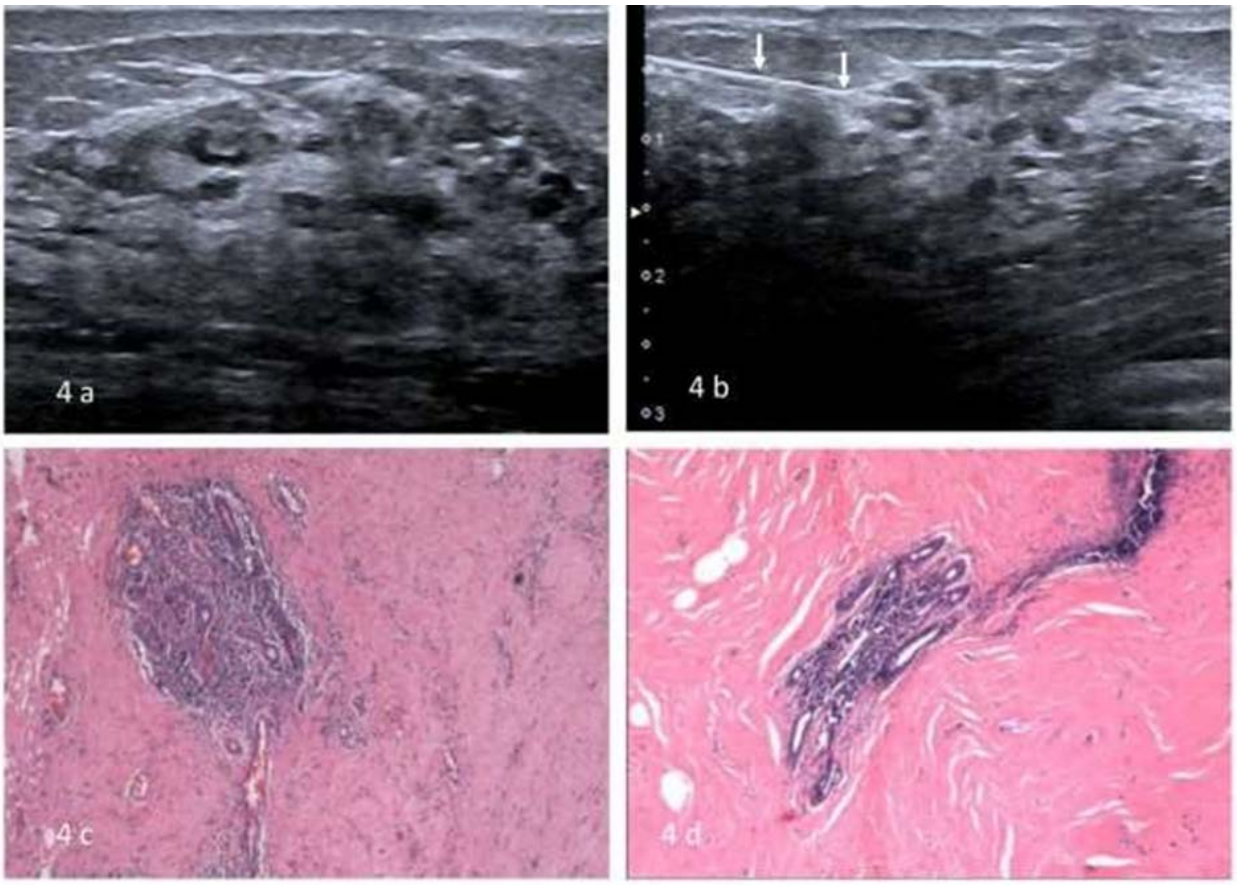

Figure 4. 4a: Ultrasound showing focal thickening of the breast parenchyma with mild architectural distortion and no underlying mass. 4b: Ultrasound guided FNA done for the same area. 4c: Light microscopy showing groups of ducts surrounded by inflammatory cells andsclerosis (H&Ex40) in the breast tissue. 4d: Light microscopy showing groups of ducts surrounded by extensive sclerosis (H&Ex40) in the breast tissue.

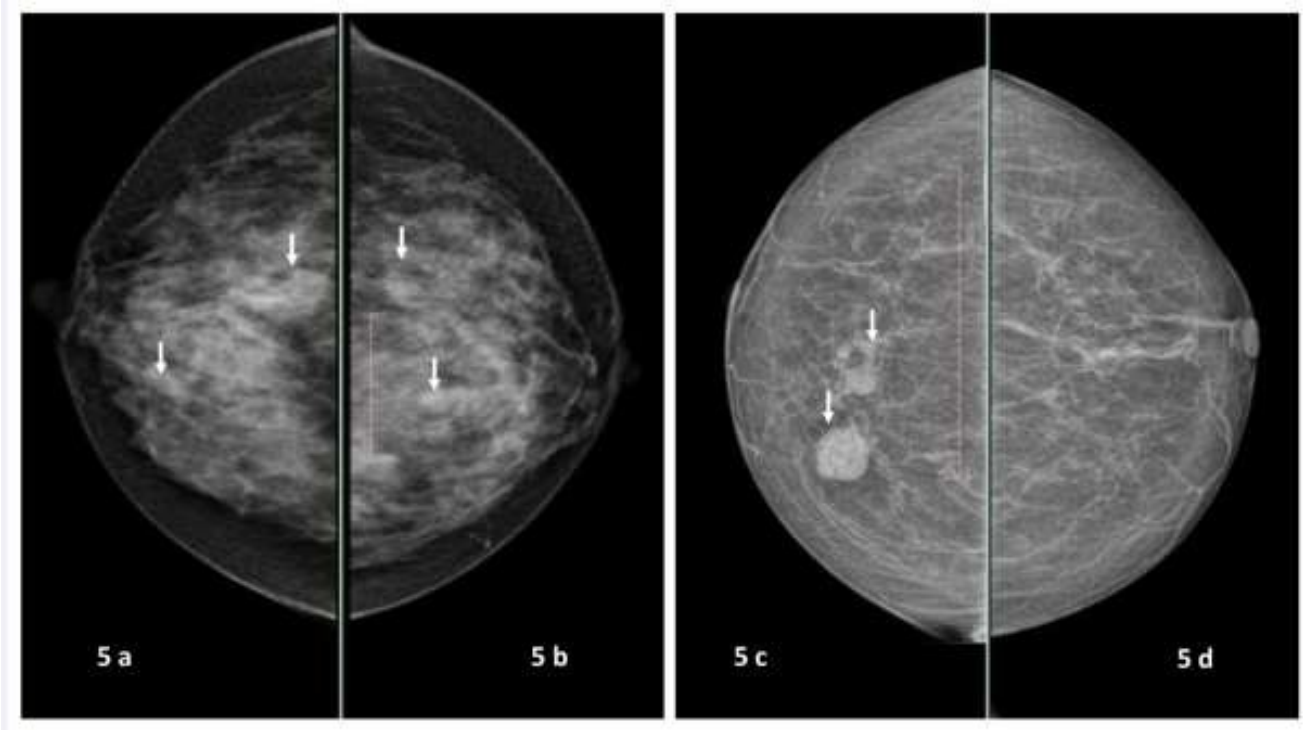

Figure 5. 5a & 5b X ray mammogram showing dense fibroglandular pattern ACR Type C, obscuring the underlying mass lesions (arrows). 5c & 5d: X ray mammogram showing round circumscribed high density lesions (arrows) in ACR Type D l-almost entirely fatty tissue.

commonly encountered pathology arising from the lobular unit of TDLU.[15] Common morphologies (Figure 6a and 6b) include tea cuplike configuration (open arrow), small rounded calcification (solid arrow), amorphous type or rod-like calcification.

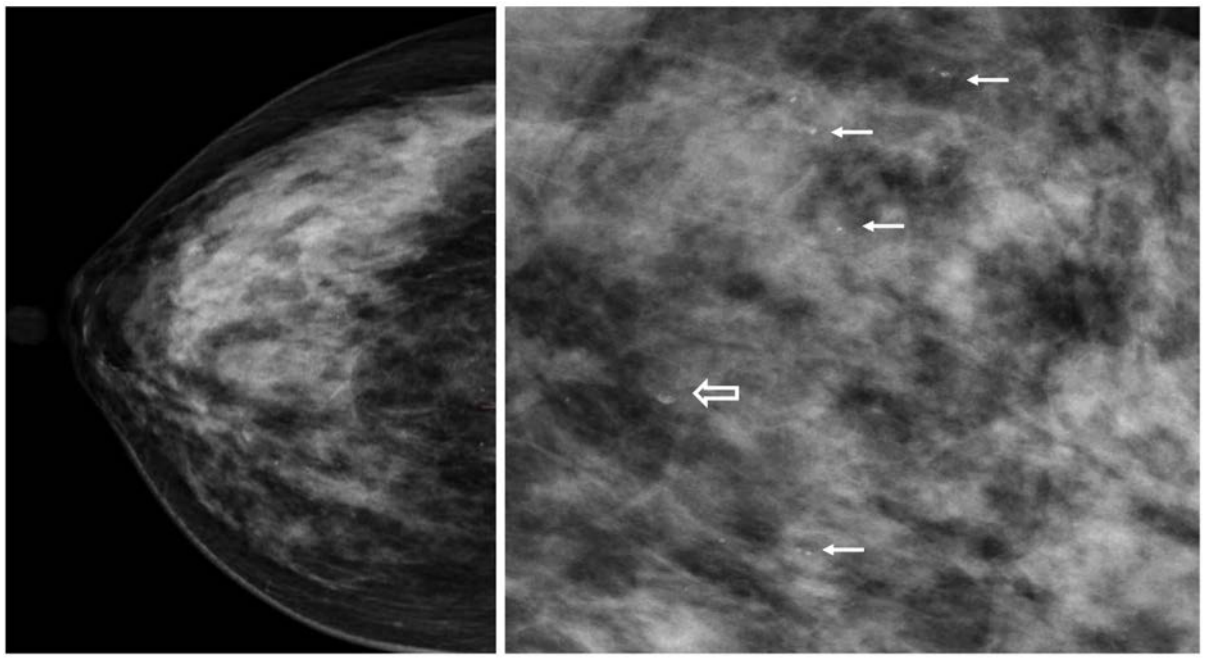

Figure 6. 6a & b: X - ray mammogram routine & magnification showing diffuse small rounded calcification (arrows) & tea cup like configuration (open arrow) in magnification (Figure 6b).

In our study the calcifications were seen in both breasts, with diffuse /regional distribution being the most common pattern. In a few patients, the calcifications were in a group and seen as three or more grouped areas of calcifications. As per ACR guidelines, the calcifications were assigned BI-RADS category in correlation with ultrasound findings.

Asymmetry and architectural distortion were also observed. Compression and magnification views were performed to differentiate from the overlapping breast tissue. Targeted ultrasound was performed and, if associated with an abnormality, it was either followed up or intervention was performed depending on ultrasound appearances. As to the correlation with imaging and pathological findings, the clear cysts and complicated cysts show features of cyst formation and epithelial hyperplasia without atypia (epitheliosis). Complex solid cystic masses, when completely excised with ultrasound guided vaccumm assisted biopsy and proven to be benign on histopathological examination, do not require any further imaging follow up or surgery.[16] Complex solid cystic masses also showed features of apocrine metaplasia, cyst formation, and epithelial hyperplasia without atypia (epitheliosis). Solid lesions were commonly sclerosing adenosis. Ductal lesions showed either simple duct ectasia, epithelial hyperplasia without atypia or intraductal papilloma. A few of the ductal lesions and complex solid cystic masses showed features of atypical ductal hyperplasia. Lesions showing features of sclerosing adenosis or epithelial hyperplasia (proliferative lesions without atypia) and epithelial hyperplasia with atypia should be followed up or surgically excised due to their association with breast malignancies.[17,18]

CONCLUSION

Fibrocystic change in the breast is one of the most common groups of breast disorders we come across in day today practice, varied imaging manifestations on ultrasound and X- ray mammogram. In our study, these cystic lesions did not reveal any abnormality as these patients had dense glandular patterns. It is essential for radiologists to be familiar with imaging and pathological findings of fibrocystic disease of the breast for further workup and management as it is not only the most common benign disease of the breast but it can also sometimes present as suspicious lesions.

ETHICAL APPROVAL

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study.

CONFLICT OF INTEREST

None.

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