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Original article

Role of Contrast Enhanced Mammography in Assessment of Asymmetric Mammographic Findings

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ABSTRACT

Background: Breast asymmetry is a common mammographic finding which encompasses a diversity of possibilities. It may be the only sign for underlying malignancy. Contrast enhanced mammography (CEM) can reveal the asymmetry underlying angiogenesis, allowing for proper diagnosis, clinical management, reducing the number of unnecessary biopsies and increasing the rate of cancer detection. At this study we aimed to assess the performance of contrast enhanced mammography in the evaluation of different types of mammographic asymmetry. **Methods:** This is a prospective study approved by our institutional review board. The study included 36 consecutive females whose mammograms revealed any type of mammographic asymmetry. After obtaining patients' informed consents, contrast enhanced mammography (CEM) examination was performed. Low energy and combined images were analyzed using the newly published contrast enhanced mammography (CEM) attachment to ACR BI-RADS® Mammography 2013 in 2022 followed by BIRADS categorization. Ultrasound was performed for all cases to verify the BIRADS category. Final diagnosis established by Ultrasound and follow-ups for benign lesions. Malignant and suspicious lesions on CEM or ultrasound were biopsied. **Results:** The performance of CEM in the detection of malignant breast lesions underlying breast asymmetry in correlation to final diagnosis was as follows: sensitivity was 94.44% with 83.33 % specificity and 88.89% accuracy. **Conclusion:** CEM is reliable for unravelling breast asymmetry underlying pathology. Analysis of low energy and combined images aids in the characterization of underlying asymmetry, directing proper clinical management and increasing cancer detection rates.

Keywords: Asymmetry; Contrast enhanced mammography; CEM

INTRODUCTION

Female breasts are widely variable in their size and parenchymal composition. Mammographic appearances range from perfectly symmetrical breasts to asymmetry. Although the presence of asymmetry is quite common and it may be an overlapping glandular tissue, hormonal effect or post-intervention, it

may be very significant and the only sign of underlying malignancy [1-2].

The American College of Radiology (ACR) developed a standardized terminology for breast asymmetry and an attachment for contrast-enhanced mammography. This lexicon aids in distinguishing asymmetry from masses and architectural distortion, identifying its various types and finally categorizing asymmetries to a final BIRADS score, which indicates the likelihood of suspiciousness of the encountered asymmetry. Based on asymmetry conspicuity, if detected on a single projection, it is categorized as asymmetry, while if depicted on two projections, it is assigned as focal asymmetry (less than one breast quadrant involvement) or global asymmetry (extending beyond one breast quadrant). The term "developing asymmetry" is reserved for newly developed asymmetries since the last scan [3-4].

Concerns about the nature of mammographic asymmetry have provoked many researchers to diligently evaluate various breast imaging modalities and assess their capabilities to detect underlying lesions such as ultrasound, tomosynthesis and MRI. Combinations of these imaging modalities were also tested to avoid missing underlying cancer and to eliminate unnecessary biopsies [5-7].

Contrast enhanced mammography is a novel procedure introduced to evaluate different breast lesions and FDA approved in 2011[8]. It provides two sets of images. The low energy images are a surrogate for 2D mammography, which is a mainstay and a widely convenient method for breast screening and diagnosis, demonstrating the characteristics of pathological lesions and their effects upon the anatomical pattern of breast structures [4,8]. The combined images provide information about abnormal angiogenesis and eliminate the obscuring effect of dense breast parenchyma. CEM and contrast enhanced MRI share neovascularity imaging with comparable performances, but CEM has the privilege of shorter examination time with less cost. It can be used in claustrophobic patients and with magnetic field incompatible implants without a patient weight limit [8-10].

In this study, we aimed to evaluate the performance of contrast enhanced mammography in the assessment of all types of mammographic asymmetry.

METHODS

This is a prospective cohort study approved by the research ethical committee of Faculty of Medicine, Zagazig University (Approval number:7075-1-7-2021) and was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. The EPI INFO 6 program was used to calculate the sample size; 36 cases with a power of 80%, a confidence interval of 95%, and a drop out of 10%. Our study was performed from January 2022 to September 2022 and included sequential patients who presented for their annual mammographic screening or for evaluation of other breast complaints and whose scans revealed mammographic asymmetry of any type, excluding patients unwilling to participate, patients with renal impairment, pregnant women and those with a history of contrast media adverse reactions. Patients' personal and medical history were obtained, kidney function tests were checked, family history of cancers, especially breast cancer and previous mammographic studies, if available, were reviewed. A detailed description of the contrast enhanced mammography technique, its value, the used contrast, method of injection and possible adverse effects were clearly explained. A written informed consent was obtained from all patients.

A contrast-enhanced mammography was performed by GE Senographe Pristina unit (GE Healthcare, Milwaukee, Wis.). The examination takes approximately 8 to 10 minutes to be performed. Initially, intravenous contrast medium was injected through an antecubital vein inserted 18G or 20G cannula. In all cases, 1.5 mL/kg of OMNIPAQUETM iohexol 300 mg/ml was used as the contrast agent. Breast compression was withheld for two minutes after the injection to ensure normal breast contrast distribution. Breast compression and imaging were performed in the standard positions; craniocaudal (CC) and mediolateral oblique (MLO) for both breasts in a two- to ten-minute

time window without specific order. During each single compression, two sets of images are obtained successively. low-energy images at 26–31 kVp (below the iodine k-edge) and high-energy images at 45–49 kVp (above the iodine k-edge). Single compression for both images reduces the overall examination time, reduces the chance for motion artefacts and enables precise subtraction of images, contrast-enhanced image generation and facilitates image analysis. After the examination was completed, we ensured that each patient was well with no side effects and they were informed to contact us if they experienced any complaints related to contrast media usage.

Images analysis was performed in a standardized method following the newly published contrast enhanced mammography (CEM) attachment to ACR BI-RADS® Mammography 2013 in 2022. To our knowledge, we are the first study that used this lexicon.

Mammography and low-energy images were used to identify breast density, the type of asymmetry and calcifications. Other associated features as; nipple, skin changes and intra-mammary or axillary lymphadenopathy. Asymmetry was recognized by missing mass and architectural distortion characters. One-sided dense area with no convex borders or radiating speculations. There are four types of asymmetries: asymmetry (formerly known as simple or one-view asymmetry), focal asymmetry, global asymmetry and developing asymmetry.

Combined images were assessed for corresponding enhancement in the region of asymmetry. Enhancement, if present, is described as either mass enhancement, non-mass enhancement or enhancing asymmetry. lesions' morphological descriptors, enhancing patterns and distributions were described.

According to the BIRADS score, the next step for management is determined. Patients with a BIRADS 1 or 2 score were confirmed by ultrasound and asked to continue their annual screening if their age more than 40 years. BIRADS 5 categorized lesions underwent excisional or core biopsies. Undetermined lesions by mammogram and CEM (BIRADS 3) were referred to ultrasound to confirm the BIRADS category. If typical features of fibroadenoma were detected, short-term follow-up after 3 and 6 months was performed. A biopsy was performed if the lesion was categorized as BIRADS 4 or suspicious ultrasound features.Final diagnoses for our detected lesions were established by biopsy (True-cut or excisional) in 19 cases and their histopathology revealed malignancy in 18 cases and 1 case was diagnosed pathologically with granulomatous mastitis.

In eight cases, the final diagnoses were deemed normal. No post-contrast enhancement or underlying lesions were detected by ultrasound. Two cases were diagnosed as breast abscesses and ultrasound guided needle aspiration revealed pus. Four cases were diagnosed as fibroadenomas by ultrasound. On follow-ups, there was no change in size or morphological changes. Three cases revealed rim-enhancing lesions, followed by ultrasound examination, which revealed fibrocystic disease.

Enlarged lymph nodes on low energy images were further assessed by combined images and ultrasound for sizes, shapes, outlines, nodal cortical thickness, hilum preservation and vascular patterns on doppler assessment. Eleven cases were suspicious and confirmed by pathological diagnosis. Three cases showed axillary lymph nodes enlargement with no suspicious features and biopsy confirmed the inflammatory nature of the underlying breast diseases.

Statistical analysis;

Data was provided to the computer and analyzed using the IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp). Numbers and percentages were used to describe qualitative data. The Kolmogorov-Smirnov test was used to verify the normality of the distribution mean, standard deviation, median, and interquartile range (IQR) were used to describe quantitative data. The significance of the obtained results was judged at the 5% level. The used tests were Chi-square test, Fisher’s exact or Monte Carlo correction.

RESULTS

This study included 36 females with ages ranging from 34 to 56 years (Mean± SD= 45.42 ± 6.63). Final diagnoses for our detected lesions were established by biopsy (True-cut or excisional) in 19 cases and their histopathology revealed malignancy in 18 cases and 1 case was diagnosed pathologically with granulomatous mastitis.

In eight cases, the final diagnoses were deemed normal. No post-contrast enhancement or underlying lesions were detected by ultrasound. Two cases were diagnosed as breast abscesses and ultrasound guided needle aspiration revealed pus. Four cases were diagnosed as fibroadenomas by ultrasound. On follow-ups, there was no change in size or morphological changes. Three cases revealed rim-enhancing lesions, followed by ultrasound examination, which revealed fibrocystic disease.Infiltrative ductal carcinoma was the most frequent type in malignant cases (8/18;22.2%). Other types were DCIS (2/18;5.6%), IDC+DCIS (3/18;8.3%) and invasive lobular carcinoma (5/18;13.9%).

Table 1 demonstrates frequencies and percentages of extracted information from mammography/low energy images correlated with their final diagnosis category: either normal, benign conditions or malignancy. Focal asymmetry was the most frequent type of asymmetry in our study. Underlying malignant lesions were detected in 50 % of cases (n = 11). 100% of developing asymmetries are pathologically proven to have malignant underlying lesions. A single case of asymmetry (1/7; 14.3%) was malignant in final diagnosis, while other cases (n = 6) revealed no underlying lesions. Global asymmetry was detected in two cases, one diagnosed as breast abscess and the other diagnosed as invasive lobular carcinoma.

Associated features such as suspicious microcalcifications and nipple retraction are signs exclusive to cases with a final malignant diagnosis (8/18; 44.4% and 5/18;27.8%). Breast skin thickening is detected in inflammatory and malignant cases. Lymphadenopathy is also detected in both inflammatory and malignant cases. Suspicious lymph nodes were detected in 11/18 (61.1%) malignant cases and confirmed by pathologic diagnosis. Inflammatory enlarged axillary lymph nodes were detected in 3 cases. Two cases were breast abscesses on clinical diagnosis, ultrasound and needle pus aspiration. The third case was diagnosed as granulomatous mastitis on core biopsy.

Table 2 demonstrates post-contrast enhanced lesions characters. Post-contrast mass enhancement (20/27; 74.1%), non-mass enhancement (6/28; 21.4%) or enhancing asymmetry (1/28; 3.6%) were observed in 27/36 mammographic asymmetries.For mass enhancing lesions; irregular shape and ill-defined margins were descriptors remarking malignancy (76.9%; 10/13). Heterogeneous enhancement was detected in (69.2% (9/13) of malignant lesions. While benign lesions showed well defined margins were 6/7 (85.7%). The enhancement pattern suggestive of benignity was rim enhancement, which was detected for cysts. Homogeneous enhancement was detected in both benign and malignant pathologies with no statistically significant difference. Heterogeneous mass-like enhancement with ill-defined borders were detected in only one benign condition diagnosed as breast abscesses.

Non-mass enhancement was detected in six cases (22%). Two of them were benign in final diagnosis (33.3%) and four were malignant (66.7%). Malignant lesions showed 50% for focal and 50% for segmental distributions. A clumped pattern of enhancement was detected in one malignant lesion (Fig.1). An enhancing asymmetry pattern was detected in only one focal asymmetry case, which was diagnosed with an invasive lobular carcinoma.

Nine cases with mammographic asymmetry showed no post-contrast enhancement. The types of asymmetry in those mammograms were asymmetry (n = 6) and focal asymmetry (n = 3). These ladies underwent further ultrasound evaluation, which also revealed no underlying pathology in eight cases and they were advised to continue their annual mammography. Only one case of non-enhanced focal asymmetry; complementary US revealed a mass with imaging features typical for fibroadenoma. Over the course of three and six months, the mass's imaging characteristics remained stable. The presence of an enhancement determines the

performance of contrast enhancement mammography in detecting asymmetry underlying lesions. The findings were as follows: 96.4% sensitivity, 100% specificity and 97.2% accuracy.

Final CEM categorization according to BIRADS was performed based on morphological characters, enhancement patterns of asymmetry regions and ancillary findings such as calcifications, skin / nipple changes and lymphadenopathy. This final CEM diagnosis is used to determine the performance of CEM in the detection of malignant breast lesions underlying breast asymmetry in correlation to final diagnosis (Table 3). The overall sensitivity of CESM to detect malignant lesions was 94.44% with 83.33 % specificity and 88.89% accuracy.

(Table 1); Extracted data from low energy images (n=36)

	Normal (n=8)		Benign (n=10)		Malignant (n=18)		^{MC}p
	No.	%	No.	%	No.	%	
ACR breast Density							
B		37.5	6	60.0	1	5.6	0.006*
C		37.5		40.0		50.0	0.831
D		25.0		0.0		44.4	0.031*
Type of asymmetry							
Focal		25.0		90.0	11	61.1	0.019*
Developing		0.0		0.0	5	27.8	0.084
Global		0.0		10.0	1	5.6	1.000
One view asymmetry		75.0		0.0	1	5.6	<0.001*
Calcifications							
No		50.0		60.0	7	38.9	0.574
Grouped micro calcification		0.0		0.0	8	44.4	0.005*
Nonsuspicious		50.0		40.0	1	5.6	0.019*
Skin changes							
No		100.0		80.0	10	55.6	0.059
Yes		0.0		20.0	8	44.4	
Nipple retraction							
No		100.0	10	100.0	13	72.2	0.079
Yes		0.0		0.0	5	27.8	
Lymph nodes involvement							
No		100.0		70.0	7	38.9	0.009*
Inflammatory		0.0		30.0	0	0.0	0.024*
suspicious		0.0		0.0	11	61.1	<0.001*

(Table 2); Extracted data of enhancing lesions on CEM recombined images (n=27).

Mass enhancing lesions (n=20)					
	Benign (n=7)		**Malignant (n=13)**		**P value**
	No.	**%**	**No.**	**%**	
Margins					
Well-defined		85.7	3	23.1	0.0166*
Ill defined		14.3	10	76.9	
Shape					
Round / Oval		85.7	3	23.1	0.0166*
Irregular		14.3	10	76.9	
Enhancement pattern					
Rim		42.85	0	0.0	0.0307*
Homogenous		42.85	4	30.8	0.6514
Heterogeneous		14.3	9	69.2	0.0573
Non mass enhancing lesions (n=6)					
	Benign (n=2)		**Malignant (n=4)**		
	No.	**%**	**No.**	**%**	
Distribution					
Multiple regions		50	0	0.0	0.3333
Focal		0.0	2	50	0.4667
segmental		50	2	50	1
Enhancement pattern					
Homogeneous		0.0	1	25	1
Heterogeneous		100	2	50	0.4667
Clumped		0.0	1	25	1
Enhancing asymmetry (n=1)					
	Benign (n=0)		**Malignant (n=1)**		
	No.	**%**	**No.**	**%**	
Homogeneous	0	0.0	0	0.0	
Heterogeneous	0	0.0	1	100	

(Table 3) : Performance of CEM for detection of asymmetry underlying lesions (n=36)

Final CESM BIRADS scoring		Final diagnosis with CESM	
BIRADS 0	**0**	**Normal & Benign (BIRADS 1, 2, &3)**	**16**
BIRADS 1	**9**		
BIRADS 2	**3**		
BIRADS 3	**4**	**Malignant/suspicious (BIRADS 4, 5 &6)**	**20**
BIRADS 4	**5**		
BIRADS 5	**15**		
BIRADS 6	**0**		

Performance of CEM for detection of asymmetry underlying lesions

CEM	Final diagnosis		Sensitivity	Specificity	PPV	NPV	Accuracy
	Underlying lesion (n=28)	No underlying lesion (n=8)					
	No.	No.					
Enhancement	27	0	96.4%	100%	100 %	88.9%	97.22%
No enhancement	1	8					

Performance of CESM for detection of malignant lesions

CEM	Final diagnosis		Sensitivity	Specificity	PPV	NPV	Accuracy
	Malignant (n=18)	Normal/benign condition (n=18)					
	No.	No.					
Malignant	17	3	94.44%	83.33%	85%	93.75%	88.89%
Normal/benign condition	1	15					

- **PPV**: Positive predictive value
- **NPV**: Negative predictive value

Figure 1

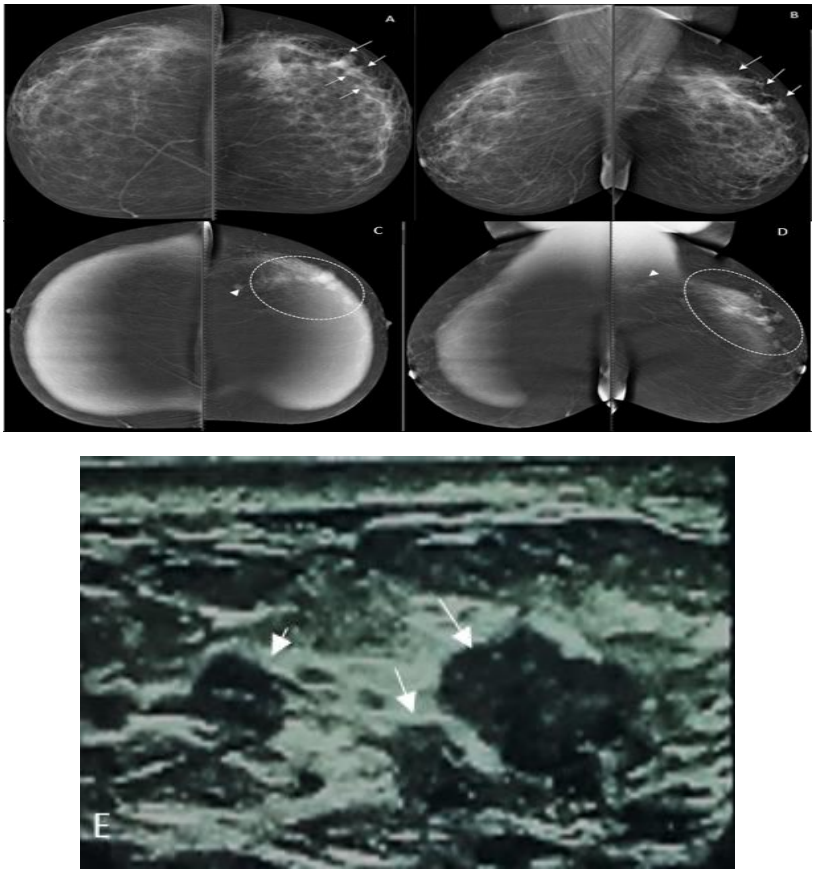
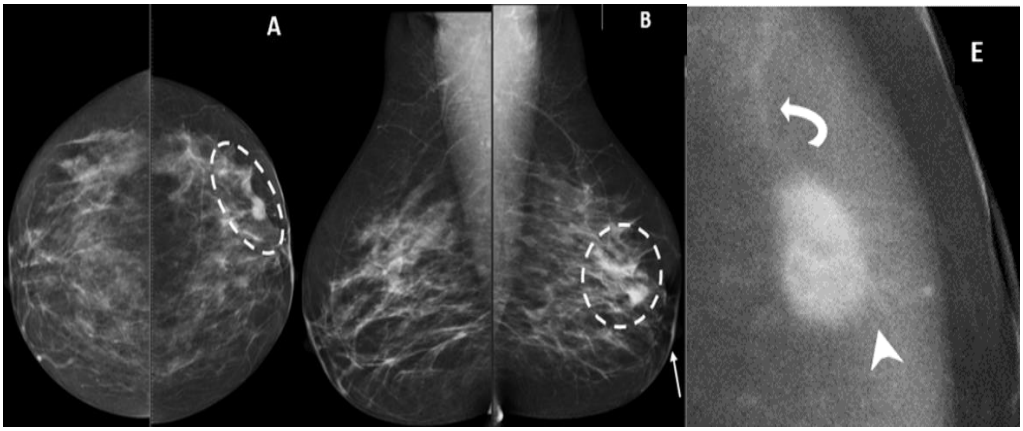


Fig. 1; (A & B); Low energy CC and MLO views;showing ACR-C breast density and a focal asymmetry at left UOQ (arrows).

(C &D); CEM recombined image in CC and MLO views showing a heterogeneous non mass enhancement of clupmed pattern (Dashed circle).Associated enlarged intrammammry and axillary lymphnodes (arrow heads). (E); Targeted ultrasound revealed multiple variable-sized hypoechoic masses with irregular shapes and not-circumscribed margins (arrows). The masses were not parallel to the skin and had no posterior acoustic features. The study categorized as BI-RADS 5. Ultrasound guided core biopsy histopathological report was concordant and reported ILC.

Figure 2



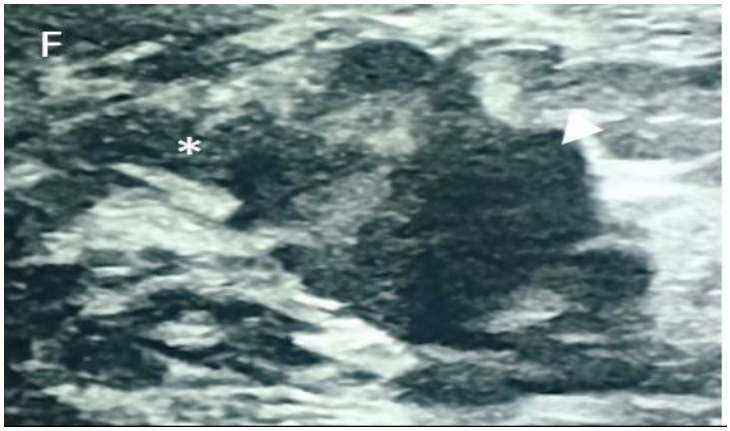


Fig. 2; (A & B); Low energy CC and MLO views showing ACR-C breast density and a focal asymmetry at left UOQ (Dashed circles) with overlapping skin thickening and retraction (white arrow). The focal asymmetry is lacking convex margins and interspersed with fat in MLO view.

(C &D); CEM recombined image in CC and LMLO views showing a heterogeneous mass-like enhancement with irregular shape and speculated margins (Dashed arrow).

(E) Magnified CC view showing a mass with speculated margins, heterogenous internal enhancement (arrow head) with long speculation off upper aspect of lesion (Curved arrow).

(F) Ultrasound showed irregular hypoechoic and non-circumscribed mass (arrow head) with long speculation (astrisk). Lesion categorized as BI-RADS 5. Excisional biopsy report proved the malignant nature of the lesion (IDC + DCIS)

Figure 3:

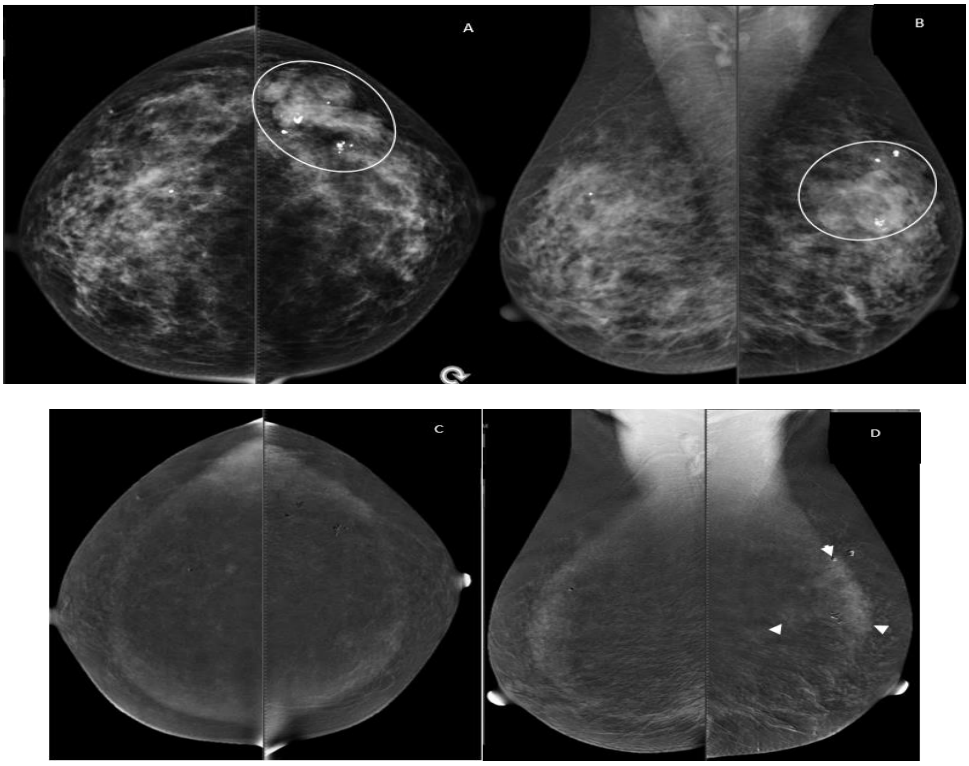


Fig. 3; (A & B); Low energy CC and MLO views showing ACR-D breast density with a focal asymmetry at left UOQ (circles).

(C & D); CEM recombined image in CC and MLO views showing a heterogeneous enhancing asymmetry noted at left MLO view (arrow heads). No corresponding CC view enhancement.

Associated enlarged axillary lymphnode is noted.

Lesion was assigned to BI-RADS 4. Ultrasound guided core biopsy revealed ILC.

Figure 4:

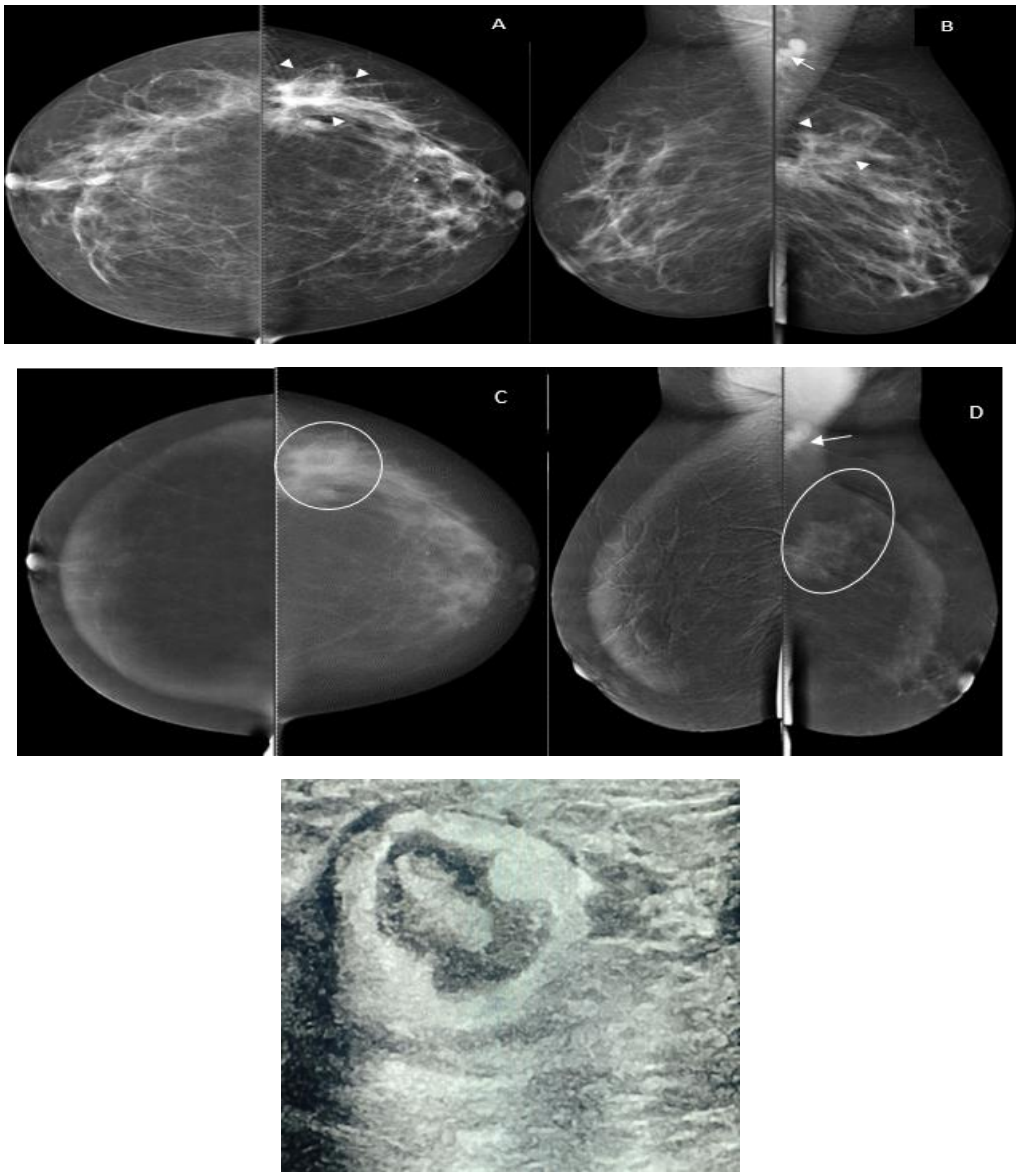


Fig. 4; A case of left Breast abscess

(A & B); Low energy CC and MLO views showing ACR-C breast density with focal asymmetry at left UOQ (Arrow heads).

(C &D); CEM recombined image in CC and MLO views showing heterogeneous mass enhancement of irregular shape and indistinct outlines (Circles) with ipsilateral axillary inflammatory enlarged lymphnodes. The lesion was assigned to BI-RADS 5. (E) Ultrasound revealed a turbid fluid collection with surrounding parenchymal edema.Ultrasound guided needle aspiration revealed pus.

DISCUSSION

Mammographic asymmetries comprise a wide range of possibilities, from normal condensed glandular tissue to malignant underlying lesions. So, these findings always require careful management to prove if there is an underlying true abnormality. Contrast enhanced mammography is a newly introduced technique that may be of credibility to untangle radiologists' concerns about mammographic asymmetries through contrast highlighting of the underlying angiogenesis.

Evaluation of mammographic asymmetries by CEM was approached by little research [11–13]. This study, Kamal et al [11] and Wessam et al [12] aimed to assess all types of mammographic asymmetries. Soliman et al. were concerned about focal asymmetries in their publication [13]. In this study, developing asymmetries were 100% underlined with malignant lesions, as in Kamal et al. [11]. But Leung et al [14] detected a lower incidence of underlying malignancy in association with developing asymmetries in screening and diagnostic mammograms. Percentages of malignancy were 12.8% and 26.7% for screening and diagnostic mammograms, respectively. Asymmetry was the least type associated with an underlying lesion. Only one asymmetry (1/7;14.3%) exhibited a heterogeneous enhancement and was malignant on histopathology diagnosis. Kamal et al reported 45% of cases to be malignant lesions detected by single-view asymmetries [11]. 50% of focal asymmetries were malignant, 41% were benign and 9% were normal on final diagnosis. In Soliman et al study, focal asymmetries with underlying malignancy accounted for 60.5% of cases; 34.2% were benign conditions and 5.2% were free of pathologies [13].

Invasive lobular carcinoma and breast abscesses were the final diagnoses of our two global asymmetry cases. A larger number is required to identify the impact of this particular type of asymmetry. Kamal et al [11] studied 128 cases and Wessam et al [12] studied 26 cases with global asymmetries. Both reported high percentages of underlying malignancies; 75.8% and 73.1%, respectively. From our perspective, any type of asymmetry should be perceived as an abnormal finding and requires further thorough evaluation to exclude underlying malignancy.

The overall performance of CEM in unravelling asymmetric findings regardless of its final diagnosis, depending on corresponding enhancement of asymmetry areas, showed 96.4 % sensitivity. This is consistent with the findings of Jochelson et al [15] and Kamal et al [16], who found 96% and 94.1% sensitivities, respectively. In asymmetry cases, Wessam et al reported a 100% sensitivity of CEM [12].

We also assessed the performance of CEM in the detection of malignant lesions. All lesions were allocated to a BIRADS category. The final BIRADS categorization of lesions helped to assess the performance of CEM in the detection of malignant ones. Sensitivity, specificity and accuracy were 94.44%, 83.33% and 88.89%. Sung et al assessed the addition of CEM for cancer detection and their results were 87.5% and 93.7% sensitivity and specificity, respectively [17].

All our non-enhanced asymmetries on combined images were normal on final diagnosis except for one non-enhancing fibroadenoma. Wessam et al [12] and Soliman et al [13] reported the same results. Kamal et al., in two studies, detected 7/21(19%) and 6/66 (9.1) malignant non-enhancing lesions [16,18].

Mass enhancing lesions' shapes and margins showed a statistically significant difference between benign and malignant lesions (p =0.0166) (Fig.2). 85.7% of benign lesions showed well defined margins and round or oval shapes, while 76.9% of malignant cases were irregular in shape with ill-defined outlines. Parallel to Soliman et al., who stated that irregular margins were noted in 87.5% of malignant cases [13]. Also, Kamal et al tested the performance of enhancing lesions' shapes and

outlines in predicting their underlying lesion nature. Their specificities for shapes and lesion outlines were 77.8% and 83.3% respectively [18].

No statistically significant difference regarding the pattern of enhancement between benign and malignant lesions detected in this study. However, homogeneous enhancement showed a slightly higher frequency between benign lesions (42.85%) than between malignant lesions (30.8%) and heterogeneous enhancement is remarkably higher between malignant cases (69.2%) than between benign cases (14.3%). Kamal et al, results revealed that heterogeneous enhancement strongly remarked the malignant nature of the lesion ($p \leq 0.001$) [18]. Soliman et al reported that the heterogeneous enhancement pattern was exclusive to malignant lesions [13]. We detected one benign heterogeneously enhancing lesion and Kamal et al [18] detected two.

A rim enhancement pattern was detected in three cases of fibrocystic disease. All cases showed subtle, thin, uniform marginal enhancement with eliminated internal lesion density on combined images, typically identified as eclipse sign [19,20]. No malignant lesion exhibited a similar pattern of enhancement. The term "ring enhancement" is used by Kamal et al [18] for marginally enhancing lesions as a substitute for "rim enhancement" and they detected this pattern in 8.7% of malignant lesions compared to 55.6% of benign lesions, contrary to Schnall et al who decided that ring-like enhancement in MRI correlates with cancer diagnosis [21].

Reasonably, marginal enhancement may be a feature of various benign and malignant lesions' enhancement. Abscesses, cancer, seromas and many other pathologies may reveal this pattern. So, we suggest separating terms of description to a typical solar eclipse enhancement without any internal enhancement, which is highly associated with cysts and non-uniform rim/ring enhancement, which encompasses a wide spectrum of possibilities. Peters et al and Neeter et al considered the eclipse pattern on recombined images is specific to cysts [22,23]. Tennant et al suggested a scale for enhancement pattern description and categorized eclipse signs as type -1 [19].In our study, regarding non-mass enhancement; there is no statistically significant difference between benign and malignant lesions regarding either distributions or patterns enhancement.

Our observations were as follows: A multiregional distribution was detected in a benign lesion diagnosed as multiple abscesses. Focal distribution was detected in only malignant lesions and segmental distribution was detected in both benign and malignant lesions. Soliman et al detected a malignant lesion with multiregional distribution, although they had assumed multiregional distribution to be associated with benignity. Ductal, segmental and regional distributions were detected in 7 benign lesions and 1 malignant lesion [13]. The study by Soliman et al also discovered that patterns of enhancement did not differ statistically [13]. Kamal et al observed that non-mass heterogeneous enhancement strongly indicates malignancy ($p \leq 0.001$) [18].

From our point of view, there is substantial overlap regarding benign versus malignant non-mass enhancement. Proper management requires consideration of additional mammographic findings such as calcifications, nipple, skin changes or lymphadenopathy, another imaging modality evaluation and biopsy if still concerned. All of our cases were evaluated by US, either aspirated or biopsied. For all non-mass enhancement lesions, Chadashvili et al recommend needle or excisional biopsy [24].

Enhancing asymmetry is a new term added to the CEM lexicon. It is used to describe an enhancement observed in one view. To our knowledge, no studies have described similar findings. In our study, we observed a similar pattern in a single malignant lesion (Fig.3).

Microcalcifications, suspicious lymphadenopathy, nipple and skin changes were significantly common for malignant cases, with a statistically significant difference between benign and malignant groups, similar to Wessam et al study [12].

All inflammatory lesions in our study had suspicious mammographic and CEM features regarding their morphological descriptors and enhancement patterns and required additional ultrasonography evaluation (Fig.4). Kamal et al

admitted using ultrasound to resolve this similarity [11]. In addition to inflammatory breast disorders, which were a pitfall and always required another imaging modality or biopsy to confirm the diagnosis, the well-defined mass border and homogeneity of enhancement should not safely exclude the possibility of underlying malignancy. A collective and structured assessment of associated signs and a targeted ultrasound assessment were of benefit to overcome these pitfalls.

The main limitations of our study are the small number of enrolled patients and the technique is new to use at our institution.

CONCLUSIONS

Each mammographic asymmetry requires identification of its nature, as it may be the only sign for a wide range of entities. CEM can play a reliable role in the assessment of mammographic asymmetries. Analysis of low energy and combined images helps with characterization of underlying pathology if present and subsequently, proper clinical management. This can undo the radiologist's concerns about the significance of an encountered asymmetry, increase the cancer detection rate and reduce the number of biopsies.

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