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Research Paper

Incidence, mammographic and sonographic imaging features of focal stromal fibrosis of the breast, diagnosed on core needle biopsy

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ABSTRACT

The purpose of the study was to determine the incidence of biopsy-proven focal stromal fibrosis of the breast, and to describe the range of sonographic and mammographic imaging features in this condition. MRI breast imaging was not part of routine screening or assessment. This is a retrospective review of cases from the National University Hospital System, Singapore (NUHS). A number of 2377 women underwent core biopsies of the breast, 89 cases having diagnosis of focal stromal fibrosis histologically, fulfilled our inclusive criteria. Imaging features for each case were analysed and compared with the histopathology findings. The incidence of focal stromal fibrosis in our study was 3.7%. Out of all cases, slightly more than half appeared as a discrete mass on ultrasound scan, less than half as a cluster of microcalcifications, and a small percentage as asymmetric density and architectural distortion. There was no uniformity of the sonographic features of the masses found to be stromal fibrosis. They have a wide spectrum of appearances: from well-circumscribed to ill-defined, from rounded to irregular, with differing echogenicity, orientation and posterior sound transmission. A range of mammographic appearances was found. Many lesions were not seen on mammography. Visible findings included spiculated mass, well circumscribed mass, asymmetric density, architectural distortion, and clustered microcalcifications. No significant histopathological differences were found in the tissues surrounding the focal stromal fibrosis. The medical histories of all the patients were followed up in 5 years. One patient developed a mucinous carcinoma from the same lesion 3.5 years later. Focal stromal fibrosis has different sonographic and mammographic appearances. It is reasonable to accept an indeterminate focal lesion being concordant with this benign histopathological diagnosis post biopsy. It is important to be aware of the broad range of imaging features found in focal stromal fibrosis, and the potential of this benign entity to mimic malignancy.

Key words: Focal stromal fibrosis, Benign focal breast lesions.

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INTRODUCTION

A retrospective review was performed to determine the incidence of biopsy proven focal stromal fibrosis of the breast in female patients, presented to the National University Hospital, Singapore, and to describe the range of mammographic and sonographic imaging features in these cases. We also analysed the histopathological entities associated closely with focal stromal fibrosis. The final diagnosis was determined by follow up patients after a period of 5 years.

Focal stromal fibrosis is a benign histopathological entity characterised by a localised areas of fibrous tissue associated with hypoplastic mammary ducts and lobules. This may present as a symptomatic mass.

Other terms have been used to describe this entity,

including:

(i) Focal fibrosis of the breast
(ii) Focal fibrous mastopathy
(iii) Fibrous breast tumour

Stromal fibrosis is usually discovered incidentally at assessment of excised breast specimen and was traditionally uncommon. Widespread screening mammography has lead to sharp increase in number of diagnosis of this condition, found by image-guided core needle biopsy.

This retrospective review was prompted by observation that a wide range of imaging findings was diagnosed as "stromal fibrosis" after core needle biopsy.

Previous reports have suggested that inadequate imaging-pathology correlation, in cases of stromal fibrosis, can be a cause of false negative diagnosis of malignancy with some patients subsequently developing cancer at the biopsy site (Suyong at al., 2013). This study addresses this issue for our cases, by following their medical records for 5 years.

METHODS

A retrospective search of the database of the Department of Anatomical Pathology at National University Hospital found 2377 cases with core needle biopsies or with surgical excision of a breast lesion, in the period from January 1, 2002 to December 31, 2004.

Of these, 116 patients had the finding of stromal fibrosis in the histopathology report, giving incidence of 4.9%. Twenty one women from the group were excluded from the study, as no lesions were visible, either on ultrasound or mammographic images. They represented only as a palpable lump and were biopsied or surgically excised under palpation guidance. They may have been cases of non-focal fibrosis being associated with fibrocystic changes in the breast. Ninety five patients with focal abnormalities on mammography, ultrasonography or both modalities were initially included in this study. In 6 patients, the lesions were highly suspicious of malignancy, BI-RADS 5, the histopathology findings of benign focal stromal fibrosis was found discordant, a second core biopsy was performed and this confirmed malignancy in 5 cases and a hamartoma in 1 patient. These patients were excluded from the study, which leave total of 89 cases. Final incidence of focal stromal fibrosis in our study is 3.7%.

All images were retrieved and analysed by two investigators. The mammograms were read from hard copies and the ultrasound images were read from PACS (Picture Archiving and Communication System). The imaging features were observed and compared directly with the histopathology slides (in conjunction with the histopathologist). Concordance of all the biopsy reports were discussed and determined.

All the patients had film-screen mammography using the Kodak Min-R 2000 system with mammograms performed on either Siemens Mammomat 3000 or GE Senographe DMR conventional mammogram units. Ultrasound scans were performed using high-resolution linear-array broadband transducers (Philips ATL HDI-5000).

Core needle biopsy was performed in all patients. All, but two patients, had 14G core needle biopsy using an automated spring loaded metal biopsy gun (14 gauge BARD Magnum TM). Two patients underwent vacuum-assisted 11G core needle biopsy under stereotactic guidance (Mammotome, 9 gauge Johnson & Johnson).

Follow-up medical history of all the patients included in the study was performed 5 years later, using the Singapore Cluster Shared Patient Record System (CPRS). CPRS includes all major hospitals in Singapore and National Cancer Centre (NCC).

RESULTS

We observed an incidence of focal stromal fibrosis in 3.7%. The clinical characteristics of our study cohort are tabulated in Table 1. The mammographic features of our study cohort are tabulated in Table 2. The sonographic features of our study cohort are tabulated in Table 3.

The majority of lesions appeared as solid, hypoechoic masses irregular in shape with margins that were generally well defined oriented parallel to the skin, with increased posterior sound transmission, mainly classified as BIRADS 4 (Figures 2, 3, 4, 5, 6, 7).

Second common appearance of focal stromal fibrosis was a cluster of indeterminate microcalcifications (Figure 1).

Accompanying histological findings

In addition to the primary diagnosis of focal stromal fibrosis, a variety of additional benign histopathological entities were described in close association with stromal fibrosis, whether the imaging abnormality was a mass or cluster of microcalcifications, such as benign epithelial hyperplasia, adenosis, pseudoangiomatous stromal hyperplasia (PASH), fibroadenomatoid changes and periductal hyalinised fibrosis.

Of 33 patients who presented as cluster of microcalcifications, the most common histopathological finding next to stromal fibrosis was that of benign breast lobules and ducts, in 19 cases (58%). The rest were either showing epithelial hyperplasia, in 5 (16.7%), fibroadenomatoid change in 3 (8.3%), periductal hyalinised fibrosis in 4 (11.1%) or adenosis in 2 (5.6%).

In 53 patients who presented as a mass, the most common histopathological finding along with stromal fibrosis, was again that of benign breast tissue in 29 (56%)

Table 1. Clinical characteristics of our study cohort.

Feature/finding	Number (Percentage)
Patient features	
Age range	22-71
Median age	49
Average age	48
Screen-detected	60 (67%)
Clinical presentation (lump)	29(33%)
Imaging & clinical	89(100%)
Ultrasound only	18(20.2%)
Mammography only	34(38.2%)
Mammography and ultrasound	37(41.6%)
Palpable	36(40.4%)
Core needle biopsy guidance	89(100%)
Mammographic stereotactic	38(42.7%)
Ultrasound	39(43.8%)
Palpation (freehand)	12(13.5%)
Location of stromal fibrosis	
Left	43(48.3%)
Right	46(51.7%)
Upper outer quadrant	48(53.9%)
Lower outer quadrant	4(4.4%)
Lower inner quadrant	6(6.8%)
Upper inner quadrant	25(28.1%)
Retroareolar/central	6(6.8%)

Table 2. Mammographic features in our study cohort.

Feature/finding	Number (Percentage)
Mammographic appearances	75(100%)
Cluster of microcalcifications	33(44.0%)
Focal density	31(41.4%)
Architectural distortion	6(8.0%)
No abnormality	5(6.6%)
Not performed	14
Microcalcifications	33(100%)
Left breast	20(60.6%)
Right breast	13(39.4)
Appearances	
Indeterminate	22(66.6%)
Pleomorphic	9(27.3%)
Suspicious	2(6.1%)
Focal mammographic density	31(100%)
Asymmetric density	17(54.8%)
Focal mass	14(45.2%)
Architectural distortion (mammography)	6(100%)
Without mass	4(66.6%)
With mass	1(16.7%)
Microcalcifications only	1(16.7%)

Table 3. Sonographic findings of abnormalities in our study.

Finding	Number (Percentage)
Clinical findings	
No palpable abnormality	27(50.9%)
Corresponding palpable lump	26(49.1%)
Location of US lesion	
Left breast	26(49.1%)
Right breast	27(50.9%)
Ultrasound size	
Range	4 —40 mm
Ultrasound finding	
Discrete mass	
Microcalcifications	53(100%)
No abnormality	
Ultrasound appearances	53
Solid mass	53
Cyst	0
Complex (mixed solid & cystic)	0
Echogenicity	
Hypoechoic	33 (62.3%)
Heterogeneous	13 (24.5%)
Hyperechoic	1 (1.9%)
Isoechoic to the gland	6 (11.3%)
Shape	
Round	6 (11.3%)
Ovoid	18 (34.0%)
Lobulated	9 (17.0%)
Irregular	20 (37.7%)
Margins	
Circumscribed	24 (45.2%)
Microlobulated	10 (19.0%)
Ill-defined	19 (35.8%)
Posterior Sound Transmission	
Unchanged	19 (35.8%)
Increased	22 (41.5%)
Decreased (shadowing)	12 (22.7%)
Ultrasound Classification	
Likely Benign BIRADS 3	13 (24.5%)
Indeterminate BIRADS 4	33 (62.3%)
Suspicious BIRADS 5	7 (13.2%)

cases, adenosis in 9 (16%) cases, fibroadenomatoid change in 8 (14%) cases, epithelial hyperplasia in 6 (12%) cases and 1 (2%) case with periductal hyalinised fibrosis.

The second most common histopathological finding for patient presenting with microcalcifications was benign breast glandular change with epithelial hyperplasia, while for patient represented by mass the second most common finding were either fibroadenomatoid changes or adenosis. There were only minor differences in histopathological features of the specimens, with no specific correlation with image presentations.

Follow up

On follow up review of all our cases on CPRS, of the study cohort, 36 patients had further medical records including mammograms. One of the patients developed Infiltrating Mucinous Carcinoma Grade 1 about 3½ years later, from the lesion diagnosed as a stromal fibrosis, represented initially as a mass (Figures 8 and 9).

Thirty eight patients did have further medical records but not related to the breasts. Fifteen patients did not have further medical records in CPRS.

DISCUSSION

The focal stromal fibrosis in the breast is a pathologic entity characterised by proliferation of stroma with obliteration of the mammary acini and ducts, which results in a localized area of fibrous tissue associated with hypoplastic mammary ducts and lobules. Stromal fibrosis is previously seen to manifest mostly in premenopausal women as a palpable mass. The cause of stromal fibrosis is unknown. Estrogen related fibroplastic proliferation, a variant of mammary involution and end stage of inflammatory processes have been suggested (Taskin at al., 2011).

In the era of breast screening, frequent use of automated spring driven core biopsy has led to an increase in focal fibrosis being diagnosed, even more in cases presented as a non-palpable mass. There have been several reports with varying findings, from authors who did not have focal stromal fibrosis presented by microcalcifications (Wiratkapun at al., 2013) to others who recorded 37% of such cases (Goel at al., 2005). Some results were similar to our study (Sklair-Levy at al., 2001; Rosen at al., 1999; Revelon at al., 2000). In general, this entity has been little reported in the imaging literature.

This must be distinguished from the long standing, inaccurate and non-histological use of "fibrosis" to describe mammographic density in DY "pattern" described by Wellings and Wolf (1978), where homogeneous sheets of density occupy more than 25% of the breast volume.

Another similar surrounding but unrelated entity is "diabetic fibrous mastopathy" or "sclerosing lymphocytic lobulitis" which has a characteristic constellation of

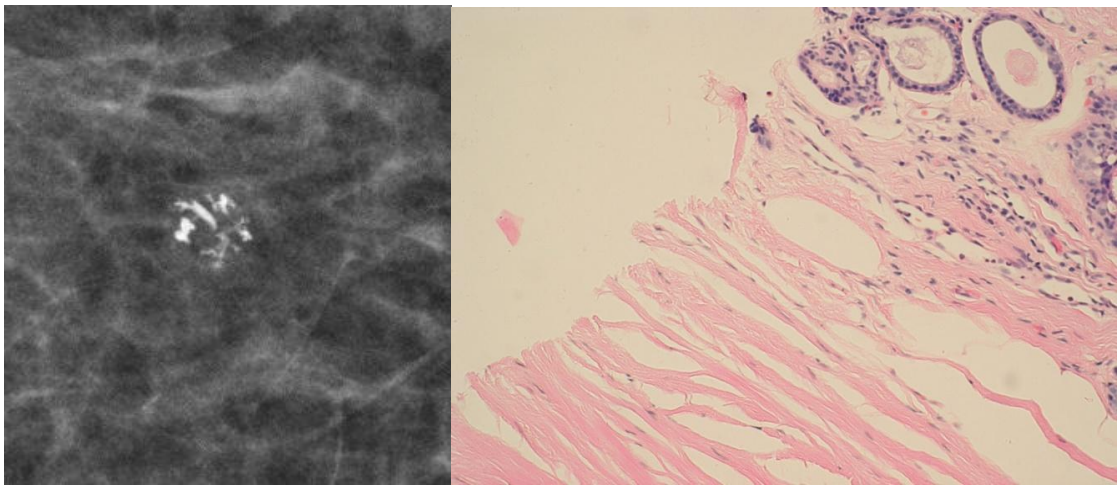

Figure 1. 63-year-old Malay woman. Mammography: Presented by tightly clusterred coarse microcalcifications, variable in size and shape, associated with small pleomorphic, branching, punctiform and linear microcalcifications, seated in RULQ; measuring 6 mm, 30 mm from nipple. Histopathology report: mostly hyalinized fibrous stroma with sccattered inflammatory cells and microcalcifications seen.

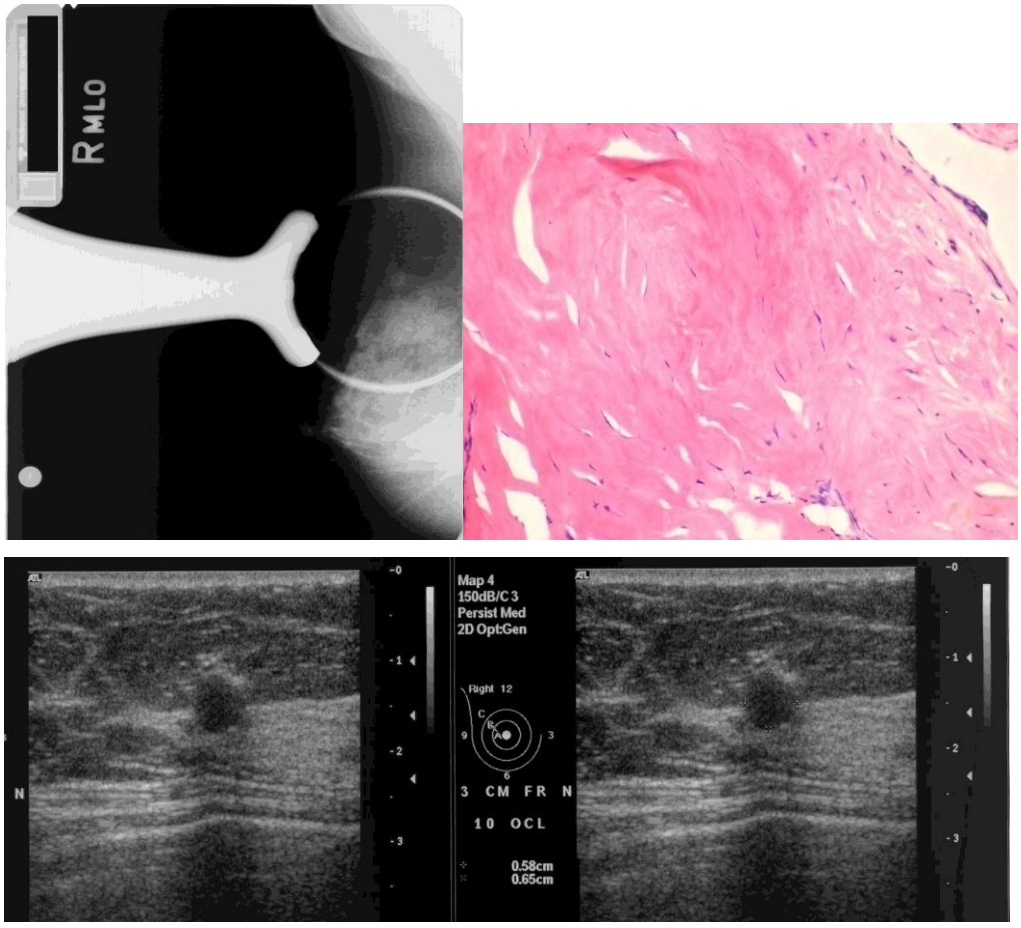

Figure 2. 53-year-old Chinese woman. Mammography: Ill-defined mass with density equal to breast tissue. Ultrasound scan: Rounded, hypoechoic, microlobulated nodule, measuring 7 mm, not parallel to the skin by orientation, had decreased sound transmission. Histopathology: Specimen shows fibrous stroma with scattered inflammatory cells.

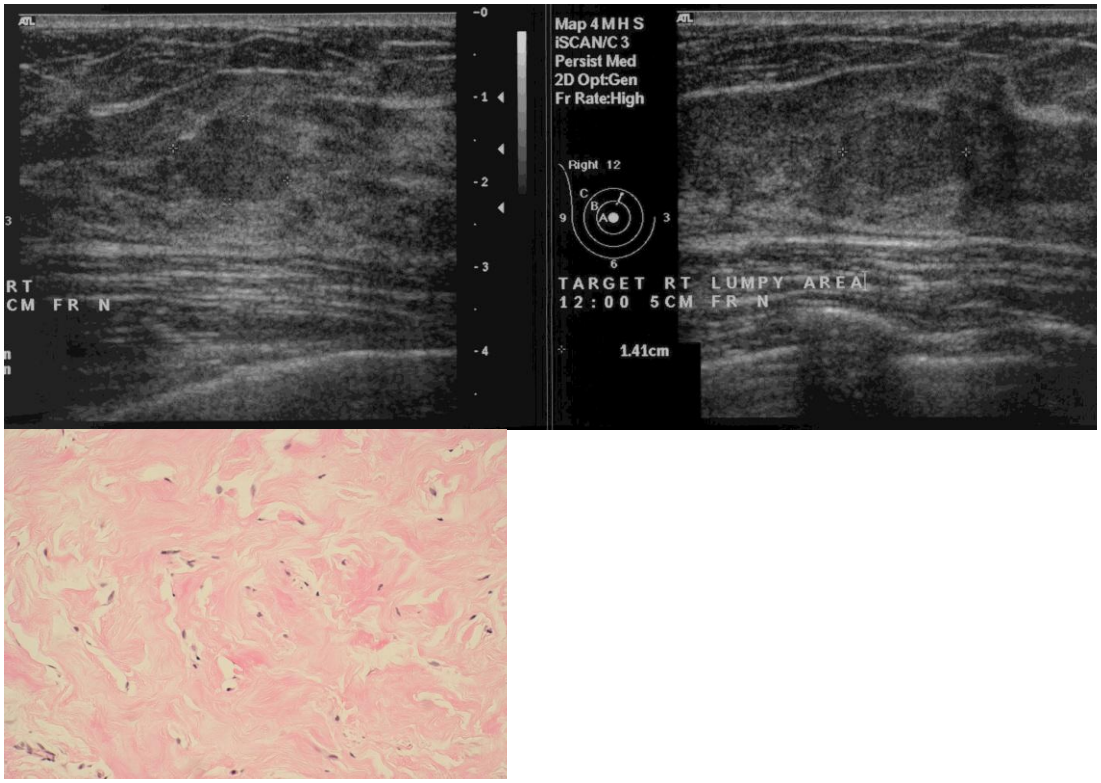

Figure 3. 29-year-old Malay woman. Presented by palpable lump. Ultrasound scan: Lobulated, isoechoic, ill-defined nodule, measuring 15 mm; parallel to the skin, increased sound transmission. Histopathology: In addition to stromal fibrosis, several slit-like spaces lined by myofibroblastic cells with appearance of pseudoangiomatous stromal hyperplasia (PASH) noted.

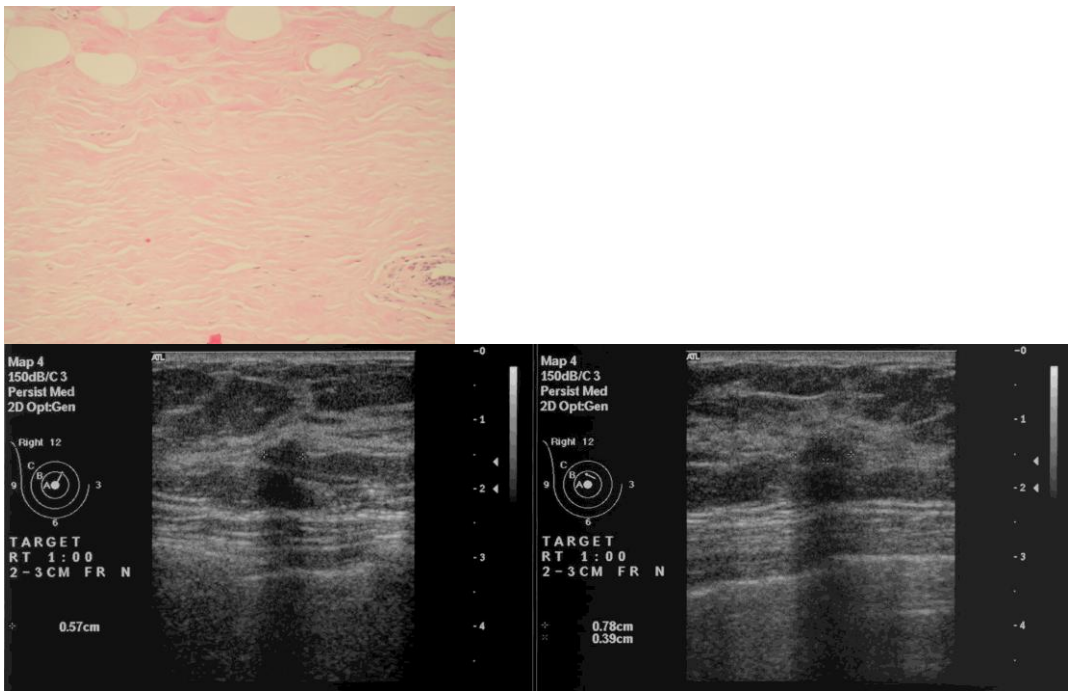

Figure 4. 30-year-old Chinese woman, presented by a palpable lump. Ultrasound scan: Irregular, ill-defined, hypoechoic nodule measuring 12 mm; parallel to the skin, decreased sound transmission. Hystopathology: Biopsy displays acellular stromal fibrosis with few fat cells on the top.

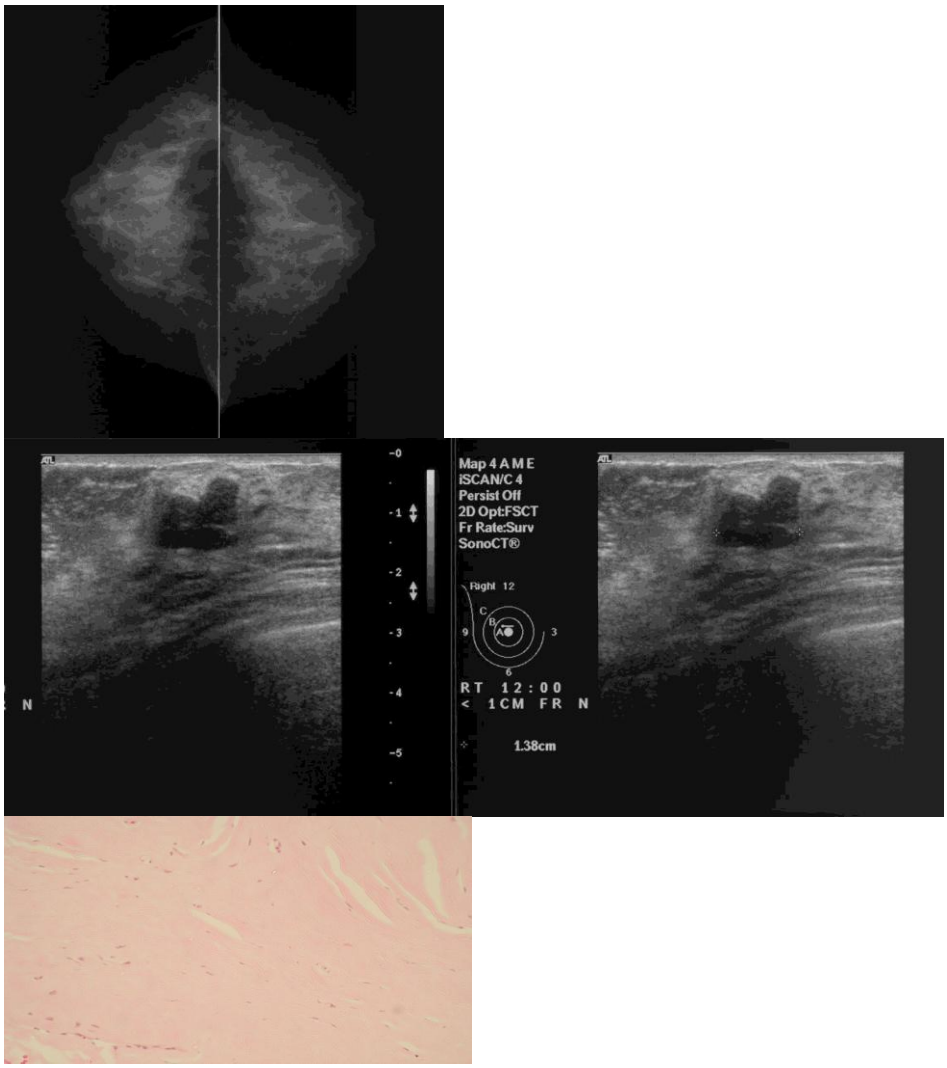

Figure 5. 50-year-old Indian woman. Mammography: Dense ill-defined mass in central right breast. Ultrasound scan: Irregular, well defined, hypoechoic nodule, measuring 15 mm, parallel to the skin, has decreased posterior transmission. Histopathology: Specimen shows hyalinized, mostly acellular fibrous stroma with scattered fibroblasts.

histological features, and is found almost exclusively in Type I diabetes (Kudva at al., 2003; Ferris, 2000). On imaging, this usually appears as a wide area of extensive markedly hypoechoic change, rather than a focal mass or cluster of microcalcifications. These features distinguish "diabetic fibrous mastopathy" from stromal fibrosis and from "focal fibrous mastopathy". Most pathologist consider focal stromal fibrosis an entity within the spectrum of fibrocystic change, others such as Haagensen (1986) believe that there is a distinct difference both clinically and histologically.

Our study describes the frequency of stromal fibrosis among lesions evaluated by core needle biopsy in women undergoing mainly routine screening mammography. We observed an incidence of focal stromal fibrosis in only 3.7%. In some studies, there were 7.9% patients reported, while in others the reported incidences were 3-4%.

Although our sample size is small, our data suggests that they account for quite a number of benign lesions being subject to core needle biopsy.

We found that the mammographic and ultrasonic features are variable. They were mainly sonographically visible masses or screen detected microcalcifications.

Mammographically they were represented as a cluster of microcalcifications, frequently in the upper outer quadrants of the breasts. Less frequently these lesions mammographically appear as relative low risk lesions, such as a focal asymmetric density, nodular density or rarely as an ill-defined density that is moderately suspicious for malignancy.

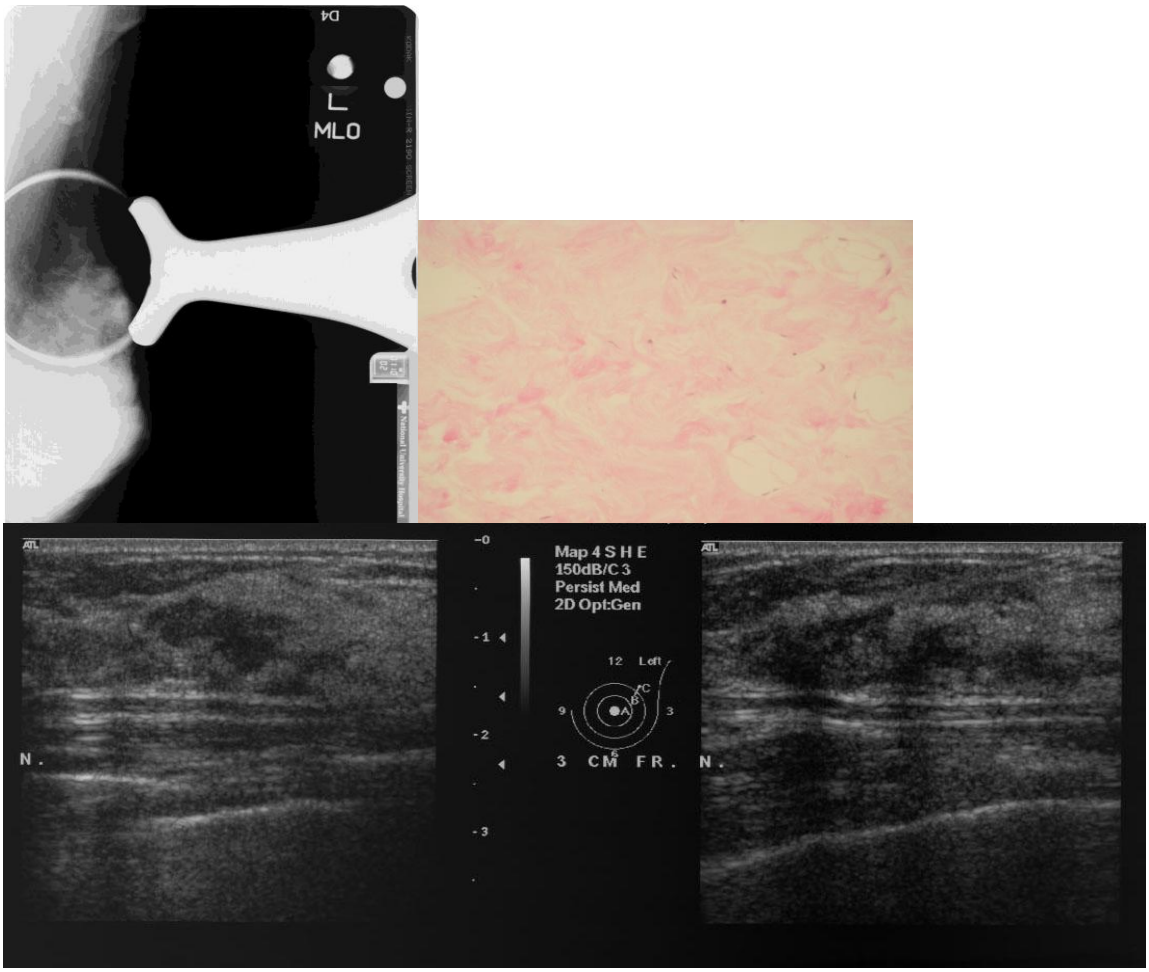

Figure 6. 46-year-old Chinese woman. Mammography: Ill-defined density. Ultrasound scan: Irregular, ill-defined nodule of mixed echogenicity, measuring 25 mm; not parallel to the skin, mixed posterior sound transmission. Histopathology: Specimen shows acellular fibrous stroma. No duct-lobular units noted.

Sonographically, the most common finding was a palpable, solid, hypoechoic, irregular mass with margins mainly well defined and with increased posterior sound transmission. Most of our cases were classified by Breast Imaging and Reporting System (BIRADS) in grade 4 (American College of Radiology BI-RADS Committee, 2003). Group of authors showed alike results in their study of nonpalpable focal stromal fibrosis, with the difference that majority of their cases were sonographically isoechoic. It was not explained either they were isoechogenic to fat or to breast tissue (Kyung at al., 2005). Several lesions appeared highly suspicious, were found discordant with the histopathological findings and were rebiopsied. In our study, out of 6 rebiopsied cases, 5 were proven malignant and one was a hamartoma. All 6 patients were excluded from our study. False negative lesions of 2.1% were reported by authors in their study after they follow up cases for 2 years, (Shin at al., 2013). We followed up the medical records of the patients for 5 years. One case was initially followed up for 2 years and the lesion showed no change in size or feature and was reported benign. 1.5 years later (a total of 3.5 years after initial diagnosis) the lesion increased significantly in size, which prompted a repeat biopsy, with outcome of mucinous carcinoma. There is no similar study for comparison, which would have 5 years follow-up cases of focal stromal fibrosis, therefore the frequency of malignant development of these lesions or dependency of the patient's age is inconclusive.

The histological subtypes of stromal fibrosis are variable, mainly represented as components of benign breast tissue. Stromal fibrosis was also thought to be an independent, incidental process from microcalcifications and thus non-specific.

Conclusion

In conclusion, focal stromal fibrosis can reveal a spectrum

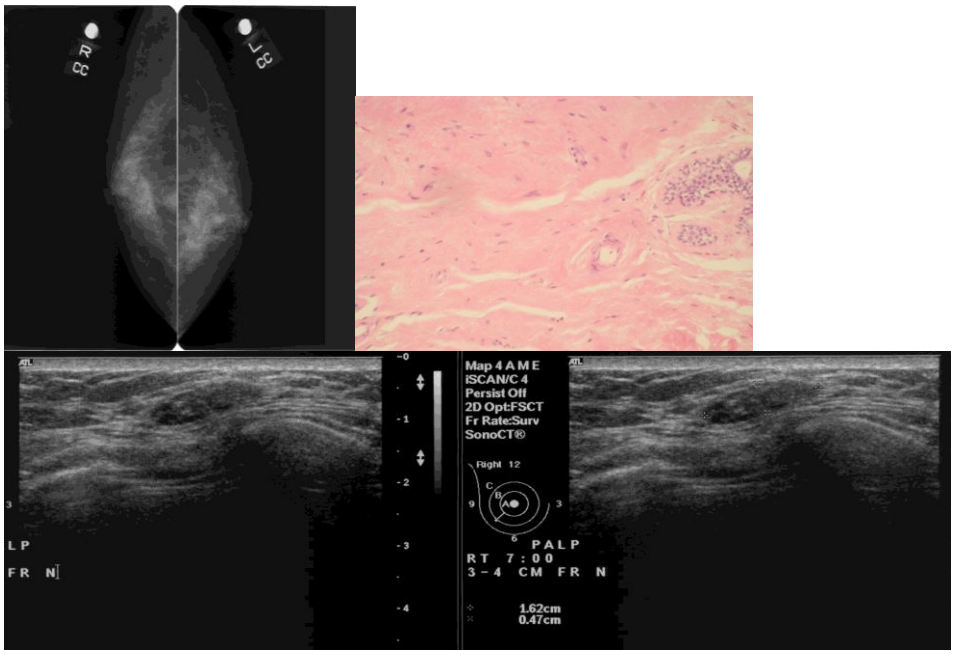

Figure 7. 50-year-old Chinese woman. Mammography: Isodense mass in central right breast. Ultrasound scan: Ovale, well defined, nodule of mixed echogenicity, measuring 18mm, not parallel to the skin, has unchanged sound transmission. Histopathology:Left half of specimen contains stromal fibrosis and right half contains prominent lobular units.

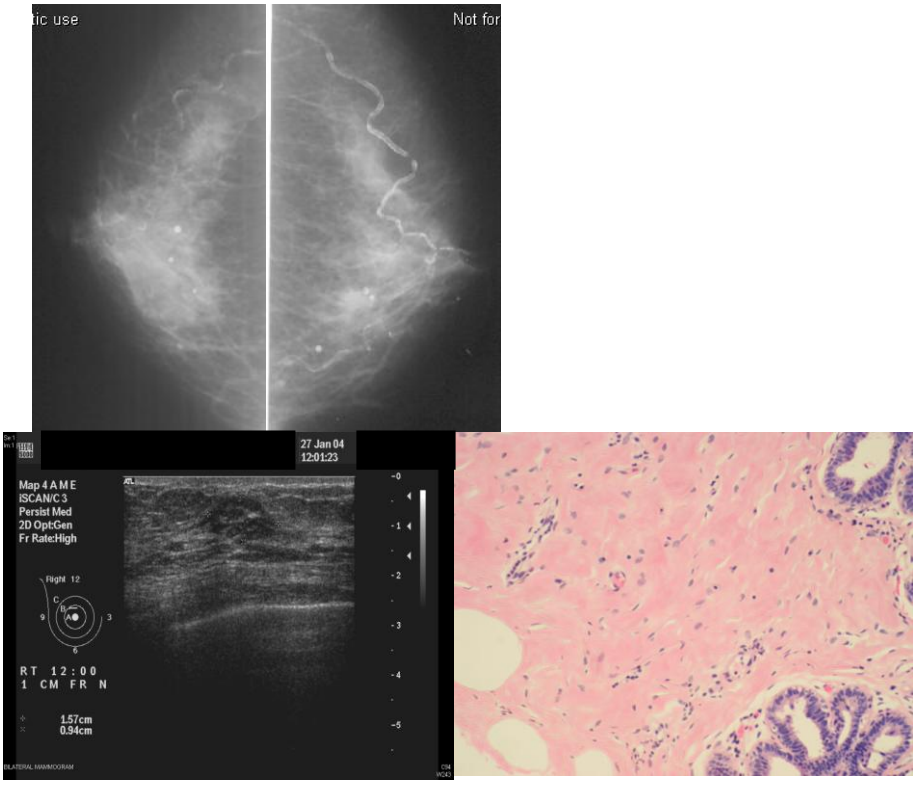

Figure 8. 73-year-old Malay woman. Presented first on January 2004 with mammography: Vague asymmetric density in right retroareolar region. Ultrasound scan: Oval, ill-defined nodule of mixed echogenicity, measuring 16×9 mm, parallel to the skin by orientation, unchanged posterior sound transmission. Histopathology: Histology shows stromal fibrosis with scattered fibroblasts and ducts. Mild usual epithelial hyperplasia of the ducts seen.

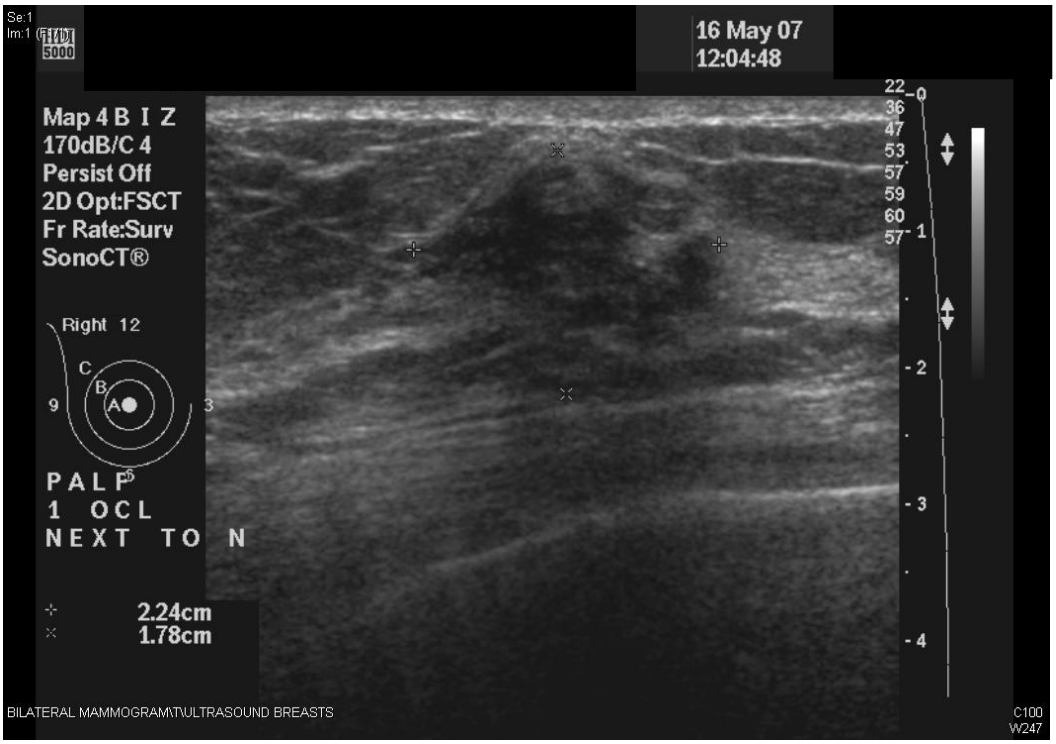

Figure 9. 76-year-old Malay woman. The feature of the same lesion 3½ years later. In May 2007, 1½ years after the last follow up examination, the same lesion in the right breast increased suddenly in size up to 24×18 mm. It was similar in feature apart from, newly developed, decreased posterior transmission. Repeated ultrasound-guided biopsy was performed with a histopathological result of an infiltrating mucinous carcinoma grade 1.The image of the lesion was stable on yearly follow-up examinations for 2 years.

of varied appearances, both mammographically and sonographically. The histological features were not significantly different between the mass lesion and microcalcifications. Our analysis does not demonstrate any definite association between imaging findings and histopathologic patterns of stromal fibrosis. Strict radiological-pathological concordance is critical and is prudent to continue regular follow up.

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