Original Article
Conventional ultrasound discriminates sclerosing adenosis involving ductal carcinoma in situ from pure sclerosing adenosis in breast

Jiejie Yao[1], Jianqiao Zhou[1], Xiaochun Fei[2], Xiaohong Jia[1], Weiwei Zhan[1]

Departments of [1]Ultrasound, [2]Pathology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China

Abstract: Objective: To investigate the diagnostic efficiency of conventional ultrasonography on sclerosing adenosis (SA), and SA involving ductal carcinoma in situ (SA-DCIS) of the breast. Methods: Clinical characteristics of 128 female patients with 136 lesions which were pathologically diagnosed as SA and SA-DCIS by ultrasonography (US) in Rui Jin Hospital Shanghai Jiaotong University School of Medicine (2011-2015) were retrospectively analyzed. All variables were analyzed by univariate and multivariate logistic regression analyses. The diagnostic efficiency of US on differentiating malignant SA-DCIS lesions from benign SA lesions was analyzed by ROC curve. Results: Eighty-six lesions in 81 patients were SA, and 50 lesions in 47 patients were SA-DCIS. A mass was visible in 70 (81.4%) SA lesions and 46 (92.0%) SA-DCIS lesions. Univariate analysis showed that SA-DCIS lesions were more likely to be larger and have an irregular shape, heterogeneous echogenicity, and high vascularity than SA lesions (all P<0.05). Multivariate analysis indicated that a larger lesion size and high vascularity were significantly and independently associated with SA-DCIS (both P<0.001). The sensitivity and specificity of US for differentiating malignant SA-DCIS lesions from benign SA lesions were 92.0% and 81.4%, the area under the curve of US was 0.844. Conclusion: SA-DCIS lesions are more likely to be larger and have higher vascularity than SA lesions verified with US.

Keywords: Sclerosing adenosis, ductal carcinoma in situ, ultrasonography, breast

Introduction

Sclerosing adenosis (SA) of the breast is a benign proliferative lesion on the terminal duct lobular unit surrounded by stromal sclerosis. Ductal carcinoma in situ (DCIS) of the breast is a neoplastic proliferation of epithelial cells confined to the ductal lobular system without tumor invasion through the basement membrane [1]. DCIS can deteriorate from SA, which usually is entirely surrounded by SA or at least focally located in the same area; namely, SA involves DCIS (SA-DCIS) [2]. However, which cases of SA will progress into carcinoma remains unclear. SA-DCIS may be an intermediate lesion [3]. Unlike SA, which is common in the breast and has been reported with contradictory imaging results in several previous studies [4], the clinical and image appearances of SA-DCIS haven't been well defined [5, 6]. To our knowledge now, only Yoshida A et al. analyzed 24 SA-DCIS cases and suggested that the rate of bilateral breast cancer and the architectural distortion on radiologic studies were higher in patients with SA-DCIS than in those with non-SA DCIS [7]. The radiological difference between SA and SA-DCIS has not been well documented, and it is unclear whether certain image features have prognostic value for malignant tumors.

With the increased awareness of breast health protection in women in Shanghai, China, the number of cases of SA and SA-DCIS detected recently has been increasing. Although mammography (MG) and magnetic resonance imaging (MRI) can identify SA and SA-DCIS, ultrasonography (US) characterization is better tolerated, less expensive as well as having a simpler and quicker detection process so it has become an important screening tool in China [8-10]. Preoperative evaluation of US features could help to select SA-DCIS patients who would benefit from surgery. It is worthy to confirm that conventional US can discriminate SA-DCIS from SA in the breast.

To date, no study has compared US characteristics of SA and SA-DCIS. Therefore, the aim of this study was to compare the ultrasonographic features of SA-DCIS and SA to assess the differentiating ability of US for SA-DCIS from SA.

Materials and methods

Study population

This retrospective study was approved by the ethical review board of Rui Jin Hospital Shanghai Jiaotong University School of Medicine, and all patients have provided informed consent. The data for all SA and SA-DCIS (including DCIS with microinvasion) lesions diagnosed by US in our hospital were from January 2011 to June 2015. All these patients received surgical resections and the lesions were pathologically reexamined.

We excluded the cases that only had core needle biopsy results, SA lesions with a variety of benign lesions, high-risk lesions or non-DCIS malignant lesions. Ultimately, our cohort was comprised of a total of 128 patients with 136 lesions.

Clinical information included the patient' age, menopausal status, hormonal replacement therapy, family history of breast cancer and symptoms. Family history was classified as negative, weak, or strong. A strong family history was defined as at least one first-degree relative with breast cancer before 50 years old, or two or more relatives with breast cancer and at least one of them was first-degree relative. Any lesser degree of breast cancer of family history was defined as weak [9].

Sonographic examinations

Real-time grayscale and color Doppler US were performed with a Mylab 60 or Mylab 90 (Esaote, Genoa, Italy) equipped with a 10-15-MHz transducer. All 128 patients with 136 lesions underwent ultrasonographic examinations prior to surgery. The sonographic examinations were performed by 2 radiologists who had over 9 years of experience in breast US examination. The ultrasonographic features of mass lesions were examined according to the 2013 version of the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS). Non-mass lesions were assessed as architectural disorder (an area with disordered organization structure compared to normal breast tissue) or a focal hypoechoic area.

The grayscale ultrasonographic features of mass lesions were assessed according to the size (maximum diameter), shape (round or oval versus irregular), orientation (parallel versus nonparallel to the skin), margins (circumscribed versus uncircumscribed), echogenicity (homogenously hypoechoic versus homogenously hyper- or isoechoic versus heterogeneous), posterior acoustic features (shadowing or combined posterior acoustic features versus no posterior acoustic features or enhancement), calcifications (absent versus present), and duct changes (absent versus present). An uncircumscribed lesion was defined as a mass with indistinct margins that was spiculated, angular, or microlobulated. The color Doppler sonographic characteristics were classified as absent blood flow (no vascular flow in the mass or in the rim around the mass), internal blood flow (orderly or disorderly blood vessels present within the mass or penetrating the margins of the mass), vessels along the rim (blood vessels were marginal and formed part or all of the rim around the mass), or combined, according to the BI-RADS lexicon. Vascularity was defined as absent, low (internal or vessels in a rim vascular flow distribution), and high (combined vascular flow distribution).

Histological analysis

All surgical specimens were specifically reviewed by a pathologist (X.C.F.) with over 13 years working experience to confirm the diagnosis results of US on SA (SA was the sole or major component in the specimens) and SA-DCIS (the specimens in which DCIS was entirely surrounded by SA or DCIS was present at least focally in an area of SA).

Statistical analysis

Data analysis was performed with SPSS 20.0 statistical software (SPSS Inc., Chicago, IL, USA). In the univariate analysis, continuous variables are presented with mean ± standard deviation (SD) and the comparison between groups were performed by independent sample t test; quantitative variables are presented as case number and percentage and the comparison between groups were performed by chi-
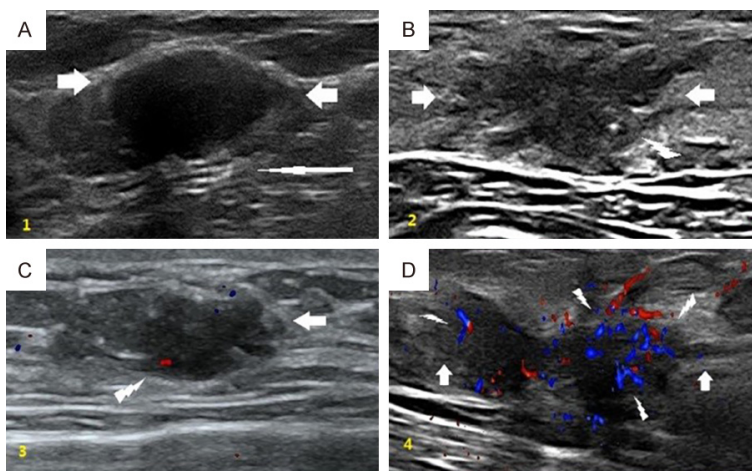
Figure 1. Representative ultrasonography images from patients with SA and SA-DCIS. A: Grayscale sonogram of SA shows an oval hypoechoic mass with circumscribed margins (short arrows) and no shadowing posterior acoustic features (long arrow); B: Grayscale sonogram of SA-DCIS shows an irregularly heterogeneous mass with indistinct margins (short arrows) and microcalcifications (jagged arrow); C: Color Doppler ultrasonogram of SA shows an irregularly hypoechoic mass with indistinct margins (short arrow) and low vascularity (jagged arrow); D: Color Doppler ultrasonogram of SA-DCIS shows an irregularly hypoechoic mass with indistinct margins (short arrows) and high vascularity (jagged arrows). SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma In Situ.

Table 1. Clinical characteristics of patients with SA and SA-DCIS

Characteristic	SA (n=81)	SA-DCIS (n=47)	P
Age (years)	46.9±7.5	48.8±9.6	0.523
Menopausal status			0.603
Premenopausal	52 (64.2)	28 (59.6)	
Postmenopausal	29 (35.8)	19 (40.4)	
Hormonal replacement therapy			0.727
Yes	23 (28.4)	12 (25.5)	
No	58 (71.6)	35 (74.5)	
Family history of breast cancer			0.813
Yes	24 (29.6)	13 (27.7)	
No	57 (70.4)	34 (72.3)	
Symptom			0.099
Palpable mass	16 (19.8)	18 (38.3)	
Mastalgia	24 (29.6)	11 (23.4)	
Nipple discharge	9 (11.1)	8 (17.0)	
Asymptomatic	32 (39.5)	10 (21.3)	

Notes: SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma Carcinoma in Situ. Patients were grouped according to the pathology results.

ed. P<0.05 was considered statistically significant.

Results

Pathologic characteristics of patients

All patients were female, with a mean age of 48 years (range, 33-65 years). A total of 128 patients with 136 lesions including 86 SA lesions in 81 patients and 50 SA-DCIS lesions in 47 patients were retrospectively analyzed. Five patients had bilateral SA, and 3 patients had bilateral SA-DCIS. Six lesions in 6 patients were SA-DCIS with microinvasion. **Figure 1** shows representative ultrasonography images from patients with SA and SA-DCIS and their clinical characteristics are summarized in **Table 1** (Patients were grouped according to the pathology results). The two groups had similar age, menopausal status, hormonal replacement therapy, family history of breast cancer, and similar clinical symptoms (all P>0.05).

Univariate and multivariate analysis of US findings

Under US examination, a mass was visible in 70 (81.4%) SA lesions and 46 (92.0%) SA-DCIS lesions. Architectural disorder was observed in 9 (10.4%) SA lesions and 4 SA-DCIS lesions (8.0%). A focal hypoechoic area was detected in 4 (4.7%) SA lesions, and no evidence of abnormality on US was detected in 3 (3.5%) cases of SA.

square or Fisher's exact tests. Multivariate logistic regression analysis was used to analyze the variables that were significant in the univariate analysis. To evaluate the diagnostic performance, the sensitivity and specificity and area under the curve (AUC) of receiver operating characteristic (ROC) curves were calculat-

The results of univariate regression analysis of the sonographic findings of masses in SA and SA-DCIS are summarized in **Table 2** (Patients were grouped according to the US results). The mean lesion size (the maximum diameter of the mass) in patients with SA-DCIS (mean diameter, 2.8 cm; range, 0.8-6 cm) was significantly

Table 2. Univariate analysis of ultrasonographic features of SA and SA-DCIS Masses

Mass	SA (n=70)	SA-DCIS (n=46)	P
Size (cm) Mean ± SD	1.5±0.9	2.8±1.4	<0.001
≤2	43 (61.4)	10 (21.7)	<0.001
>2	27 (38.6)	36 (78.3)	
Shape			0.023
Oval/round	24 (34.3)	7 (15.2)	
Irregular	46 (65.7)	39 (84.8)	
Orientation			0.827
Parallel	52 (74.3)	35 (76.1)	
Not parallel	18 (25.7)	11 (23.9)	
Echogenicity			0.033
Homogenously hypoechoic	27 (38.6)	8 (17.4)	
Homogenouslyhyper-or isoechoic	9 (12.8)	5 (10.9)	
Heterogeneous	34 (48.6)	33 (71.7)	
Margins			0.136
Circumscribed	26 (37.1)	11 (23.9)	
Not circumscribed	44 (62.9)	35 (76.1)	
Posterior acoustic features			0.485
None or enhancement	32 (45.7)	18 (39.1)	
Shadowing or combined	38 (54.3)	28 (60.9)	
Calcification			0.557
Absent	45 (64.3)	32 (69.6)	
Present	25 (35.7)	14 (30.4)	
Duct changes			0.085
Absent	57 (81.4)	31 (67.4)	
Present	13 (18.6)	15 (32.6)	
Vascularity			<0.001
Absent	29 (41.4)	5 (10.9)	
Low	26 (37.1)	13 (28.3)	
High	15 (21.4)	28 (60.9)	

Note: SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma In Situ. Patients were grouped according to the US results.

Table 3. Multivariate analysis of sultrasonographic findings

Variable	B	Wald	df	P	OR (95% CI)
Size >2 cm	0.869	17.463	1	<0.001	2.519 (1.218-4.594)
High vascularity	1.096	20.569	1	<0.001	2.878 (1.371-5.873)
Constant	-1.845	63.587	1	<0.001	0.189

Note: SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma In Situ. B, the regression coefficient; CI, Confidence Interval; OR, the Odds Ratio.

larger than that in patients with SA (mean diameter, 1.5 cm; range, 0.5-4.8 cm; P<0.05). Larger lesion size (78.3% versus 38.6%), irregular shape (84.8% versus 65.7%), and heterogeneous echogenicity (71.7% versus 48.6%) as well as high vascularity (60.9% versus 21.4%) were significantly more common in the SA-DCIS group (all P<0.05). Other BI-RADS US descriptors, including orientation, margins, posterior acoustic features, calcification and duct changes showed no significant difference between the groups (all P> 0.05).

Multivariate analysis revealed that a lesion size >2 cm (P<0.001; OR, 2.519; 95% CI, 1.218-4.594) and high vascularity (P<0.001; OR, 2.878; 95% CI, 1.371-5.873) were significantly and independently associated with SA-DCIS (**Table 3**). However, there was no association between sonographic results and clinical characteristics (all P>0.05; **Table 4**).

The diagnostic efficiency of US

The sensitivity, specificity and the area under the ROC curves (AUC) of US for differentiating malignant SA-DCIS lesions from benign SA lesions were 92.0%, 81.4% and 0.844, respectively (**Table 5** and **Figure 2**).

Discussion

In 1994, Ichihara S. et al. first reported a case of DCIS entirely surrounded by SA and suggested that DCIS originated in the tubules of SA [11]. Recent studies have proved that SA usually coexists with proliferative lesions as well as malignancies and most of them are DCIS [8, 12, 13]. Currently, few studies have described the imaging features of SA-DCIS, except some case reports. Therefore, this is the first study to compare the clinical and ultrasonographic features between SA-DCIS and SA with a relatively large sample size.

Table 4. Correlation of clinical characteristics with lesion size and vascularity in SA and SA-DCIS

| Clinical Characteristic	size (cm)		P	Vascularity		P
	>2	≤2		High	Low/Absent	
Menopausal status			0.364			0.673
Premenopausal	42 (66.7)	31 (58.5)		26 (60.5)	47 (64.4)	
Postmenopausal	21 (33.3)	22 (41.5)		17 (39.5)	26 (35.6)	
Hormonal replacement therapy			0.656			0.921
Yes	19 (30.2)	14 (26.4)		12 (27.9)	21 (28.8)	
No	44 (69.8)	39 (73.6)		31 (72.1)	52 (71.2)	
Family history of breast cancer			0.427			0.744
Yes	16 (25.4)	17 (32.1)		13 (30.2)	20 (27.4)	
No	47 (74.6)	36 (67.9)		30 (69.8)	53 (72.6)	
Symptom			0.058			0.251
Palpable mass	24 (38.1)	10 (18.9)		16 (37.2)	18 (24.7)	
Mastalgia	16 (25.4)	17 (32.1)		12 (27.9)	21 (28.8)	
Nipple discharge	10 (15.9)	6 (11.3)		7 (16.3)	9 (12.3)	
Asymptomatic	13 (20.6)	20 (37.7)		8 (18.6)	25 (34.2)	

Note: SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma In Situ. Data are presented as numbers (percentages).

Table 5. The diagnostic efficiency of US

Methods		Pathology		Total
		SA-DCIS	SA	
US	SA-DCIS	46	16	62
	SA	4	70	74
Total		50	86	136

Note: SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma In Situ.
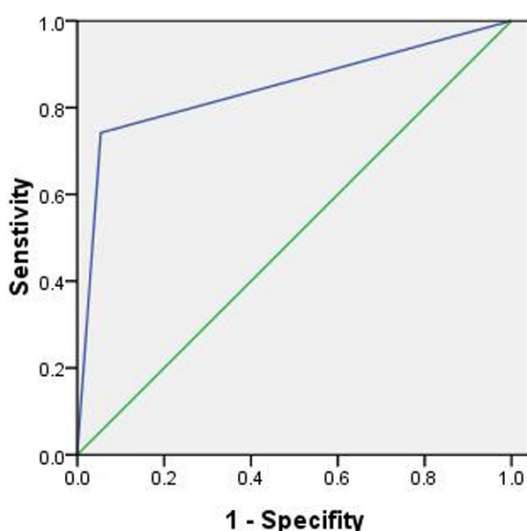
Figure 2. ROC curve of Color Doppler ultrasonogram of SA-DCIS. SA, Sclerosing Adenosis; SA-DCIS, SA involving Ductal Carcinoma In Situ.

Clinically, SA is frequently observed in the premenopausal age group and is correlated with both an abnormal hormonal environment and a family history of breast cancer [14, 15]. However, the contribution of age and menopausal status to breast cancer in previous studies is controversial [7, 16-18]. Our study also found that age, menopausal status, hormonal replacement therapy, and family history of breast cancer had no association with SA-DCIS, which was inconsistent with previous studies. Early published results suggest that SA-DCIS can present with a variety of clinical symptoms, including a palpable mass or nipple discharge [19]. It is also common for an asymptomatic case of SA-DCIS to be diagnosed during a radiological screening examination. SA has also been reported to be asymptomatic and noted microscopically and may form a palpable mass as a result of confluence of the affected lobules [20, 21]. However, although our study also found that patients with SA-DCIS were more likely to have a palpable mass (38.3% versus 19.8%) and less asymptomatic mass (21.3% versus 39.5%) than patients with SA, but these differences were not statistically significant (P>0.05).

The size of SA lesions has been considered a way to differentiate the risk of cancer [22, 23]. Our study also found that patients with SA-DCIS had significantly larger lesion size than those with SA.

Malignant tumors have a tendency to show increased vascularization, but avascular tu-

mors as well as hypervascular benign tumors have been discovered as well [24]. However, few studies have been published about the vasculature of SA-DCIS and SA lesions. Malignant lesions tend to show enlarged and twisted vessels inside breast lesions and penetrating vessels and spiculated or radial vessels in the periphery, whereas benign lesions mainly show peripheral annular vessels [24-26]. In our experience, the vascular flow distribution was significantly different between benign and malignant lesions on Doppler images. The combined vascular flow distribution involving internal vessels and vessels along the rim were more commonly detected in SA-DCIS lesions than in SA lesions. Our study results showed that a larger mass size, irregular shape, heterogeneous echogenicity, and high vascularity were more common in SA-DCIS lesions than in SA lesions. However, multivariate analysis indicated that neither irregular shape nor heterogeneous echogenicity were associated with DCIS, a larger lesion size and a high vascularity were significantly and independently associated with SA-DCIS.In addition, when correlating with clinical information, our study also found that neither a larger lesion size nor high vascularity on US were associated with clinical characteristics. Hence, careful imaging examination of the breast in patients with SA lesions is recommended because these lesions may lack evident clinical manifestations for predicting malignancy.

In our cohort, we achieved 92.0% sensitivity and 81.4% specificity for the differentiation of SA-DCIS lesions from benign SA lesions. The AUC of US is 0.844. The sensitivity and diagnostic efficiency are high. In addition, a combination of US, MG and MRI might be recommended to increase the diagnostic performance.

Our study had several limitations. First, it was retrospective in design; second, our study only used conventional US, not 3-dimensional US, elastography, or superb microvascular imaging to compare SA and SA-DCIS lesions, because these US technologies were not widely used during the study period. Therefore, a prospective, multicenter cohort study will be performed in the future to verify our results.

In conclusion, SA-DCIS lesions were more likely to be larger in size (>2 cm) and to have high vascularity than SA lesions. Although patients may lack evident clinical manifestations, those with these sonographic features tended to have malignant lesions, which should alert the clinician to the possibility of DCIS.

Disclosure of conflict of interest

None.

Address correspondence to: Weiwei Zhan, Department of Ultrasound, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, No. 197 Ruijin Second Road, Shanghai 200025, China. Tel: +86-18917762563; E-mail: zhanweiweiiu98@163.com

References

[1] Preece PE. Sclerosing adenosis. World J Surg 1989; 13: 721-725.

[2] Pinder SE. Ductal carcinoma in situ (DCIS): pathological features, differential diagnosis, prognostic factors and specimen evaluation. Mod Pathol 2010; 23 Suppl 2: S8-13.

[3] Cui X and Wei S. Carcinoma in situ involving sclerosing adenosis: seeking the salient histological characteristics to prevent overdiagnosis. Ann Clin Lab Sci 2017; 47: 529-534.

[4] Yu BH, Tang SX, Xu XL, Cheng YF, Bi R, Shui RH, Tu XY, Lu HF, Zhou XY and Yang WT. Breast carcinoma in sclerosing adenosis: a clinicopathological and immunophenotypical analysis on 206 lesions. J Clin Pathol 2018; 71: 546-553.

[5] Günhan-Bilgen I, Memiş A, Ustün EE, Ozdemir N and Erhan Y. Sclerosing adenosis: mammographic and ultrasonographic findings with clinical and histopathological correlation. Eur J Radiol 2002; 44: 232-238.

[6] Chen YL, Chen JJ, Chang C, Gao Y, Wu J, Yang WT and Gu YJ. Sclerosing adenosis: ultrasonographic and mammographic findings and correlation with histopathology. Mol Clin Oncol 2017; 6: 157-162.

[7] Yoshida A, Hayashi N, Akiyama F, Yamauchi H, Uruno T, Kikuchi M, Yagata H, Tsugawa K, Suzuki K, Nakamura S and Tsunoda H. Ductal carcinoma in situ that involves sclerosing adenosis: high frequency of bilateral breast cancer occurrence. Clin Breast Cancer 2012; 12: 398-403.

[8] Huang N, Chen J, Xue J, Yu B, Chen Y, Yang W, Shao Z and Wu J. Breast sclerosing adenosis and accompanying malignancies: a clinicopathological and imaging study in a Chinese population. Medicine (Baltimore) 2015; 94: e2298.

[9] Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, Vierkant RA, Maloney SD, Pankratz VS, Hillman DW, Suman VJ, John-

son J, Blake C, Tlsty T, Vachon CM, Melton LJ and Visscher DW. Benign breast disease and the risk of breast cancer. N Engl J Med 2005; 353: 229-237.

[10] Mendelson EB, Böhm-Vélez M, Berg WA, Whitman GJ, Feldman MI and Madjar H. ACR BI-RADS ultrasound. ACR BI-RADS Atlas, Breast Imaging Reporting and Data System. 5th edition. Reston, VA: American College of Radiology; 2013. pp. 1-173.

[11] Ichihara S and Aoyama H. Intraductal carcinoma of the breast arising in sclerosing adenosis. Pathol Int 1994; 44: 722-726.

[12] Ogura K, Horii R, Oosako T, Iwase T and Akiyama F. A clinico-pathological study on cancer in sclerosing adenosis. Breast Cancer 2014; 21: 732-737.

[13] Fukai S, Yoshida A, Akiyama F, Tsunoda H, Lefor AK, Kimura J, Sakamoto T, Suzuki K and Mizokami K. Ductal carcinoma in situ of the breast in sclerosing adenosis encapsulated by a hamartoma: a case report. Int J Surg Case Rep 2018; 45: 9-12.

[14] Jensen RA, Page DL, Dupont WD and Rogers LW. Invasive breast cancer risk in women with sclerosing adenosis. Cancer 1989; 64: 1977-1983.

[15] Oiwa M, Endo T, Ichihara S, Moritani S, Hasegawa M, Iwakoshi A, Sato Y, Morita T, Hayashi T and Kato A. Sclerosing adenosis as a predictor of breast cancer bilaterality and multicentricity. Virchows Arch 2015; 467: 71-78.

[16] Bertrand KA, Tamimi RM, Scott CG, Jensen MR, Pankratz V, Visscher D, Norman A, Couch F, Shepherd J, Fan B, Chen YY, Ma L, Beck AH, Cummings SR, Kerlikowske K and Vachon CM. Mammographic density and risk of breast cancer by age and tumor characteristics. Breast Cancer Res 2013; 15: R104.

[17] Ashbeck EL, Rosenberg RD, Stauber PM and Key CR. Benign breast biopsy diagnosis and subsequent risk of breast cancer. Cancer Epidemiol Biomarkers Prev 2007; 16: 467-472.

[18] Taşkin F, Köseoğlu K, Unsal A, Erkuş M, Ozbaş S and Karaman C. Sclerosing adenosis of the breast: radiologic appearance and efficiency of core needle biopsy. Diagn Interv Radiol 2011; 17: 311-316.

[19] Visscher DW, Nassar A, Degnim AC, Frost MH, Vierkant RA, Frank RD, Tarabishy Y, Radisky DC and Hartmann LC. Sclerosing adenosis and risk of breast cancer. Breast Cancer Res Treat 2014; 144: 205-212.

[20] Kundu UR, Guo M, Landon G, Wu Y, Sneige N and Gong Y. Fine-needle aspiration cytology of sclerosing adenosis of the breast: a retrospective review of cytologic features in conjunction with corresponding histologic features and radiologic findings. Am J Clin Pathol 2012; 138: 96-102.

[21] Gill HK, Ioffe OB and Berg WA. When is a diagnosis of sclerosing adenosis acceptable at core biopsy? Radiology 2003; 228: 50-57.

[22] Shaaban AM, Sloane JP, West CR, Moore FR, Jarvis C, Williams EM and Foster CS. Histopathologic types of benign breast lesions and the risk of breast cancer: case-control study. Am J Surg Pathol 2002; 26: 421-430.

[23] Sloane JP and Mayers MM. Carcinoma and atypical hyperplasia in radial scars and complex sclerosing lesions: importance of lesion size and patient age. Histopathology 1993; 23: 225-231.

[24] Kim S, Lee HJ, Ko KH, Park AY, Koh J and Jung HK. New Doppler imaging technique for assessing angiogenesis in breast tumors: correlation with immunohistochemically analyzed microvessels density. Acta Radiol 2018; 59: 1414-1421.

[25] Lee SW, Choi HY, Baek SY and Lim SM. Role of color and power doppler imaging in differentiating between malignant and benign solid breast masses. J Clin Ultrasound 2002; 30: 459-464.

[26] Xiao XY, Chen X, Guan XF, Wu H, Qin W and Luo BM. Superb microvascular imaging in diagnosis of breast lesions: a comparative study with contrast-enhanced ultrasonographic microvascular imaging. Br J Radiol 2016; 89: 20160546.