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## Sclerosing Adenosis of the Breast: Report of Two Cases and Review of the Literature

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### Summary

**Background:**

Sclerosing adenosis is a benign, usually asymptomatic lobulocentric proliferative process that involves both the epithelial and the mesenchymal component of the breast. It is commonly an incidental finding in perimenopausal women undergoing screening mammography.

**Case Report:**

We reported on two patients with sclerosing adenosis assessed with mammography, ultrasound, and contrast-enhanced magnetic resonance imaging. Case 1 was a 21-year-old woman with a palpable lesion in her right breast that was depicted as an irregular mass on contrast-enhanced magnetic resonance imaging. Case 2 was an asymptomatic 42-year-old woman with suspicious ultrasound findings in her left breast; contrast-enhanced magnetic resonance imaging showed regional non-mass-like enhancement associated with increased vascularity. Both patients underwent ultrasound-guided vacuum-assisted biopsy. Sclerosing adenosis does not have distinctive radiological features and can mimic a malignant growth process, thus requiring a diagnostic biopsy.

**Conclusions:**

SA is a common, benign, generally asymptomatic proliferative lesion of the breast. It is associated with a doubling of the risk of developing breast carcinoma, even though its role in carcinogenesis remains to be elucidated. It does not exhibit distinctive MG, US or even MRI features. Since it may mimic a carcinoma it requires further investigation with a diagnostic biopsy.

**MeSH Keywords:**

**Breast • Fibrocystic Breast Disease • Magnetic Resonance Imaging • Mammography**

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### Background

Sclerosing adenosis (SA) is a benign lobulocentric proliferative process of the breast that is associated with a doubling of the risk of developing breast carcinoma [1]. It may be a component of other benign or malignant proliferative processes [2]. It is commonly asymptomatic and is generally an incidental finding in perimenopausal women undergoing screening mammography (MG), where it can present as opacity, focal asymmetry, architectural distortion, or

microcalcifications, mimicking a carcinoma [3]. Ultrasound (US) usually demonstrates no focal abnormality, or it may show a mass or focal acoustic shadowing without a mass [4]. On histopathology, its infiltrating-like appearance and dilated ducts, due to sclerosis, may mimic a carcinoma.

We report on two patients with SA that were assessed with MG, US, and contrast-enhanced magnetic resonance imaging (CE-MRI).

## Case Report

### Case 1

A 21-year-old woman with a family history of breast carcinoma underwent lumpectomy for tubular adenoma (maximum lesion size, 30 mm) in her left breast in 2012. In October 2013, a self-examination revealed a nodule in the right breast. US scanning performed at another institution depicted a hypoechoic area with ill-defined margins between the upper quadrants of the right breast, whose maximum size was 40 mm (image not available). She underwent CE-MRI examination at our institution with a 1.5 T scanner (Signa Excite HD; GE Healthcare, Milwaukee, WI, USA) and a dedicated breast coil (GE 4-channel breast array coil). MRI examination disclosed an irregular mass with spiculated borders between the upper quadrants of the right breast, measuring 23 mm (antero-posterior diameter) × 20 mm (longitudinal diameter) × 23 mm (transverse diameter). The mass exhibited rim enhancement and predominant type II curves except for some SA foci which showed early washout (type III curve). The mass demonstrated intermediate intensity on T1-weighted images and inhomogeneous hyperintensity on T2-weighted images (FSE with fat saturation). Diffusion-weighted imaging (DWI) showed a hyperintense mass without diffusion restriction (Apparent Diffusion Coefficient [ADC] mass  $1.53 \times 10^{-3}$  mm<sup>2</sup>/s vs. ADC corpus mammae  $1.45 \times 10^{-3}$  mm<sup>2</sup>/s). MG examination showed a distortion of breast parenchyma with inhomogeneous density and star-like appearance, without a radio-opaque nucleus. The latter finding was best depicted in the mediolateral oblique view. Six tissue samples were collected in US-guided vacuum-assisted biopsy (Ethicon Endo-Surgery, Hamburg) using an 11-gauge needle. Histopathological examination demonstrated fibrocystic breast tissue where an SA lesion was associated with columnar cell metaplasia/hyperplasia and subacute-chronic inflammation at both intra- and extraductal sites also involving histiocytes (Figure 1A–1E).

Twelve months after breast biopsy the lesion is clinically and radiologically stable, without signs of malignant change.

### Case 2

In December 2013, a 42-year-old woman with a family history of breast carcinoma underwent CE-MRI at our institution to investigate an asymptomatic non-nodular hypoechoic area associated with some microcysts found by US in the superomedial quadrant of the left breast (image not available) while MG performed at the same time was negative. CE-MRI examination showed regional clumped non-mass-like enhancement in the superomedial quadrant of the breast (maximum axial diameters, 4×16 mm, longitudinal diameter, 18 mm) and time-signal intensity curves type I and II. On T2-weighted images (FSE with fat saturation), only some microcysts whose maximum size was 5 mm could be visualized at the site of the non-mass-like enhancement, whereas DW sequences showed slight diffusion restriction (ADC lesion  $1.32 \times 10^{-3}$  mm<sup>2</sup>/s vs. ADC corpus mammae  $1.78 \times 10^{-3}$  mm<sup>2</sup>/s). Asymmetrically increased vascularity was also noted in the same area.

Histopathological examination of 6 tissue samples collected in US-guided vacuum-assisted biopsy (Ethicon Endo-Surgery) using an 11-gauge needle at our institution demonstrated a complex SA lesion associated with epithelial proliferation that was reminiscent of usual ductal hyperplasia (UDH) including florid and papillary aspects as well as columnar cell metaplasia/hyperplasia with evidence of flat epithelial atypia (Figure 2A–2E).

At 9 months, the lesion is sonographically stable and has not undergone malignant transformation.

## Discussion

SA is a benign proliferative lesion of the breast that is found in 27.8% of benign biopsies and in 3.1% of breasts in post-mortem studies [1,3].

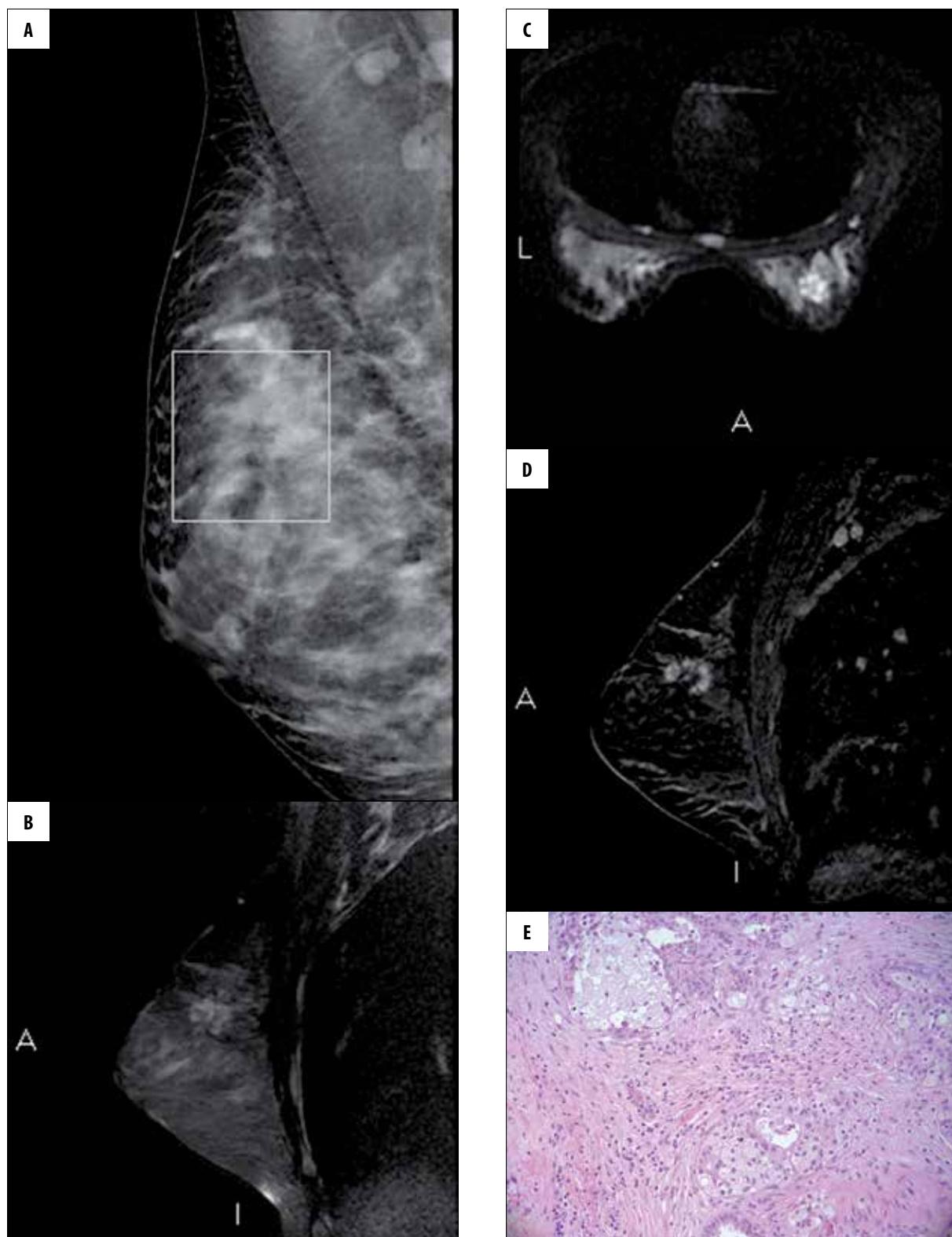
It is more common in perimenopausal women; in those with a strong family history (at least one 1<sup>st</sup>-degree relative, or 2 or more relatives [with at least one of 1<sup>st</sup> degree] developing breast carcinoma by the age 50 years); in those undergoing postmenopausal hormone therapy, and among multiparous women [1].

Its causes are unknown. Haagensen defined SA as "a phenomenon of the menstrual phase of life", suggesting that oestrogens induce the epithelial proliferation that predisposes to the development of adenosis and other epithelial tumours [3].

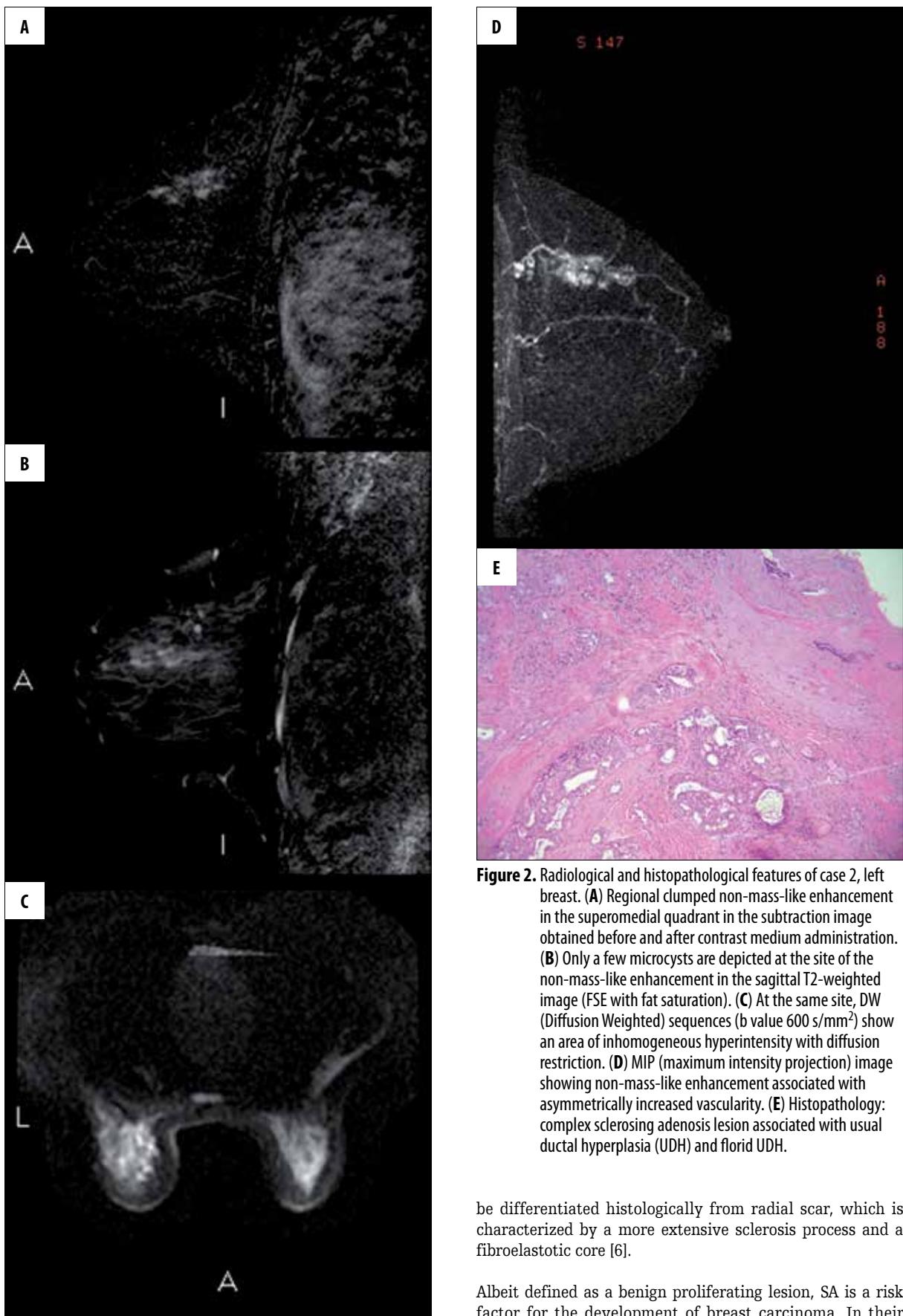
SA is frequently asymptomatic and is an incidental finding on mammographic screening or histopathological examination performed for other reasons, where it is detected as a focal or diffuse lesion [3,5].

When it presents as a palpable mass, it is defined as "nodular sclerosing adenosis" or "adenosis tumour"; this variant is generally found in patients with a broader age range, where most women are aged 30 to 45 years [3].

Histologically it is a complex lobulocentric lesion characterized by enlarged, distorted lobules containing duplicated and crowded acini (ductuli) whose luminal epithelial and myoepithelial components and basal membrane are however preserved [1]. Stromal fibrosis involves at least half of the terminal duct lobular unit (TDLU), which is elongated, distorted and compressed by the sclerosis [6]. Lesion extension ranges from microscopic foci smaller than a normal lobule to a confluent process where the marked cellularity and the involvement of both the epithelial and the mesenchymal compartment mimic a carcinoma on gross and microscopic examinations. The preserved lobular architecture that can be appreciated at low magnification is useful in the differential diagnosis from carcinoma, even though SA may extend to adipose tissue or even invade perineural structures [2,7]. At high magnification, identification of myoepithelial cells and the intact basal membrane allow confirmation of the non-invasive nature of the process. In cases where the extensive sclerosis hampers identification of the myoepithelial layer, immunohistochemical assays (p63, calponin, α-SMA, CD10, SMMHC, CK14) confirm the benign nature of the lesion [7]. SA should also



**Figure 1.** Radiological and histopathological features of case 1, right breast. (A) Right mediolateral oblique view: distortion of breast parenchyma between the upper quadrants showing inhomogeneous density and star-like appearance, but no radio-opaque nucleus. (B, C) Irregular mass between the upper quadrants exhibiting heterogeneous hyperintensity in sagittal T2-weighted images (FSE with fat saturation) (B) and hyperintensity on DW (Diffusion Weighted) sequences ( $b$  value  $600 \text{ s/mm}^2$ ) without diffusion restriction (C). (D) Irregular mass with spiculated margins showing rim enhancement and persistent enhancement in the sagittal subtraction images obtained before and after contrast medium administration. (E) Histopathological examination: fibrocytic breast tissue with a sclerosing adenosis lesion and columnar cell metaplasia/hyperplasia.



**Figure 2.** Radiological and histopathological features of case 2, left breast. (A) Regional clumped non-mass-like enhancement in the superomedial quadrant in the subtraction image obtained before and after contrast medium administration. (B) Only a few microcysts are depicted at the site of the non-mass-like enhancement in the sagittal T2-weighted image (FSE with fat saturation). (C) At the same site, DW (Diffusion Weighted) sequences ( $b$  value  $600 \text{ s/mm}^2$ ) show an area of inhomogeneous hyperintensity with diffusion restriction. (D) MIP (maximum intensity projection) image showing non-mass-like enhancement associated with asymmetrically increased vascularity. (E) Histopathology: complex sclerosing adenosis lesion associated with usual ductal hyperplasia (UDH) and florid UDH.

be differentiated histologically from radial scar, which is characterized by a more extensive sclerosis process and a fibroelastotic core [6].

Albeit defined as a benign proliferating lesion, SA is a risk factor for the development of breast carcinoma. In their

study of the biopsies of 13,434 patients with benign lesions collected from 1967 to 2001 (follow-up 15.7 years), Visscher and colleagues [1] found SA in 3,733 patients (27.8%). They calculated that their standard incidence ratio (SIR) of developing carcinoma was 2.10 compared with 1.52 in 9,701 women without SA, entailing a double risk of developing breast carcinoma that was in line with earlier studies [3,8].

SA may be associated with benign lesions (cystic changes, apocrine metaplasia, fibroadenoma, intraductal papilloma) as well as malignant changes (carcinoma *in situ*, invasive ductal carcinoma) [5]. It is also commonly found in biopsy tissue showing columnar cell changes and atypical hyperplasia, either ductal or lobular [1].

Although according to some studies [1,3] the simultaneous presence of SA lesions and other benign proliferative changes with or without atypia would not affect the stratification of the risk of developing invasive carcinoma, Oberman and co-workers found that women in whom SA was associated with atypical hyperplasia had a 2.1-fold risk of developing carcinoma compared with a 1.7-fold risk when women with atypical hyperplasia were excluded [8]. Tavassoli and colleagues examined 82 patients with atypical ductal hyperplasia and found that 17% of those who had SA went on to develop invasive carcinoma compared with 4% of those without SA [2].

SA may coexist with a lobular or ductal carcinoma, invasive or *in situ*. The carcinoma may originate from or close to the SA focus, resulting in secondary infiltration [9]. According to Ogura and colleagues, ductal carcinoma *in situ* arising in the SA area often exhibits bilateral biological features, is of non-comedo type and HER2-negative [9].

On MG, SA may present as a focal or diffuse lesion with a variety of patterns that include microcalcifications, opacities (with well-defined, ill-defined or spiculated margins), focal asymmetry, and architectural distortion [4].

Gunhan-Bilgen and co-workers assessed the mammographic and sonographic features of 43 SA and found that 81% (35/43) were detected on MG as microcalcifications (55.8%), opacity (11.6%), focal asymmetry (6.9%), and architectural distortion (6.9%) [3]. Taskin and colleagues [5] examined the MG features of 41 benign lesions in which SA was the main diagnosis; 90% were visualized on MG as opacity (39%), microcalcifications (39%), architectural distortion (7.3%), and focal asymmetry (4.7%).

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SA may be associated with intralobular microcalcifications – punctate, powdery, amorphous or pleomorphic – that are more often clustered than diffused [5,10,11].

When it presents as a spiculated opacity, SA enters into differential diagnosis with other spiculated lesions, either benign (surgical scar, radial scar, fat necrosis, tuberculosis) or malignant (ductal carcinoma *in situ*; tubular carcinoma, invasive lobular or ductal carcinoma) [6]. Even though carcinoma tends to have a more radio-opaque nucleus, it is not easy to differentiate between the two diseases.

US often fails to depict a focal abnormality, even though in a few cases it demonstrates a circumscribed mass or focal acoustic shadowing. In the study by Gunhan-Bilgen and colleagues, 44.2% of SA lesions were depicted on US: 77.9% presented as a mass (63.1% with irregular margins; 15.8% as a well-circumscribed mass) and 21% as focal acoustic shadowing without a mass [3]. In the study by Taskin and colleagues, 56.1% of the lesions where SA was the main component were depicted on US as a mass in 78.3% of cases (43.5% with well-defined margins; 26.1% with ill-defined margins; 8.7% with spiculated margins); as acoustic shadowing/focal heterogeneity without a mass in 17.4%, and as a cluster of microcalcifications in 4.3% [5].

SA does not seem to present distinctive features on CE-MRI. Lesions may be depicted as ductal enhancement or as a homogeneously-enhancing oval or round mass with lobulated or angular margins showing rapid early enhancement and delayed persistent or washout kinetics [12].

Oztekin and co-workers described a case of bilateral SA whose clinical presentation was that of multiple palpable masses depicted on MRI as round, oval, or lobulated masses with smooth borders, intermediate signal intensity on T1- and T2-weighted sequences and type I and III curves [13].

## Conclusions

SA is a common, benign, generally asymptomatic proliferative lesion of the breast. It is associated with a doubling of the risk of developing breast carcinoma, even though its role in carcinogenesis remains to be elucidated. It does not exhibit distinctive MG, US or even MRI features. Since it may mimic a carcinoma, it requires further investigation with a diagnostic biopsy.

## Conflict of interest

The authors declare that they have no conflict of interest to the publication of this article.

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