Radiological and clinical findings in sclerosing adenosis of the breast

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Abstract

To study the imaging and clinical features of breast sclerosing adenosis (SA), and to enhance the recognition of this disease, as well as to help the clinic to give a correct diagnosis.

Imaging findings were retrospectively reviewed in 47 women with SA lesions confirmed by pathology (including 39 cases of mammography, 40 cases of ultrasound [US], and 34 cases magnetic resonance imaging [MRI]).

Of 47 patients confirmed with SA, 18 cases were pure SA, and 29 cases coexist with other proliferative lesions and malignancies; the maximum diameter of SA lesions was 0.5 to 3.5 cm with an average of 1.6 cm. On the mammogram of 39 SA cases, the percentage of architectural distortion, calcifications, mass/nodular, asymmetric density, and mass combining with calcifications were 30.8%, 23.1%, 17.9%, 12.8%, and 7.7%, respectively; and 3 cases had no abnormal findings. On the sonogram (excluding 5 normal finding cases), the majority of lesions showed regular shaped (57.1%), well defined margin (60.0%), heterogenous low echo (71.4%) nodulus. 85.3% lesions showed high signal on T2-weighted images, and all lesions were enhanced markedly, including 82.4% lesions appearing mass-like enhancement (17 star-shaped enhanced masses included); and the percentage of the time-intensity curve in type 1, type 2, and type 3 were 52.9%, 41.2%, and 5.9%, respectively. If the category breast imaging-reporting and data system ≥4b was considered to be a suspicious malignant lesion, the misdiagnostic rates of mammography, US, and MRI would be 17.9%, 17.5%, and 35.3%, respectively.

The SA lesions are small and can occur with other diseases histologically. The majority of SA lesions showed distortion or calcifications on mammograms, low echo-level nodules with heterogenous echo on US and mass-like lesion with or without star shape on enhanced MRI.

Abbreviations: BI-RADS = breast imaging-reporting and data system, CDFI = colour Doppler flow imaging, MRI = magnetic resonance imaging, SA = sclerosing adenosis, US = ultrasound.

Keywords: breast imaging, magnetic resonance imaging, mammography, sclerosing adenosis, ultrasound

1. Introduction

Sclerosing adenosis (SA) is a benign, usually asymptomatic lobulocentric proliferative process that involves both the epithelial and the mesenchymal component of the breast. It is usually an incidental finding in perimenopausal women undergoing screening mammography or histopathological examination performed for other reasons.\textsuperscript{[1]} SA can be observed as a component of other benign or malignant proliferative processes. Though SA is not considered a premalignant lesion, it is associated with a doubling of the risk of developing breast carcinoma; and some studies have demonstrated a 1.7 to 3.7 times relative risk for the development of invasive breast carcinoma in patients with SA.\textsuperscript{[2–5]} The etiology of this disease is still unknown.

 Clinically, SA is usually small and frequently asymptomatic; however, it may form a palpable mass named as adenosis tumor or nodular SA. Most palpable SA lesions may be poorly delineated and firm with during physical examination, which may be considered as malignant lesions by clinician. Pathologically, SA is characterized by proliferating fibrous and myoepithelial tissue that is disposed in whorls and distorts the normal glandular structures.\textsuperscript{[6–7]} And this infiltrating-like appearance on histopathology in SA sometimes leads to mimicking invasive carcinoma regardless of clinical and radiological reports.\textsuperscript{[8–12]} Especially, its mammographic patterns of calcifications in some SA may be difficult to differentiate from carcinoma.\textsuperscript{[13]}

However, imaging findings of SA have been reported insufficiently, and there are only a few articles which emphasize the mammographic and sonographic findings of SA\textsuperscript{[7–8,12–15]} and few articles describes the magnetic resonance imaging (MRI) features of SA of the breast.\textsuperscript{[9,12]} The purpose of this study is to describe and assess the clinical features and image findings of SA...
on mammograms, sonograms, and MRI as well as to discover the best method for accurately determining this disease.

2. Materials and methods

2.1. Patient population

The clinical and imaging records of 47 SA patients with the approval of the ethics committee of Henan Provincial People’s Hospital and informed consent provided were retrospectively reviewed. All 47 patients had biopsy or surgical pathology confirmed as SA between January 2011 and August 2015. Of 47 patients, 39 cases had preoperative mammography records, 40 cases had preoperative ultrasound (US) records, and 34 cases had preoperative MRI records. There were all female patients with an age range of 29 and 73 years old (mean: 46.1 years old). Of these 47 patients, 36 were premenopausal and 11 were postmenopausal state. Clinically, 37 patients presented with a breast lump, and 1 patient presented with nipple discharge. The duration of the symptoms was between several days and 9 years. Among these patients, 8 cases had a family history of breast cancer, and 3 patients were combined with the surgical history of contralateral breast cancer.

2.2. Imaging techniques

Bilateral digital mammography was performed using the GE Senographe™ 2000D (GE Medical Systems, San Francisco, CA) or the Hologic Selenia (Hologic Medical Systems, Bedford, MA). Bilateral breast images were obtained in the craniocaudal and mediolateral oblique views. Bilateral whole-breast ultrasound was performed before biopsy using a linear array broadband transducer (Aloka 5500 [Hitachi, Tokyo, Japan]; IU 22 [Philips, Andover, MA]; ACUSON [Siemens, Washington, DC]) with a center frequency of 3.5 to 10 MHz. Ultrasound was performed by 3 ultrasound technologists with 3 to 15 years of experience in breast ultrasound. MRI was performed on a 1.5 T or 3.0 T Twin Speed scanner (Signa Twin speed Excite; GE Medical Systems, Milwaukee, WI). Patients were positioned prone in the dedicated breast coil. Routine sagittal and axial T1-weighted high-resolution images were obtained before and after the administration of contrast material, with time of repetition (TR) = 500 ms, time of echo (TE) = 10 ms. T2-weighted acquisition was performed using a fat-suppressed 2D fast spin-echo sequence with TR = 3200 ms, TE = 85 ms, a 5 mm slice thickness, and a 1 mm intersection gap. Dynamic imaging was performed utilizing a T1-weighted 2D fast spoiled gradient recalled echo sequence, with TR = 200 ms, TE = 5 ms, flip angle = 80°, matrix size = 256 × 160, number of excitations = 1, and field of view between 32 and 38 cm for bilateral axial view imaging. The contrast medium (Magnevist; Schering, Berlin, Germany, 0.2 mmol/kg) was administered as a bolus injection followed by a 20 mL saline flush. The scans began at times after contrast injection of 0, 1, 2, 4, and 7 minutes, with a scanning time of 45 minutes. A type 1 (persistent enhancement) pattern was assigned if the signal intensity increased steadily throughout the dynamic period; a type 2 (plateau) pattern was assigned if the peak signal intensity was reached soon after the injection of the contrast agents and followed by a signal intensity plateau in the remaining dynamic series; a type 3 (washout) pattern was assigned if the peak signal intensity was reached in the early phase and was immediately followed by a loss of signal intensity soon after the injection of the contrast agent.

2.3. Imaging interpretation and data analysis

All patients’ images (including mammography and MRI) were independently interpreted by 2 experienced radiologists with 5 or more years of radiological experience. Radiologists were blinded to the final pathological results, and the imaging features were described according to the breast imaging reporting and data system (BI-RADS) lexicon. US findings were interpreted by 2 experienced ultrasound experts. The features of the lesion, including echogeneity, shape, margin, and vascularity, were recorded and classified according to the ultrasound BI-RADS description. To evaluate the blood vessels in SA in color Doppler flow imaging (CDFI), we used a semi-quantitative analysis method. The vascularity was classified into 3 grades: grade I, in which the blood vessels are not present or not assessed; grade II, in which >3 punctate or rod-like blood vessels are present in the lesion or immediately adjacent to the lesion, and grade III, in which >3 punctate or rod-like blood vessels are present in the lesion or the surrounding tissue.[16] If the 2 readers differed in their assignment of a BI-RADS category, they reached a consensus through discussion. BI-RADS categories 1–3 is considered benign, 4a is defined as a low-grade suspicious malignant lesion, and 4b–5 is considered a malignant tumor; category 0 is considered an incomplete diagnosis. The non-palpable and vaguely palpable lesions were preoperatively localized by using a needle-wire system placed under mammographic guidance. In these cases, specimen radiography was obtained to confirm removal of the lesion. Imaging findings then correlated with the pathological findings.

3. Results

All 47 patients had unilateral breast SA lesions, including 27 lesions locating in the left breast and 20 lesions in the right breast. Histopathologically, 18 (38.3%, 18/47) cases were pure SA, and 29 (61.7%, 29/47) cases coexist with other proliferative lesions as well as malignancies, such as 14 patients combination with cyclomastopathy, 5 cases of calcifications, 3 cases of adenomatous hyperplasia, each 2 cases combination with intracanalicular papilloma and metaplasia apocrine, and another 3 patients combination with breast carcinoma. The lesions were located in the upper outer quadrant (n = 25, 53.2%), upper inner quadrant (n = 10, 21.3%), lower outer quadrant (n = 4, 8.5%), lower inner quadrant (n = 6, 12.8%), and the central region (n = 2, 4.2%). The maximum diameter of SA lesions was 0.5 to 3.5 cm with an average of 1.6 cm. On physical examination, 41 cases had physical signs, including 29 firm palpable masses with indistinct margins, 10 local thickness of mammary gland, 1 flexible mass and 1 moderately hard mass; 6 cases had no abnormal findings.

Of these 47 patients, 39 cases underwent mammography, and the mammographic findings are listed in Table 1. On mammograms, 69.2% (27/39) of patients had heterogeneously dense or extremely dense mammary glands; the percentage of architectural distortion, simple calcifications, mass/nodular, asymmetric density, and mass combining with calcifications were 30.8% (12/39), 23.1% (9/39), 17.9% (7/39), 12.8% (5/39), and 7.7% (3/39), respectively; and 3 cases had no abnormal findings. Of 12 cases presented with architectural distortion, 6 lesions had small local radiolucent shadow in the central region of the architectural disorder (Fig. 1). Nine cases of simplification calcifications displayed as small punctate, granulom, or irregular coarse calcifications with focal or diffuse scattered distribution (Fig. 2). Otherwise, there
were no definite malignant calcifications in the 3 patients with mass and calcification. Of the 7 high-dense mass/nodule lesions, 5 showed ill-defined margin (Fig. 3A). No patient had skin change, nipple discharge, or enlarged axillary lymph nodes in our series.

Of these 47 SA patients, 40 cases had preoperative sonography. The sonographic findings are shown in Table 2. On ultrasonograms, 5 patients exhibited breast normal sonograms, while the majority of SA patients showed lesions that were regular shape (57.1%, 20/35), well defined margin (60.0%, 21/35), heterogenous low echo (71.4%, 25/35) nodule (Fig. 4). The signal from the blood in CDFI showed grade I, grade II, and grade III blood flow in 13 (37.1%), 19 (54.3%), and 3 (8.6%) lesions, respectively. Echo attenuation was found in 16 (45.7%, 16/35) cases.

Of 47 SA patients, 34 had preoperative MRI. All 34 SA lesions were visible using MRI, and the MRI findings are shown in Table 3. On plain images, 64.7% lesions showed low signal on T1-weighted images; 85.3% lesions showed high signal on T2-weighted images. After contrast administration, all 34 lesions were enhanced obviously, including 28 (82.4%, 28/34) mass-like enhanced lesions. For the 28 mass-like enhanced lesions, 24 lesions were irregular shaped, 2 were round-shaped, and each 1 had oval and lobulated shape; 17 lesions showed an ill-defined
spiculated shape mass (radial-shaped mass) (Fig. 5), including 1 patient with SA lesion coexisting with lobular carcinoma in situ (Fig. 6), 7 lesions had coarse margins and 4 with smooth border. Nineteen lesions showed a heterogeneous enhancement with punctuate unenhanced low signal (Fig. 7), and 7 mass-like lesions demonstrated homogeneous enhancement, while another 2 lesions exhibited dark internal septation enhancement (Fig. 3B). In the 6 non-mass-like lesions, 3 lesions had multiple focal area enhancement, 2 lesions showed linear enhancement, and 1 lesion showed rind enhancement.

**Table 2**

| Sonographic findings         | n  | Percentage (%) |
|------------------------------|----|----------------|
| **Lesion description**       |    |                |
| Nodule                       | 35 | 87.5           |
| Normal                       | 5  | 12.5           |
| **Lesion morphology**        |    |                |
| Regular                      | 20 | 57.1           |
| Irregular                    | 15 | 42.9           |
| **Lesion echo**              |    |                |
| Hypoecho                     | 35 | 100.0          |
| Iso/hyperecho                | 0  | 0.0            |
| **Lesion margin**            |    |                |
| Well defined                 | 21 | 60.0           |
| Poorly defined               | 14 | 40.0           |
| **Lesion homogeneity**       |    |                |
| Homogeneous                  | 10 | 28.6           |
| Heterogeneous                | 25 | 71.4           |
| **Lesion vascularity**       |    |                |
| Grade I                      | 13 | 37.1           |
| Grade II                     | 19 | 54.3           |
| Grade III                    | 3  | 8.6            |

SA = sclerosing adenosis.
and 1 lesion appeared regional enhancement (Fig. 8). In 34 SA lesions, the percentage of the time-signal intensity curve in type 1, type 2, and type 3 were 52.9% (18/34), 41.2% (14/34), and 5.9% (2/34), respectively. Skin changes, nipple discharge, or enlarged axillary lymph nodes were not found in our series.

In our study, 3 cases imaged by mammography and 5 cases imaged by sonography were not positively detected; however, all 34 lesions were successfully identified using enhanced MRI. Table 4 shows the BI-RADS category assigned through mammography, US, and MRI at diagnosis. The BI-RADS categories with the highest number of patients were category 1–3 on mammography (33.3%, 13/39), category 1–3 on sonography (52.5%, 21/40), and Category 4a on MRI (56.9%, 14/34). On mammography and sonography, there were each 7 cases with BI-RADS category of 4b, including 5 cases of architectural disorder on mammograms and 6 cases of low echo nodulus with regular shape and ill-defined margin on sonograms. For MRI, of 12 cases with BI-RADS category ≥4b, 9 cases showed obvious enhanced radial-shaped masses. If lesions labeled higher than BI-RADS category 4b are considered to be malignant lesions, the rate of misdiagnosis under mammography, US and MRI would, therefore, be would be 17.9% (7/39), 17.5% (7/40), and 35.3% (12/34), respectively.

### 4. Discussion

SA is a benign proliferative disease of the breast that has an increased incidence among reproductive-age and perimenopausal women, especially between 35 and 50 years of age.[1–2,7] The pathological manifestations of SA are complex and various, and it can coexist with other proliferative lesions as well as malignancies. Previous studies have demonstrated that SA had a risk for the development of invasive breast carcinoma,[1,2–5] and it sometimes was regarded as precancerous lesions. Clinically, the majority of SA presented with a painless breast lump, partial patients were occasionally found with calcifications on mammograms during physical examination. Hence, SA lesions always were misdiagnosed by clinics. In our study, 61.7% (29/47) cases coexisted with other proliferative or malignant lesions; the age of the patients ranged from 29 to 73 years old with a mean age of 46.1 years, and 36 of 47 patients were premenopausal state; and the maximum diameter of SA lesions were 0.5 to 3.5 cm with an average of 1.6 cm. And these findings were agreed well with the
above reports. Because SA lesions are usually with small size, complex, and various pathological/imaging manifestations, a correct diagnosis for SA is challenging.

Both mammography and ultrasound are the most common methods for the diagnosis of breast diseases. On mammograms, SA may present as a focal or diffuse lesion with a variety of patterns that include microcalcifications, masses, focal asymmetry, and architectural distortion. And our results were consistent well with the findings above, while, the difference was the various frequency of mammographic appearances in different series. In our study, architectural disorder was the most common mammographic finding. While some reports described microcalcifications was the most common mammographic appearance, and 53% (17/32) lesions in Gill’s study and 44% (18/41) lesions in Taşkin’s series manifested as masses. These differences may be due to the various stages during the development of SA. However, these findings were nonspecific, especially when SA lesions showed architectural disorder and clustered microcalcifications, which were difficult to be distinguished from breast carcinoma. And small local low density was found in the central region of the architectural disorder in our study, which was confirmed as fatty tissue on histopathology. This may correlate with the normal fatty component surrounded by proliferative distorted lobules and stromal fibrosis. And this feature may also be found in radial scars, which is a little different from the architectural disorder demonstrating central dense core found in breast malignancy. However, not all architectural disorders had central small local low density on the

Figure 6. SA coexists with lobular carcinoma in situ in the left breast for a 60-yr-old woman, and the patient has the surgical history of contralateral breast cancer. Axial and sagittal T1-weighted enhanced MR images show a notable enhanced radial-shaped mass (A, B). MR = magnetic resonance, SA = sclerosing adenosis.

Figure 7. SA of the right breast in a 34-yr-old woman. Axial T1-weighted enhanced MR images show a small ill-defined star-shaped mass, and the lesion is enhanced heterogeneously with internal punctuate unenhanced low signal. MR = magnetic resonance, SA = sclerosing adenosis.
mammograms for SA. Calcification was another common finding of SA in our study. And the calcifications of SA in our study displayed as small punctate, granulum, or irregular coarse calcifications with focal or diffuse scattered distribution. Some microcalcifications have the similarity in size to those found in breast carcinoma, while, typical malignant calcifications of ductal carcinoma in situ (DCIS), with clustered linear, branching, or sand-like calcifications were rare in SA lesions.\(^\text{21-22}\) Otherwise, the SA patients are always young, and have dense or extremely dense mammary gland. And these factors influence the diagnosis of SA on mammogram. In our study, 3 patients had no abnormal mammographic findings. US is another common method for diagnosing breast diseases, which can detect more details about the morphology and internal feature of SA lesions than mammography. In our series, the majority of SA lesions showed regular shaped (57.1%), well defined margined (60.0%), heterogenous low echoed (71.4%) nodulus, always with few or morderate blood flow (91.4%). And these findings are in accordance with those of the previous reports.\(^\text{7-8}\) Echo attenuation was found in 16 (45.7%) cases, and this may have some relationship with more fibrous tissue in the lesions of SA.\(^\text{7-8}\)

MRI features of SA described in the published literature are scarce.\(^\text{9,12}\) These reports state that SA has a wide spectrum of appearances, such as enhancing mass, non-mass enhancement, structure distortion, even negative or not specified, which are mainly consistent with our findings. The majority of SA lesions showed low signal on T1-weighted images, high signal on T2-weighted images, and mass-like enhancement after the contrast agent administration in our series. Of 28 (82.4%), 28/34 lesions appearing mass-like enhancement in our study, 24 lesions were irregular shaped, 17 lesions showed an ill-defined spiculated shape enhanced mass (star-shaped mass); and these manifestations were very difficult to differentiate from breast carcinoma with the same appearances, especially for lack of sufficient cognition on MR features of SA.\(^\text{23}\) There were no skin changes, nipple discharge, or axillary lymph node enlargement in our series. Dynamic enhanced MRI could reflect the lesion’s features of hemodynamics, so it can be useful to distinguish benign and malignant diseases. Of our 34 patients, 32 cases had type 1 or type 2 on time-signal intensity curve. Hence, the type of time-signal intensity curve can give some certain reference value when the morphological features are difficult to distinguish SA lesions from breast carcinoma. In our study, star-shaped enhanced mass was the most common, and this should be differential diagnosis from some diseases with the similar appearance, such as postoperative scar, radial scar, fat necrosis, tuberculosis, and tubular carcinoma.\(^\text{24}\)

According to American College of Radiology BI-RADS criterion, the BI-RADS categories with the highest number of patients were category 1–3 on mammography (33.3%), category 1–3 on sonography (52.5%), and Category 4a on MRI (56.9%). If lesions labeled BI-RADS category ≥4b are considered to be malignant lesions, the rate of misdiagnosis under mammography, US, and MRI would, therefore, be would be 17.9% (7/39), 17.5% (7/40), and 35.3% (12/34), respectively. The reason why the rate of misdiagnosis in MRI was high in our study may be due to insufficient understanding of MRI appearances in SA, as well as its complex and various pathological manifestations. Hence, further study with more cases is needed.

In our study, 3 of the 39 cases imaged using mammography and 5 of the 40 cases imaged using US were not positively detected; however, all the SA lesions were detected by enhanced

### Table 4
The BI-RADS category of SA among mammography, US and MRI.

| BI-RADS | Mammography (n = 39) | US (n = 40) | MRI (n = 34) |
|---------|---------------------|------------|-------------|
|         | 0 1–3 4a 4b 4c 5    | 0 1–3 4a 4b 4c 5 | 0 1–3 4a 4b 4c 5 |
| Case (%) | 9 13 10 7 0 0       | 0 21 12 7 0 0   | 0 8 14 10 2 0 |
| Rate of misdiagnosis * (%) | 17.9 | 17.5 | 35.3 |

*BI-RADS=breast imaging-reporting and data system, MRI=magnetic resonance imaging, SA=sclerosing adenosis, US=ultrasound.

If the lesions with BI-RADS category ≥4b are considered as malignant lesions, then this is the misdiagnosis rate.
MRI. Though, 69.2% patients had heterogeneously dense or extremely dense mammary glands in our series, mammography is still an important method to detect SA lesions. Because mammography can well detect architectural distortion and calcifications, and this role cannot be instead of by US or MRI. The features of SA on US are nonspecific, while US can help detect more benign signs in SA lesions. Breast MR has emerged as a highly sensitive modality for the imaging of breast diseases, and all the lesions in our study were detected by enhanced MRI. In our series, the percentage of BI-RADS category ≥4b was 35.3% (12/34), which was higher than that of mammography and US. The reasons maybe include 2 aspects, one is the higher percentage of BI-RADS category 0 on mammography, the other one may be due to insufficient cognition of MRI appearances in SA. Therefore, when a focal lesion with notable mass-like enhancement and type 1 dynamic curve on enhanced MRI, especially for a small star-shaped enhanced mass, the diagnosis of SA should be considered. Otherwise, the imaging of SA cases coexisting with breast carcinoma was not discussed independently because of only 3 cases in our study. Hence, improving case number and carrying out further study are needed.

On mammograms, a differential diagnosis should be made for the appearances of cluster microcalcifications and architectural disorder that include both malignant lesions (eg, invasive breast carcinoma, tubular carcinoma, DCIS) and benign lesions (eg, postoperative scar, radial scar, fat necrosis, tuberculous).\[10\] Invasive breast carcinoma tends to have a denser center than either SA or radial scar.\[10\] Microcalcifications are often present in association with suspicious breast carcinoma but may also occur in benign lesions including SA, radial scar, and fat necrosis. On MRI, SA should also distinguish from both malignant lesions mimicking invasive breast carcinoma, tubular carcinoma, DCIS) and benign lesions (eg, postoperative scar, radial scar, fat necrosis, tuberculous).\[10\] If the abnormalities that occur on mammogram or MRI suspected as SA lesions, a core needle biopsy should be needed in the diagnosis of SA because of some SA lesions mimicking invasive breast carcinoma.

5. Conclusion

In conclusion, SA lesions are small and usually occur with other diseases and various complex clinical and pathological manifestations. The diagnosis of SA should be considered when architectural disorder on mammograms, well defined heterogenous low echo nodule on ultrasound or small star-shaped enhanced mass on MRI are detected. However, as the imaging findings of SA are not specific, pathological evaluation should be made for final diagnosis.

Author contributions
Conceptualization: Hongna Tan, Zhidan Lei, Meiyun Wang. Data curation: Hongna Tan, Huiyu Zhang, Zhidan Lei, Fangfang Fu. Formal analysis: Hongna Tan, Huiyu Zhang. Funding acquisition: Hongna Tan. Methodology: Hongna Tan, Fangfang Fu. Writing – original draft: Hongna Tan. Writing – review and editing: Hongna Tan.

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