Letter to the Editor

Rare desmoid-type fibromatosis of the breast in young female patients: a description of three cases and literature analysis

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Introduction

Desmoid-type fibromatosis (DF), which falls within the major category of fibroblast and myofibroblast tumors, is classified as intermediate and locally aggressive according to the 2020 World Health Organization (WHO) classification of soft tissue tumors and has an annual incidence of 4–5 cases per million individuals (1-3). Due to the incidence rate of DF in the breast being only 0.2% and its clinical and imaging features partially overlapping with those other breast diseases such as breast cancer, accurate diagnosis is often considerably challenging (4). To the best of our knowledge, there have been limited published cases documenting the diagnosis of DF in the breast thus far. We therefore performed a more comprehensive radiological examination and feature analysis of breast DF as compared to previous studies (5,6).

Case presentation

All procedures performed in this study were in accordance the ethical standards of the Ethics Committee of the West China Hospital of Sichuan University and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Case 1

Chief complaints

A 29-year-old female was referred to our hospital due to a painful right breast space-occupying lesion.

History of past illness

The patient indicated that she had a history of right breast trauma related to cycling.

Ten years prior to arriving to our center, the patient had inadvertently noticed a small right breast lump without signs of redness, swelling, or pain. One year prior, the patient noticed a gradual increase in the size of her right breast lump and occasional pain. Three months prior, the patient found that the right breast mass was still growing, with an increased frequency of pain.

Physical examination

Bilateral breast asymmetry was observed, characterized by swelling in the upper and outer quadrants of the right breast accompanied by localized skin indentation. No signs of redness, orange peel skin, nipple retraction, or nipple discharge were observed (Figure S1).

Imaging examinations

Ultrasound examinations

On conventional grayscale ultrasound, a huge solid mass (measuring 130 mm × 30 mm × 100 mm size) at the outer

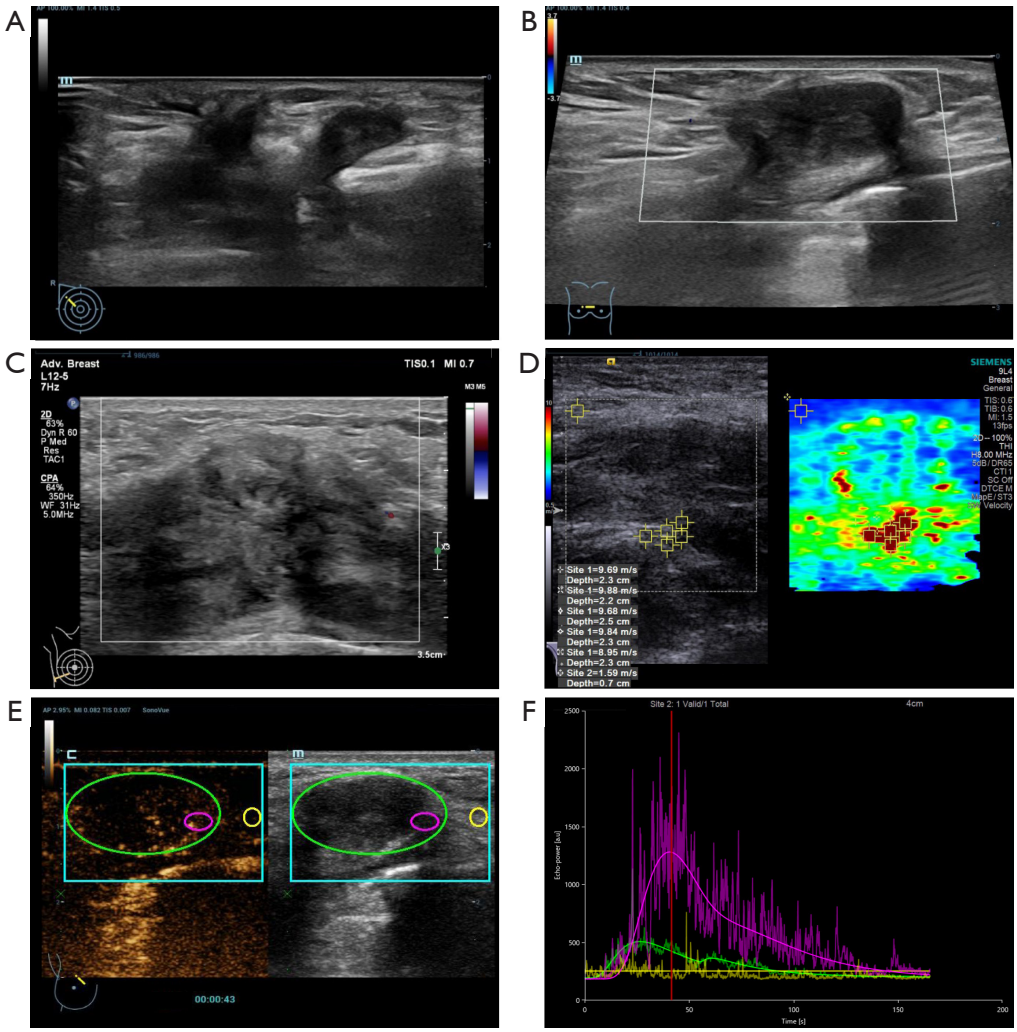

Figure 1 Ultrasound images of desmoid-type fibromatosis of the breast (case 1). (A) Conventional grayscale ultrasound showed a hypoechoic mass close to the muscle layer in the right breast. (B) Color Doppler flow imaging revealed sparse blood flow signals within the smaller mass. (C) Power Doppler flow imaging displayed sparse blood flow signals within the larger mass. (D) Shear wave elastography demonstrated a higher hardness of the larger mass. (E) Contrast-enhanced ultrasound image revealed slightly higher nodular enhancement in some areas of the smaller mass. (The green circle covers the entire mass, the red circle covers a portion of the mass, the yellow circle covers the surrounding contrasting tissue, and the blue box contains areas of interest and control). (F) The contrast pattern was progressively enhanced in the smaller mass. CPA, color propagation angle.

quadrant and a relatively small solid mass (measuring 25 mm × 12 mm × 25 mm in size) at the upper inner quadrant were found within the right breast. The aforementioned masses exhibited hypoechoic characteristics, irregular shape, indistinct margins, nonparallel orientation, absence of calcification, posterior echo attenuation, distorted surrounding tissue architecture, infiltration into the subcutaneous layer, and a retro-mammary space [classified as grade 5 in Breast Imaging Reporting and Data System (BI-RADS); *Figure 1A*]. Doppler flow imaging showed sparse blood flow signals around the masses consistent with Adler grade I (*Figure 1B*,*1C*). Additionally, the lesions exhibited a relatively high level of hardness, and shear velocity measurements indicated a median variable speed of 9.69 m/s within the larger lesions (*Figure 1D*).

Moreover, the patient underwent a contrast-enhanced ultrasound (CEUS) examination with a bolus injection of 5 mL of contrast agent (SonoVue; Bracco, Milan,

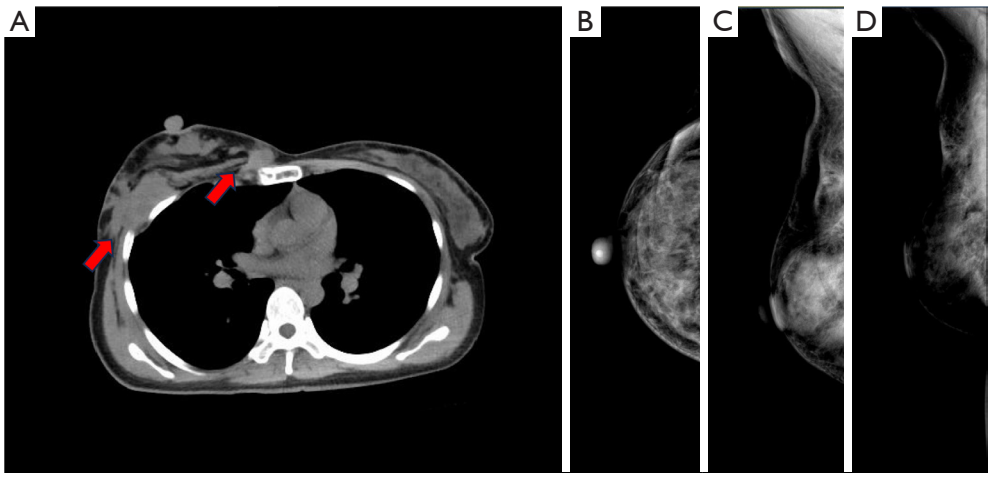

Figure 2 The CT and X-ray images of desmoid-type fibromatosis in the breast (the red arrows mark the location of the mass in case 1). (A) The CT scan demonstrated multiple irregular soft tissue masses with indistinct margins in the posterior chest wall of the right breast. (B-D) X-ray revealed distortion and retraction of the skin in the upper outer quadrant of the right breast, which was accompanied by disorganized structures in the posterior gap. CT, computed tomography.

Italy) followed by a 3-mL injection of saline through the antecubital vein. Both lesions exhibited heterogeneous enhancement, characterized by a progressive enhancing pattern (*Figure 1E,1F*).

X-ray and computed tomography (CT) examination

The X-ray revealed an irregular structure, dermal depression, and disordered arrangement within the posterior gap of the right breast. An unenhanced thoracic CT provided a more comprehensive depiction compared to X-ray, revealing the presence of multiple soft tissue masses in the posterior chest wall located behind the right breast, with no bony involvement of underlying ribs (*Figure 2*).

Magnetic resonance imaging (MRI) examination

Enhanced breast MRI (*Figure 3*) was performed. and isointense T1- and hyperintense T2-weighted signal masses were observed in the outer quadrant and upper inner quadrant of the right breast chest wall area, with involvement of the local chest wall muscles; the former extended upwards toward the right axillary tail region and downward to the level of the fifth rib in the pectoralis major muscle area, causing adjacent organizations to deform and exhibiting an indistinct demarcation with breast tissue; meanwhile, the latter extended to the area below the third rib. Moreover, diffusion-weighted imaging (DWI) of the lesions demonstrated a high signal, with the apparent diffusion coefficient (ADC) value measuring 2.42. The two lesions both exhibited heterogeneous enhancement.

Pathology results

An ultrasound-guided core needle biopsy was carried out to obtain tissues from the masses. The histopathology result showed that the masses were spindle cell proliferative disease. Further immunohistochemistry and genetic testing were performed.

Immunohistochemistry revealed partially nuclear smooth muscle actin (SMA) positivity, scattered nuclear β-catenin positivity, and scattered nuclear desmin positivity in spindle cells. Meanwhile, genetic testing identified a missense mutation in the *CTNNB1* gene, which is associated with β-catenin. No mutations were identified in the *APC* gene, which is associated with familial adenomatous polyposis (FAP). Finally, the masses were confirmed to be DF (*Figure 4*).

Treatment intervention

A multidisciplinary diagnosis and treatment meeting was held to discuss the therapeutic options for this case. Given the patient' s younger age and the large size of the masses, it was believed that extensive resection of chest wall mass and muscles would affect organismal function. It was thus decided to decrease the size of the masses so as to reduce risk of surgery trauma and recurrence.

Case 2

A 30-year-old woman had been experiencing a

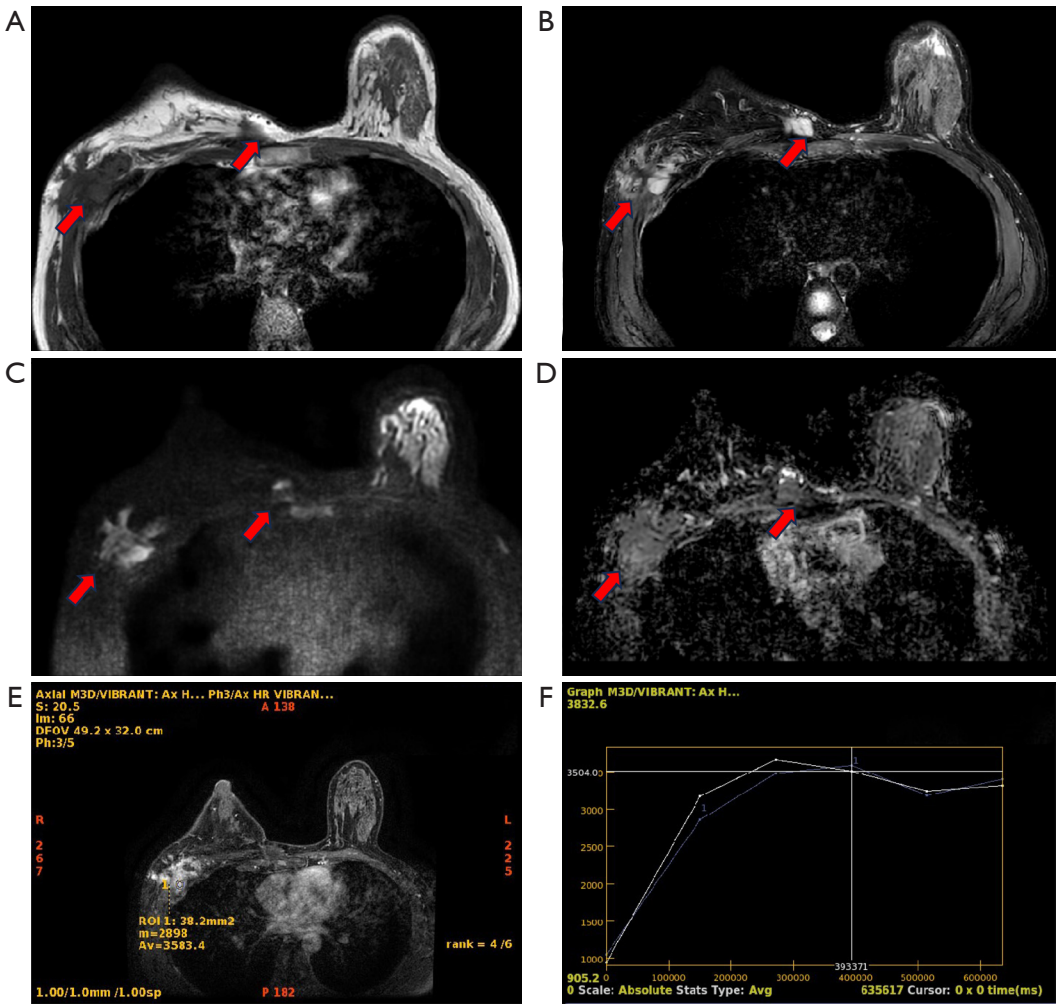

Figure 3 The MRI images of desmoid-type fibromatosis of the breast (the red arrows mark the location of the mass in case 1). (A) The masses exhibited low signal intensity on T1WI. (B) The masses displayed high signal intensity on T2WI. (C) The masses demonstrated high signal intensity on DWI. (D) The masses do not show significant reduction in signal intensity on ADC. (E) The larger mass exhibited heterogeneous enhancement on imaging. (F) The enhancement pattern demonstrated progressive enhancement followed by gradual fading in the larger mass (X axis: time; Y axis: enhancement value). MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient.

palpable lump in her right breast for over a year. Ultrasonography revealed a mass measuring 103 mm × 81 mm × 31 mm in size in the right breast. The mass exhibited hypoechoic characteristics, irregular shape, indistinct margins, nonparallel orientation, calcification, posterior echo attenuation, distorted surrounding tissue architecture, infiltration into the subcutaneous layer and retromammary space consistent with Adler grade I. The median variable speed was 9.68 m/s, and there was heterogeneous enhancement on CEUS (BI-RADS 5; *Figure 5A-5C*). The CT scan revealed the presence of a soft tissue mass in the right breast, while the MRI demonstrated a right breast mass involving the chest wall accompanied by nipple retraction. Pathology confirmed that the mass was DF.

Case 3

A 40-year-old woman indicated the presence for over a month of an inconspicuously palpated mass in her left

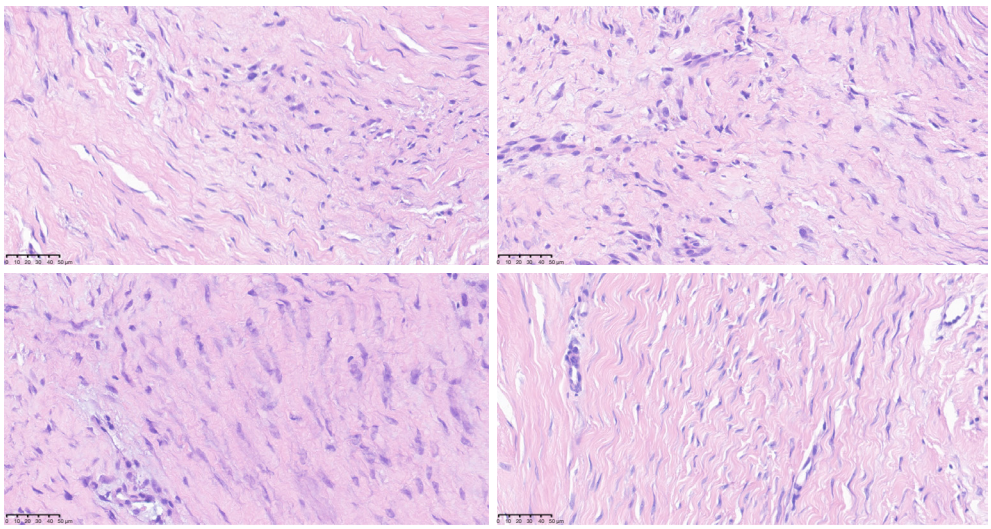

Figure 4 Histopathological section of desmoid-type fibromatosis of the breast stained with hematoxylin and eosin (case 1; 40×).

breast. Ultrasound examination revealed a hypoechoic mass measuring 26 mm × 18 mm × 21 mm in size located at the 4 o'clock position, approximately 2 cm from the nipple. The mass exhibited irregular shape and blurred boundaries with unparallel orientation. No calcifications were observed within the mass, but the posterior echogenicity was attenuated. Surrounding tissue structure remained changed with signs of infiltration (BI-RADS 5). Elasticity analysis indicated a mean variable speed of 5.61 m/s for the mass. Adler grade I and heterogeneous enhancement were observed in the lesion (*Figure 5D-5F*). X-ray findings showed structural distortion in the outer quadrant of the left breast. DF was ultimately confirmed by pathology.

Discussion

Comprehensive overview of pathological conditions

The 2020 WHO Classification of Soft Tissue Tumors (fifth edition) encompasses 11 primary categories and 176 subtypes, with DF being listed as a rare, locally aggressive, nonmetastasizing mesenchymal tumor. The pathogenesis of DF is associated with genetic, endocrine, and traumatic factors. DF can be classified into three types: extra-abdominal, abdominal wall, and intra-abdominal. Extra-abdominal DF (EADF), which is more commonly observed in adolescent patients, tends to present in the extremities, chest wall/paraspinal region, head, and neck. Abdominal wall DF (AWDF) has a high prevalence among women in their reproductive years and exhibits a greater incidence within the rectus abdominis muscle. Intra-abdominal DF (IADF) is a rare condition that is often associated with FAP/Gardner syndrome. Superficial DF may be amenable to surgical excision without compromising functionality. The National Comprehensive Cancer Network (NCCN) and Desmoid Tumor Working Group guidelines recommend active surveillance or systemic therapy for tumors that are not amenable to surgical resection, such as DF located in the mesentery or neck and adjacent to critical structures (2,7-15).

Distinguishing between DF and breast lesions

This disease typically affects patients at a young age and exhibits a high likelihood of recurrence following surgery; thus, imaging serves as the preferred modality for both the staging of DF and postoperative surveillance. Ultrasound is a convenient imaging modality, lacks ionizing radiation, and is particularly valuable in assessing DF in superficial diseases, such as with AWDF and EADF (5,16,17). DF presents as a fusiform or lobulated mass growing along muscle fibers and fascia, exhibiting sparse blood flow, infrequent liquefaction necrosis, and calcification. In addition, the literature includes two documented characteristic ultrasound features of DF: linear extension of lesions along the fascial plane—referred to as the fascial tail sign—and finger-like extension of lesions into the muscle—known as the staghorn sign (18). The degree of DF reinforcement is correlated with the ratio of fibroblasts to collagen fibers arranged in a shuttle shape, exhibiting a

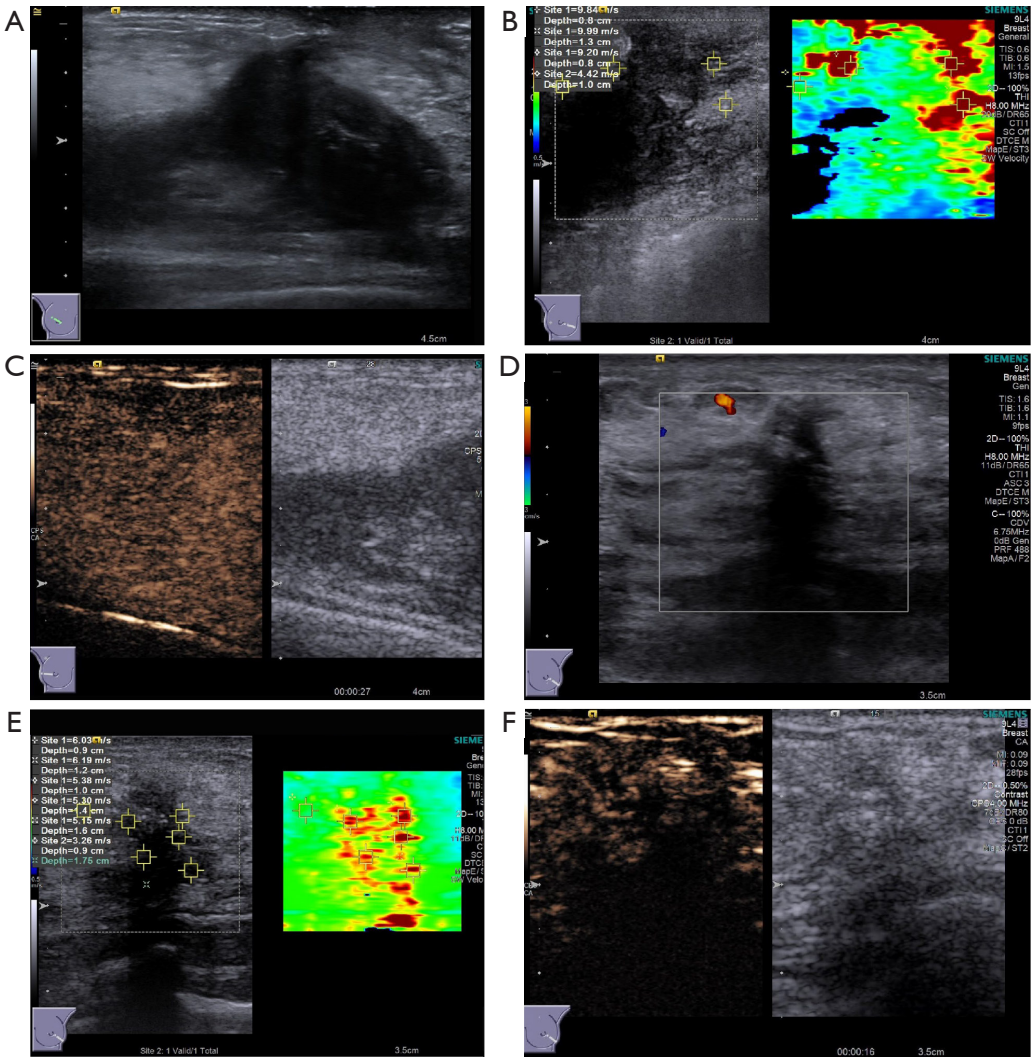

Figure 5 Ultrasound images of desmoid-type fibromatosis of the breast. Case 2: (A) conventional grayscale ultrasound showed a hypoechoic mass close to the muscle layer in the right breast. (B) Shear wave elastography demonstrated higher hardness of the larger mass. (C) Contrast-enhanced ultrasound revealed heterogenous enhancement in the mass. Case 3: (D) power Doppler flow imaging displayed sparse blood flow signals within the mass in the left breast. (E) Shear wave elastography demonstrated moderate hardness of the mass. (F) Contrast-enhanced ultrasound image revealed heterogenous enhancement in the mass.

significant augmentation in the densely populated fibroblast region compared to the collagen-rich area (19).

The differential diagnosis of the cases described in this report encompassed considerations of breast cancer, mastitis, sclerosing adenosis, fibroadenoma, borderline phyllodes tumor, and soft tissue sarcoma of the chest (*Table 1*, *Figure 6*); the differential features of these conditions are described below: (I) the differential features of breast cancer are microcalcification and heterogeneous hyperenhancement on CEUS with crab foot infiltration or radiation sign. (II) Mastitis usually requires a combination of whether the patient is breastfeeding and has a history of redness, swelling, heat, and pain. The lesion is rich in blood flow and CEUS shows an enlarged lesion. (III) Sclerosing adenosis is categorized as an advanced stage of breast hyperplasia, predominantly observed in middle-aged and older adult females. Ultrasound examination demonstrates a notable posterior acoustic attenuation of the lesion, while imaging reveals low enhancement and limited field of view on CEUS. (IV) Fibroadenomas are typically

Table 1 Features for the differential diagnosis of desmoid-type fibromatosis and other lesions of the breast

Entities	Details
Desmoid-type fibromatosis	A firm mass, closely associated with the muscular layer, lacking calcification or liquefaction, and demonstrating a progressive enhancement followed by gradual fading on CEUS
Breast cancer	A mass exhibiting microcalcification and heterogeneous hyperenhancement and crab foot infiltration or radiation sign on CEUS
Mastitis	A lesion with an expanding range and evident vascular or ring enhancement in the surrounding area on CEUS, which may exhibit an internal filling defect when accompanied by an abscess
Sclerosing adenosis	A mass with notable reduction in posterior echo attenuation and low enhancement and characterized by a limited field of view on CEUS
Fibroadenoma	A well-defined, slightly lobulated mass demonstrating homogeneous enhancement with a limited extent on CEUS
Borderline phyllodes tumor	A mass characterized by prominent hyperenhancement followed by gradual washout on CEUS
Soft tissue sarcoma	A mass often exhibiting liquefied necrosis and calcification, with heterogeneous hyperenhancement on CEUS

CEUS, contrast-enhanced ultrasound.

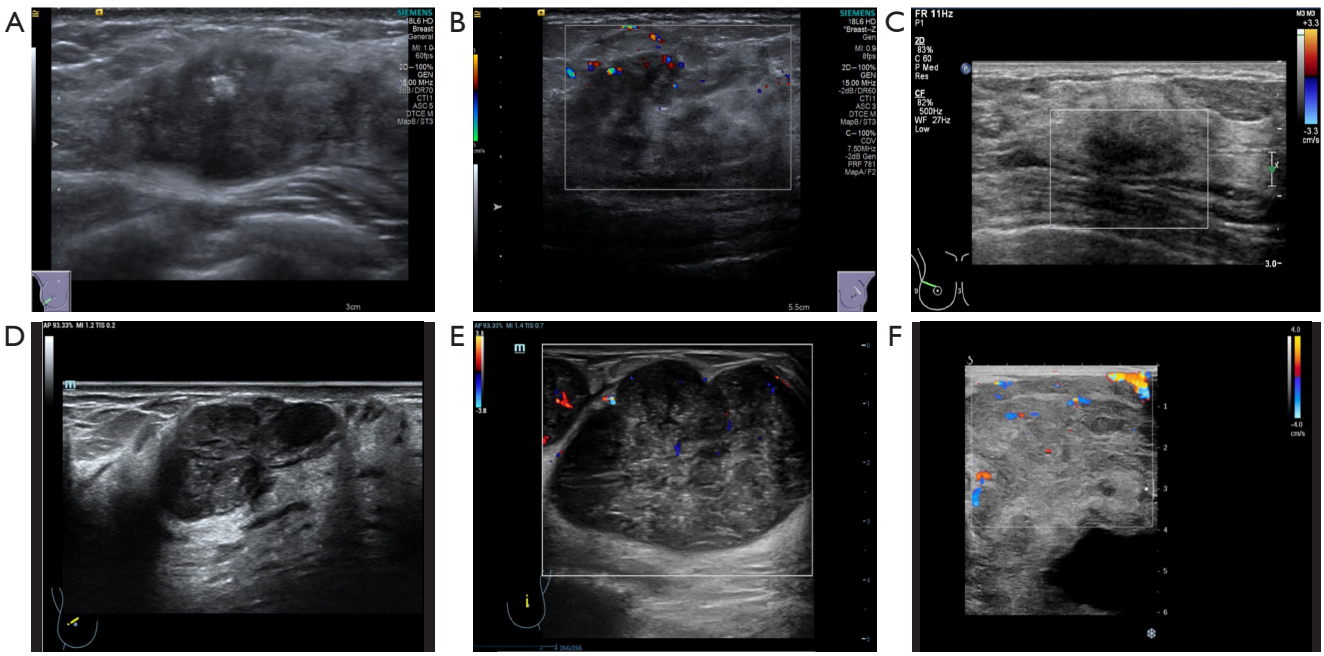

Figure 6 Relevant cases for the differential diagnosis of desmoid-type fibromatosis of the breast. (A) A case of breast cancer in a 28-year-old woman with a mass presenting with blurred borders (burr sign) and visible micro and gross calcifications. (B) A case of mastitis in a 29-year-old woman with a mass presenting with blurred borders, distorted surrounding tissue structure, and an Adler grade of III. (C) A case of sclerosing adenosis in a 52-year-old woman with a mass presenting with vague borders, marked posterior echogenic attenuation, and hardness. (D) A case of fibroadenoma in a 27-year-old woman with a mass presenting with slightly lobulated, limited margins; parallel orientation; and enhanced posterior echogenicity. (E) A case of a 47-year-old woman with borderline phyllodes tumor presenting with well-defined borders, parallel orientation, and enhanced posterior echogenicity. (F) A case of an 18-year-old woman with rhabdomyosarcoma presenting with liquefaction necrosis and an Adler grade of III.

Table 2 Features for the differential diagnosis of desmoid-type fibromatosis and other soft tissue lesions

Entities	Details
EADF and AWDF	A firm mass, closely associated with the muscular layer, lacking calcification or liquefaction, and demonstrating a progressive enhancement followed by gradual fading on CEUS
Soft tissue sarcoma	A mass often exhibiting liquefied necrosis and calcification, with heterogeneous hyperenhancement on CEUS
Nodular fasciitis	A mass predominantly observed in the upper extremities and presenting as a rapidly proliferating tender nodule
Intramuscular hemangioma	A vascular network with enhanced blood flow upon compression
Neurofibroma	An eccentrically expanding neoplasm along the nerves, characterized by a spindle-shaped appearance, rat tail sign, and encapsulation
Endometriosis	Purplish-brown lesions at the site of a cesarean section incision, accompanied by cyclic pain associated with menstruation

EADF, extra-abdominal desmoid-type fibromatosis; AWDF, abdominal wall desmoid-type fibromatosis; CEUS, contrast-enhanced ultrasound.

well-defined and slightly lobulated, exhibiting limited and homogeneous enhancement on CEUS. (V) Borderline phyllodes tumors are characterized by rapid growth within a short duration accompanied by prominent enhancement and demonstrate a pattern of swift progression followed by gradual regression on CEUS. (VI) Soft tissue sarcoma, such as rhabdomyosarcoma, frequently manifests as liquefied necrosis and calcification and is accompanied by abundant blood flow. Imaging reveals heterogeneous hyperenhancement on CEUS.

In addition, it is imperative to distinguish EADF and AWDF from soft tissue sarcoma, nodular fasciitis, intramuscular vascular malformation, neurofibroma, and endometriosis (*Table 2*).

Additional imaging characteristics of DF

MRI is the preferred modality for the preoperative assessment and postoperative surveillance of AWDF and EADF, while CT is more suitable for assessing IADF. Both primary and recurrent DF often appears as masses with a fascicular configuration and heterogeneous contrast enhancement on MRI. Apart from fascia tail sign on ultrasound, MRI further demonstrates the following characteristics: (I) band sign, presenting as an enhanced mass accompanied by a linear low signal intensity band; (II) separation fat sign, indicating the presence of strip-shaped fat signal between the tumor and muscle; and (III) flame sign, characterized by lesions with feather-like edges resembling flames and equivalent to staghorn sign in ultrasound. It is worth mentioning that an increase in T2 signal intensity on MRI imaging indicates a rise in cell density, thus suggesting an elevated level of invasiveness of the tumor (7,20-23).

This case serves as a reminder that breast lumps may not originate solely from the breast tissue. The presence of tumors with infiltrative growth in the breast should not be immediately diagnosed as breast cancer, and accurate diagnosis of disease requires considering imaging features in combination with clinical history. In case 1, X-ray and CT only indicated disorder in the retromammary space of the breast, while MRI enhancement only suggested the presence of tumor lesions due to an insufficiently elaborated medical history. However, through the integration of ultrasound features and given the clinical history of trauma to the right chest wall, we successfully arrived at a diagnosis of DF. The indispensable advantage of ultrasound examination lies in the ability to effectively communicate with patients and gather comprehensive clinical history during the process of ultrasound examination.

Conclusions

DF is frequently observed in young adults aged 20 to 40 years and is often associated with a history of surgery/trauma or Gardner syndrome. Ultrasound imaging shows DF as a spindle-shaped or lobulated mass in close relation to the muscle layer, demonstrating sparse blood flow and frequently lacking liquefaction, necrosis, and calcification. DF usually appears as fascicular configuration

on MRI, which can accurately confirm the extent of muscle involvement. Meanwhile, CT can assess bone and periosteum destruction in patients with DF.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1586/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance the ethical standards of the Ethics Committee of the West China Hospital of Sichuan University and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patients for publication of this article and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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Supplementary

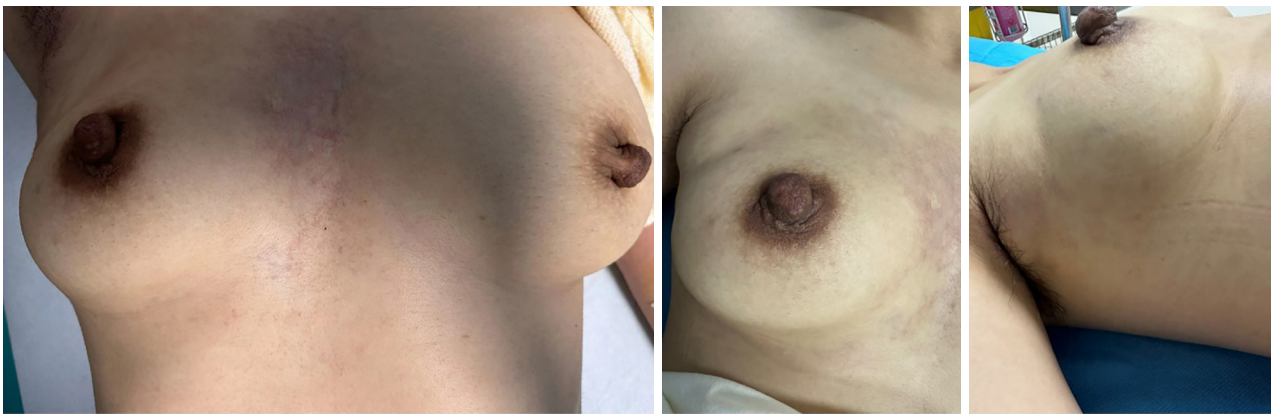

Figure S1 Swelling in the upper and outer quadrant of the right breast with local skin depression. (These images have been published with the patient's consent).