Letter to the Editor

Misdiagnosis of breast cancer after augmentation injection of stromal vascular fraction gel: a case description

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Introduction

Stromal vascular fraction gel (SVF-gel) is an adipose tissue-derived product and an autologous injectable filler that contains condensed adipose tissue extracellular matrix (ECM) fibers, adipose-derived stem cells (ADSCs), and vascular endothelial cells (1). The ADSCs and vascular-related growth factors promote angiogenesis and adipocyte differentiation and prevent cell apoptosis, therefore, they can improve the survival rate of the graft recipient area (2-4). Initially, SVF-gel was frequently used in facial rejuvenation (5); later it was used for breast reconstruction to maintain the fat volume and prevent reabsorption (6). Studies from various countries have shown that augmentation mammaplasty patients do not bear an increased risk of breast cancer (7,8). However, reports show that breast augmentation can influence breast cancer diagnosis by decreasing the sensitivity of imaging techniques (i.e., mammography) (9,10). Several breast cancer cases have been reported after breast implants, but there are no reports on SVF-gel as the material in the augmentation injection (11-17).

This report details a case of breast cancer misdiagnosis in a patient following an augmentation injection of SVF-gel, which could provide helpful information for the differential diagnosis of breast cancer in this specific condition.

Case presentation

Patient information

A 31-year-old woman who had a left breast mass for 6 months presented at the Shenzhen People's Hospital Clinic, Shenzhen, China, on 29 May 2020. The patient had undergone breast augmentation with high-density fat combined with SVF-gel injection after breastfeeding for 12 months. The left breast mass was palpated 12 months after the implant operation. The patient had no family history of breast cancer or other malignancies.

Clinical finding

Based on the physical examination, the bilateral breasts were noted to have good symmetry without skin abnormalities or surgical scars. A mass was located at 3 o'clock on the left breast, was palpable, and measured 30 mm × 20 mm. The mass was hard and tender with an irregular surface, unclear borders, and poor mobility, although it was not fixed to the chest wall.

Diagnostic assessment

Mammography was performed on 29 May 2020 using a film-screen mammogram (MammoMat II 2000; Siemens, Munich, Germany). Focal asymmetry was found in the central area of the left breast (*Figure 1A*,*1B*). The asymmetry area was approximately 27 mm × 15 mm without calcification. The asymmetry was categorized using the Breast Imaging Reporting and Database System Score (BI-RADS) as zero, which indicated that the mammogram images were difficult to interpret. A further ultrasound examination was recommended.

A breast color Doppler ultrasound was carried out on

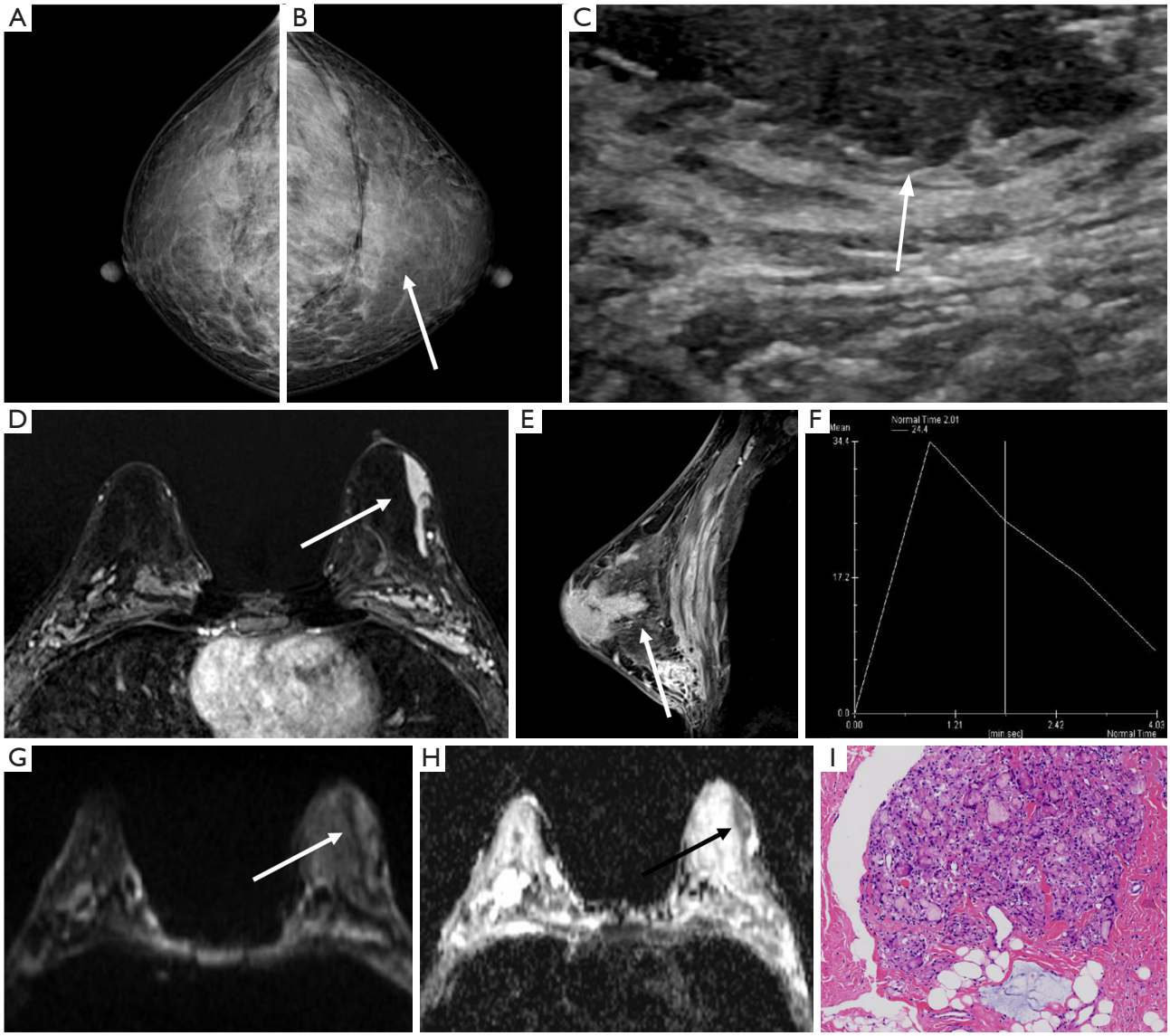

Figure 1 Images related to the case. (A,B) The craniocaudal view (CC view) of mammography (A shows the right breast and B shows the left breast). Focal asymmetry in the central area of the left breast was indicated (B, white arrow). (C) Abnormal fusiform echo (white arrow) of the left breast in the breast ultrasound examination. (D) The breast MRI showed an abnormal enhancement of non-mass (white arrow) in the outer quadrant of the left breast. (E) The sagittal position MRI indicated the abnormal enhancement (white arrow). (F) The TIC showed a type I (fast-rising-descending type). (G) The DWI in b-value of 800 showed a high signal (white arrow). (H) The ADC was (0.9–1.0)× 10^{-3} mm^2/s (black arrow). (I) The histological image showed atypia and multinucleated giant cells (HE, ×400). MRI, magnetic resonance imaging; DWI, diffusion weighted imaging; TIC, time of intensity curve; ADC, apparent diffusion coefficient; HE, hematoxylin and eosin.

9 June 2020 using a GE Logiq 700 scanner (GE Medical Systems, Milwaukee, WI, USA). An abnormal echo was seen at 3 o'clock on the left breast next to the nipple (*Figure 1C*). The mass was 29 mm × 28 mm × 10 mm. The mass had a fusiform shape, an unclear boundary, and an uneven internal echo. It was hypoechoic, and there was no change in the echo for the background area. There was no side sound or shadow on both sides of the mass. The color Doppler flow imaging showed abundant blood flow signals in and around the abnormal mass shadow. The speed of the internal blood flow had a peak systolic velocity (PS) of 8 cm/s with a resistance index of 0.57. The injected

prosthesis tissue was observed in the back of the glandular layers of both breasts with honeycomb-shaped disordered echoes. The diagnosis based on the ultrasound examination was as follows: (I) abnormal sound image in the left breast; (II) BI-RADS 4A, which indicated a suspicious abnormality; and (III) postoperative changes in bilateral breast augmentation (BI-RADS 2).

To further confirm the diagnosis, breast magnetic resonance imaging (MRI) was performed on 19 June 2020 at 3.0 T (Philips, Best, Netherlands). The left breast MRI flat scans showed abnormal signal shadows. The T1-weighted image (T1WI) showed that the left breast was isointense, and the T2-weighted image (T2WI) with fat suppression showed a low signal. In addition, scattered, irregular, and flake shaped (both T1-weighted and long T2-weighted) long signal shadows were located behind the pectoralis major in the bilateral posterior space. The dynamic enhancement scan showed an abnormal non-mass enhancement in the outer quadrant of the left breast that extended from the nipple to the chest wall with an uneven internal signal and a segmental distribution (*Figure 1D,1E*). The time of intensity curve (TIC) was type I (fast-rising-descending) (*Figure 1F*). The diffusion-weighted MRI (DWI) in *b* values of 800 showed a high signal (*Figure 1G*) and an apparent diffusion coefficient (ADC) of (0.9–1.0)× 10^{-3} mm^2/s (*Figure 1H*). In addition, multiple clockwork sheet-like abnormal enhancements were observed behind the glands. Based on the MRI examination, the diagnosis was as follows: (I) the left breast segmental distribution of non-mass enhancement with BI-RADS 4; and (II) bilateral breast augmentation changes.

Ultrasound-guided core needle biopsy (CNB) was performed on the left breast mass by a sonologist with 13 years of experience on 9 June 2020, using a 14-gauge automatic biopsy gun (TSK Laboratory, Oisterwijk, the Netherlands). The patient did not provide her breast augmentation history to the pathologist during the CNB procedure. The CNB results showed diffuse nodular hyperplasia of atypical cells with scattered mitotic images, unclear borders, and pushing around of the normal tissues under the hematoxylin and eosin (HE) staining microscope. Multinucleated giant cells were also observed. The atypical cells with abundant cytoplasm were spindle-shaped, polygonal, and epithelioid. According to the CNB, the diagnosis was suspicious invasive breast cancer but required further confirmation through post-surgical immunohistochemical examination.

Primary diagnosis

The following primary diagnosis was made on 10 June 2020 based on the patient's information, clinical findings, and diagnostic examinations: (I) a left breast mass, suspected to be breast cancer, and (II) bilateral breast augmentation changes.

Therapeutic intervention

The patient was admitted to the breast surgery department of our hospital on 12 June 2020, and underwent breast surgery 3 days later. The tumor was in the upper outer quadrant of the left breast, with a size of about 30 mm × 15 mm. The lump tissue was tough, had a clear boundary and an irregular surface, and there were no obvious capsules. Further, gelatinous substances were found around the glands, and the substances did not have fixed shapes or clear boundaries. Some of the gelatinous substances were located under the skin and in front of the chest wall. The patient was discharged on 23 June 2020, after the incision had healed.

Postoperative pathology showed similar findings of preoperative puncture (*Figure 1I*) but confirmed that the mass was not breast cancer. The heteromorphic cells were non-epithelial-derived cells, which were composed of prokaryotic cells and necrotic cells. Immunohistochemistry showed the presence of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, human epidermal growth factor receptor 2 (HER-2) negative, CK (–), Vimentin (+), S100 (–), MDM2 (–), CD34 (vascular +), CD30 (–), P16 (+), KI-67 (about 20%), CD20 (a little +), ALK (–), and P63 (–).

Based on the postoperative pathological results, the final diagnosis was as follows: (I) a granulomatous response after fat necrosis, and (II) bilateral breast augmentation changes.

Follow-up

A follow-up visit was made on 21 April 2021. The patient stated that no tenderness or palpable masses had occurred in the left breast since discharge. An ultrasound examination showed the changes after breast augmentation on both breasts. No sound images of abnormal masses in either breast or enlarged lymph nodes in the axilla were found.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki

Declaration (as revised in 2013). Written informed consent was provided by the patient before publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

High-density fat combined with SVF-gel is an expensive modern cosmetic material that is mainly used to correct suborbital depression and laceration by suborbital injection (5). In the 1990s, the traditional injection of breast augmentation in China's beauty institutions mainly used polyacrylamide hydrogel, which was simple, quick, and bio-compatible, but had complications such as inflammation, infection, and even breast cancer (18). The patient in the present case was a young woman who had experienced a reduction of breast tissue tone after breastfeeding. Therefore, to improve breast elasticity, she underwent breast augmentation with high-density fat combined with an SVF-GEL injection. According to the postoperative pathological findings, extensive tissue cells and multinucleated giant cell responses with lymphocyte infiltration were observed at the injection site. The left breast mass, which was originally suspected to be breast cancer, was shown to be a granulomatous reaction caused by high-density fat necrosis after the SVF-gel injection.

Routine injection for breast augmentation can influence the diagnostic sensitivity of mammography (9,10). In contrast, MRI dynamic enhancement can distinguish whether the lesion originated from the prosthesis or the gland itself. Leakage or overflow of the prosthesis shows no enhancement. However, lesions originating from their own glands are abnormally enhanced, distinguishing from benign to malignant by dynamic enhancement and diffusion weight (19). The mammography in this case only showed focal asymmetry, and it was difficult to determine whether it was a self-glandular lesion or whether it had appeared post-injection. Therefore, the mass was defined as Bi-RADS zero. In addition, the ultrasound examination revealed an irregular mass with rich blood flow signals, which was assessed as BI-RADS 4A. The MRI showed segmental distribution and non-mass enhancement; DWI showed a high signal, and the ADC value was $(0.9–1.0)\times10^{-3}$ mm^2/s. All these diagnostic assessments suggested that the lesion may be malignant. However, the segment distribution was related to the location and approach of injection of high-density fat and SVF-gel mixture. In addition, because high-density fat is rich in vascular-related growth factors, the proliferation index is high after injection, and blood vessel hyperplasia occurs, resulting in abnormally rich blood flow that typically signals a tumor on ultrasound imaging and abnormal non-mass enhancement on MRI similar to breast cancer. Therefore, it is easy to misdiagnose this type of mass as a malignant space-occupying lesion.

In the present case, the patient came to the doctor because of breast mass enlargement and mild pain. A CNB was performed under the guidance of an ultrasound. The postoperative pathology of this case was consistent with the percutaneous biopsy. The consistency between the CNB results and postoperative pathology was 94% (20). The percutaneous biopsy showed diffuse proliferation of epithelioid and cytoplasmic atypia with lymphocytic infiltration. Hyperplasia cells have certain atypia with mitosis, which is easily misdiagnosed as triple-negative breast cancer by morphology (21). For personal reasons, the patient concealed her breast augmentation history during the first puncture diagnosis. Therefore, CNB easily made a misdiagnosis of breast cancer without considering the post-augmentation changes. However, the follow-up immunohistochemistry after mass surgery defined that the mass was not breast cancer. After recalling the medical history and the diagnostic assessment findings, the patient's final diagnosis was a granulomatous response after fat necrosis.

The breast lesions were easily misdiagnosed as malignant lesions after high-density fat combined with SVF-gel injection. Difficulties in diagnosis occur because high-density fat combined with SVF-gel injection for breast augmentation is rare, and percutaneous biopsy after breast augmentation is not routinely performed. This case has implications for the diagnosis of breast lesions after SVF-gel augmentation. The materials used during breast augmentation and the pathological changes that are prone to occur after injection should be fully evaluated in imaging and include percutaneous biopsy.

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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-22-165/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 with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient before the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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