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Massive breast fat necrosis with invasive breast cancer: A case report

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Abstract. Breast fat necrosis is a relatively uncommon benign breast condition, while invasive breast cancer is one of the most common types of breast cancer. Coexistence of massive breast fat necrosis with invasive breast cancer is relatively uncommon. The present study reported the case of a 74-year-old female patient who was diagnosed with breast cancer based on mammography findings; breast MRI indicated fat necrosis; subsequent surgical resection confirmed the coexistence of breast fat necrosis with invasive breast cancer using histopathological and immunohistochemical analysis. The relatively uncommon combination of these two conditions poses notable diagnostic challenges for radiologists. The present study reported relevant imaging findings to improve the understanding of radiologists on this disease, highlighting the clinical and radiological features.

Introduction

Breast fat necrosis is a relatively uncommon benign breast condition, with an overall incidence of ~0.6%, accounting for 2.75% of all benign breast lesions (1). The pathogenesis of fat necrosis includes a non-suppurative inflammatory process of adipose tissue, fundamentally caused by aseptic fat saponification. Common causes of fat necrosis include trauma, surgery, radiotherapy, anticoagulant therapy or idiopathic factors (2). It is key to diagnose fat necrosis because it often mimics breast cancer, which can lead to unnecessary biopsies of breast lesions. Breast cancer is a heterogeneous disease influenced by both genetic and environmental factors. Key genetic factors involve high-penetrance mutations (e.g., BRCA1/2) and family history, the latter conferring a 2-3-fold risk increase with an affected first-degree relative. Modifiable risks encompass prolonged estrogen exposure, lifestyle factors like postmenopausal obesity and alcohol use, and reproductive history such as nulliparity and late first birth (3). Globally, it is one of the most common female cancers, representing 25% of new cases and accounting for 2.1 million diagnoses in 2018 (3). Invasive breast cancer is the most frequent subtype, with the main pathological types being invasive ductal carcinoma (70-80%) and invasive lobular carcinoma (5-15%) (3). The occurrence of massive breast fat necrosis associated with a small focus of invasive breast cancer is relatively uncommon, with, to the best of our knowledge, only 5 cases reported in the literature, all including a history of seatbelt trauma from road traffic accidents (4). The imaging differentiation between breast fat necrosis and breast cancer presents notable diagnostic challenges. Breast fat necrosis can mimic several imaging features of breast cancer, such as spiculated margins due to fibrosis or inflammatory reactions, calcification foci resulting from saponification of necrotic cells and irregular enhancement patterns on contrast-enhanced scans similar to those seen in malignant tumors (5-7). This notable overlap in imaging manifestations has led to breast fat necrosis being termed the 'great mimicker' (8,9). While current studies primarily focus on differentiating between these two entities, the imaging characteristics of their coexistence remain insufficiently explored (10-12). The present study reported a case primarily characterized by the relatively uncommon coexistence of massive breast fat necrosis with invasive breast cancer, emphasizing the key role of imaging findings in diagnosis to prevent overlooking malignant foci hidden within benign lesions.

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Case report

A 74-year-old female patient was admitted to The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi) (Zunyi, China) in March 2023 with a 2-month history of a palpable nodule in the left breast, accompanied by intermittent swelling and self-perceived distending pain. On physical examination, a mass measuring ~2.0x1.0 cm was identified at the 2 o'clock position of the left breast, 4 cm from the nipple. The mass was hard, had an irregular surface, poorly defined margins and an irregular shape, with limited mobility and no tenderness. When the patient and their family were queried regarding a relevant medical history, the patient and their family denied having a history of trauma, surgery, radiotherapy, anticoagulant therapy or other relevant medical histories. No notable abnormalities were identified in other examinations.

In March 2023, mammography revealed an irregular, high-density mass in the upper outer quadrant of the left breast, located 8.6 cm from the nipple, with a diameter of ~2.1 cm. The lesion exhibited indistinct margins and spiculated edges (Fig. 1A). The mammographic findings suggested a mass in the upper outer quadrant of the left breast, highly suspicious for breast cancer.

In March 2023, MRI revealed an irregular lesion in the upper outer quadrant of the left breast, 7.0 cm from the nipple, measuring ~2.2x1.2x1.2 cm. The lesion had poorly defined margins and spiculated edges. On T1-weighted imaging (T1WI), it appeared hypointense with small focal areas of hyperintensity (Fig. 1B). On fat-suppressed T1WI, the focal areas appeared hypointense. On fat-suppressed T2WI, the lesion exhibited slightly hyperintense signals with focal hypointense areas that were lower in intensity compared with surrounding fat, forming a 'black hole sign' (Fig. 1C). Diffusion-weighted imaging (DWI) revealed heterogeneous hyperintensity, while apparent diffusion coefficient (ADC) mapping revealed hypointensity. A contrast-enhanced MRI demonstrated marked heterogeneous enhancement in the early phase, with patchy non-enhancing areas within the lesion (Fig. 1E). The time-intensity curve (TIC) displayed a washout pattern (Fig. 1D). Maximum intensity projection images indicated a rich blood supply to the mass (Fig. 1F). Based on MRI findings, the lesion in the upper outer quadrant of the left breast was considered consistent with fat necrosis.

In March 2023, surgical excision of the mass and surrounding normal glandular tissue (weighing 50 g) was performed. A gross examination of the specimen revealed extensive gray-yellow necrotic fat interspersed with white, speckled cancerous foci (Fig. 2A). The histopathological analysis performed in March 2023 using hematoxylin and eosin (H&E) staining (Fig. 2B) confirmed invasive breast carcinoma with focal fat necrosis in the surrounding tissue. For H&E staining, surgical specimens were fixed in formalin at room temperature for 12 h, followed by paraffin embedding and sectioning into 4-μm slices. The sections were baked at 70˚C for 1 h, deparaffinized in xylene and rehydrated through a graded alcohol series at room temperature. The sections were stained with hematoxylin for 5 min and eosin for 1 min at room temperature. Subsequently, the sections were dehydrated through a graded alcohol series, cleared in xylene and mounted with neutral balsam for examination under a DM750 light microscope (Leica Microsystems). Immunohistochemical analysis was conducted manually on 4-μm formalin-fixed, paraffin-embedded tissue sections. After baking at 70˚C for 1 h, sections were deparaffinized in xylene and rehydrated through a graded alcohol series. Antigen retrieval was performed under high pressure at 100˚C using either EDTA (pH 9.0) or citrate-based buffer (pH 6.0) according to the specific requirements of each primary antibody (7 min at full pressure followed by 5 min standing). Following cooling and PBS rinses, endogenous peroxidase activity was blocked with 3% H_2O_2 for 10 min at room temperature. Sections were then incubated with primary antibodies from Tongling Biotechnology (50-100 μl/section) at 37˚C for 1 h, all primary antibodies were used at ready-to-use concentration including Ki-67 (cat. no. AM0241; EDTA pretreatment), erythroblastic oncogene B-2 receptor (c-erbB-2) (cat. no. AM0037; EDTA), non-metastatic protein 23 (nm 23) (cat. no. AM0382; EDTA), estrogen receptor (ER) (cat. no. AR0710; CBS), progesterone receptor (PR) (cat. no. AR0711; CBS), E-cadherin (cat. no. AR0240; EDTA), epidermal growth factor receptor (EGFR) (cat. no. AR0251; EDTA), cytokeratin 5/6 (CK5/6) (cat. no. AM0101; EDTA), p63 (cat. no. AM0186; EDTA), and p120 (cat. no. AM0268; EDTA). After PBS washes, sections were incubated with HRP-conjugated secondary antibody (cat. no. DD13; Tongling Biotechnology) at 37˚C for 30 min, followed by DAB development (cat. no. KS-005A/B; Tongling Biotechnology) for 5 min at room temperature. Counterstaining was performed with hematoxylin for 1 min at room temperature, followed by differentiation in 1% hydrochloric acid-alcohol solution (1% HCl in 70% ethanol). Finally, sections were dehydrated through graded alcohols, air-dried and mounted for examination under a DM750 light microscope (Leica Microsystems). In March 2023, immunohistochemical staining revealed positive expression of Ki-67 (+; ~45%) (Fig. 2C), E-cadherin (+) (Fig. 2D), ER (3+; ~90%) (Fig. 2E), PR (+; ~50%) (Fig. 2F), c-erbB-2 (+) (Fig. 3A), p120 (on the tumor cell membrane +) (Fig. 3B) and nm23 (+) (Fig. 3C), while EGFR (Fig. 3D), CK5/6 (Fig. 3E) and p63 (Fig. 3F) were negative. The date of last follow-up was September 2025, with annual telephone follow-ups conducted.

Discussion

Breast fat necrosis is a common benign breast condition with imaging features that often mimic breast cancer, such as spiculated margins due to fibrosis or inflammatory reactions, calcification foci resulting from saponification of necrotic cells and irregular enhancement patterns on contrast-enhanced scans similar to those seen in malignant tumors (5-7). Breast fat necrosis is characterized by granulomatous inflammation resulting from the enzymatic liquefaction of necrotic tissue. The process of fat necrosis has four stages: i) The hyperacute stage; ii) the acute inflammatory stage; iii) the oil cyst formation stage; and iv) the chronic granulomatous reaction stage. Each stage exhibits distinct imaging characteristics. When the imaging findings resemble those of malignancy, a pathological examination is required for a definitive diagnosis (5,8). Invasive breast cancer is defined by the penetration of cancer cells through the basement membrane into the breast stroma, resulting in a higher degree of malignancy and an increased risk of metastasis compared with non-invasive breast cancer (13,14).

The patient was admitted to The Third Affiliated Hospital of Zunyi Medical University (The First People's Hospital of Zunyi); Zunyi, China) in March 2023 due to a palpable left breast nodule for >2 months, accompanied by self-perceived distending pain that occurred intermittently. Although the patient reported no history of breast trauma or surgery, imaging examinations are of notable necessity (15). This is

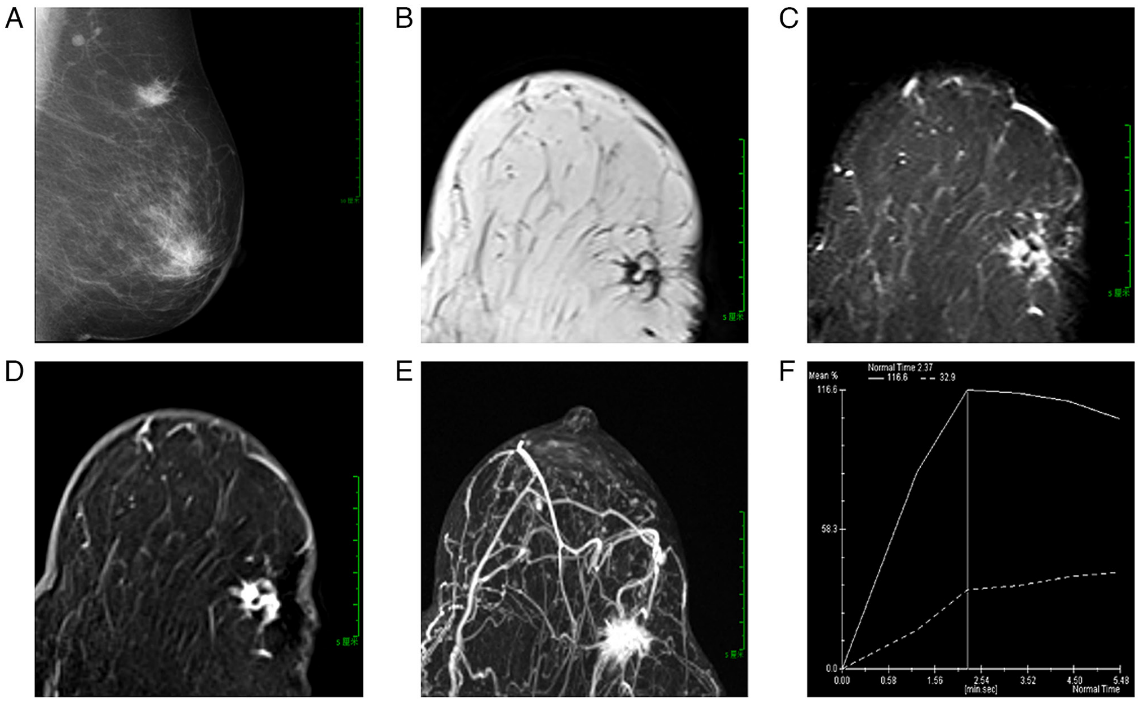

Figure 1. (A) The mammographic mediolateral oblique view reveals an irregular high-density mass in the upper outer quadrant of the left breast, with indistinct, spiculated margins. (B) Axial T1-weighted MRI exhibits an irregular mass in the upper outer quadrant of the left breast with indistinct, spiculated margins. The lesion exhibits low signal intensity with small focal areas of high signal intensity within. (C) Axial fat-suppressed T2-weighted MRI demonstrates slightly high signal intensity within the mass, with small focal areas of low signal intensity. These areas are lower in signal intensity than the surrounding fat, displaying the characteristic 'black hole sign'. (D) Axial post-contrast MRI exhibits heterogeneous enhancement of the mass with patchy non-enhancing areas. (E) Maximum intensity projection reveals slightly increased vascularization of the mass. (F) The time-signal intensity curve demonstrates a washout pattern.

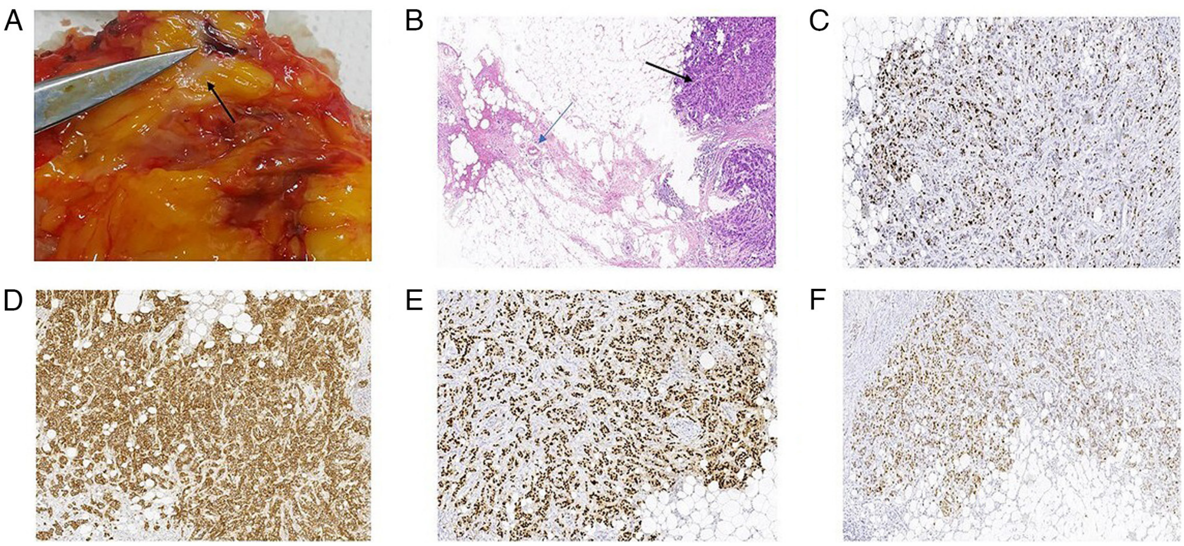

Figure 2. (A) The gross specimen exhibits extensive gray-yellow necrotic fat with white spot-like cancer foci (indicated by the black arrow). (B) Fat necrosis and invasive breast cancer (H&E stain): The area indicated by the blue arrow displays ruptured or disrupted adipocytes, with their normal round structure destroyed. Macrophages are visible. The area indicated by the black arrow displays highly heterogeneous cancer cell morphology and size, with an increased nucleus-to-cytoplasm ratio. The cancer cell cytoplasm stains light pink, and the cancer cells infiltrate the surrounding fibrous stroma in a cord-like pattern (magnification, x5). (C) Invasive breast cancer (Ki-67): Ki-67$^+$ cells have brownish-yellow-stained nuclei. The positive staining is confined to the cell nucleus, with no staining in the cytoplasm. (D) Invasive breast cancer (E-cadherin): E-cadherin(+) displays brownish-yellow positive staining on the cancer cell membranes, with staining primarily localized to the cell membrane, suggesting that the cancer cells still retain some adhesive function. (E) Invasive breast cancer (ER): ER$^+$ cells have brownish-yellow-stained nuclei. (F) Invasive breast cancer (PR): PR$^+$ cells have brownish-yellow-stained nuclei (magnification, x10). ER, estrogen receptor; PR, progesterone receptor.

because imaging examinations can make up for the limitations of palpation, clearly display the detailed characteristics of the nodule such as its size, shape, boundary, internal echo, density or signal and whether it is accompanied by calcification, and can even detect 'occult or tiny nodules' that cannot be identified by palpation (16).

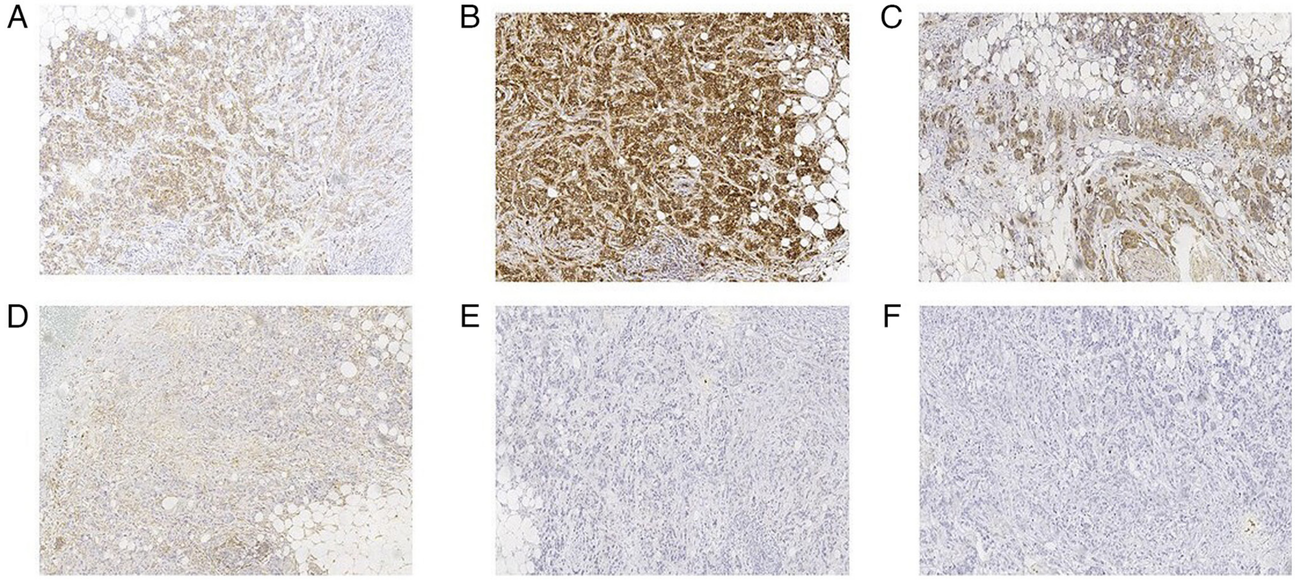

Figure 3. (A) Invasive breast cancer (c-erbB-2): c-erbB-2$^+$ with brownish-yellow staining observed on tumor cell membranes. (B) Invasive breast cancer (p120): p120$^+$ with brownish-yellow staining in tumor cells. (C) Invasive breast cancer (nm23): nm23$^+$ with brownish-yellow cytoplasmic staining in tumor cells. (D) Invasive breast cancer (EGFR): EGFR$^-$ with no staining observed in tumor cells. (E) Invasive breast cancer (CK5/6): CK5/6$^-$ with no staining in tumor cells. (F) Invasive breast cancer (p63): p63$^-$ with no staining detected in tumor cells (magnification, x10). c-erbB-2, erythroblastic oncogene B-2 receptor; nm23, non-metastatic protein 23.

Breast fat necrosis and breast cancer can have similar imaging appearances, which makes them difficult to distinguish. On mammography, fat necrosis often presents as round or oval low-density cysts with fat-fluid levels caused by the separation of oil and serous fluid (17). As the condition progresses, calcifications may develop (5). By comparison, breast cancer appears on mammography as an irregular, high-density mass with spiculated margins. The calcifications associated with breast cancer are often described as clustered microcalcifications or fine, irregular microcalcifications (18). In the present case, mammography revealed an irregular, high-density mass with unclear borders and spiculated edges, features highly suggestive of breast cancer. However, mammography has limited tissue-specific resolution and previous reports have indicated that fat necrosis can mimic malignant tumors (8,9,12). Therefore, breast MRI is necessary, as it provides more detailed information using multiparametric imaging techniques.

In breast MRI, fat necrosis often appears as a hyperintense lesion on T1WI and T2WI, becoming hypointense on fat-suppressed images, with a typically clear border. However, fibrosis or inflammation may cause slight spiculation. On enhanced scanning, it often exhibits no enhancement or only rim enhancement. However, enhancing fat necrosis mimicking malignancy can exhibit irregular mass enhancement (9), with a varied TIC to a certain extent similar to breast cancer, making differentiation difficult (5). Notably, on inversion recovery sequences, most intracellular lipids, such as those in lipid-rich mammary lesions (19) and the triglyceride droplets of breast hamartomas (20) indicate marked signal reduction. However, fat necrosis has a lower signal intensity compared with surrounding normal fat, termed the 'black hole' sign, considered specific for fat necrosis. This is because the necrotic fat is replaced by fibrosis, calcification or fluid, with a narrower distribution of T1 relaxation times around the inversion time (TI), the specific time delay used in an MRI inversion recovery pulse sequence, leading to more complete fat suppression at specific TI times. The 'black hole sign' often presents in the oil cyst formation stage (where the necrotic region undergoes cystic change and liquefied fat is confined within the cyst cavity) and the chronic granulomatous reaction stage (where the central necrotic area is completely fibrotic, with or without calcification) of fat necrosis. By contrast, breast cancer often lacks this sign (19,21,22). The 'black hole' sign seen in the breast MRI of the present case suggested fat necrosis. However, apart from the characteristic 'black hole' sign of fat necrosis on MRI, other imaging features were similar to those of breast cancer, making differentiation difficult and prompting clinical vigilance and biopsy. The histopathological analysis of the surgical specimen suggested that the coexistence of massive mammary fat necrosis with invasive breast cancer, which is a relatively uncommon clinical presentation with only a few documented cases in the literature (4).

Previous studies have predominantly focused on differentiating fat necrosis from breast cancer, yet they have overlooked their imaging manifestations when they coexist (10-12). In the present case, performing MRI after mammography was necessary for accurate preoperative assessment of the lesion's size and delineating the extent of the lesion. Firstly, mammography has relatively weak tissue resolutions due to the interference of breast glands (23,24), while the multi-parametric imaging technology of MRI provides more detailed information, thus serving a complementary role (25). Furthermore, MRI can evaluate the condition of the contralateral (healthy side) breast. It is worth noting that when mammography suggests a malignant lesion, MRI becomes particularly key, as it serves a key role in diagnosis and treatment (26). The present case highlighted that even with the characteristic 'black hole' sign of fat necrosis on MRI, if other imaging features resemble breast cancer and are indistinguishable, the possibility of coexisting breast cancer within fat necrosis should be considered.

Under the microscope, fat necrosis is characterized by ruptured adipocytes, infiltration of inflammatory cells, saponification of fat, formation of foam cells and fibrosis (2,21,27,28). The pathological features of invasive ductal carcinoma of the breast include cellular atypia, loss of normal glandular architecture (14,29), and immunohistochemical staining results demonstrated negative expression for myoepithelial markers CK5/6 and p63 and positive expression of p120 and E-cadherin. Fat necrosis is a proliferative condition often induced by hypoxia (27). Following ischemic injury, adipocyte rupture alters the tumor microenvironment, creating conditions that may promote cancer development (30).

The differential diagnosis between breast fat necrosis and invasive breast cancer requires distinguishing it from conditions such as breast sarcoma, inflammatory breast cancer (IBC) and simple invasive breast cancer. Breast sarcoma often includes the entire breast, with rare calcification and axillary lymphadenopathy. On T1WI, it reveals isointensity or hyperintensity, except in necrotic or cystic areas. The TIC of breast sarcoma demonstrates washout, indicating slow enhancement and heterogeneous signal intensity (SI) distribution (31). IBC presents with specific mammography and MRI features, such as breast enlargement and diffuse or nodular skin thickening. Lesions are often multifocal and widespread, making accurate tumor size measurement challenging (32). Pure infiltrating ductal carcinoma generally appears on mammography as an irregular, spiculated, dense mass with malignant calcification. On MRI, it exhibits mixed T2WI signals, with SI dependent on internal components. Enhancement can be homogeneous, heterogeneous or rim-like, and TIC demonstrates washout. On DWI, it demonstrates hyperintense and hypointense signals on ADC, indicating restricted diffusion (33,34). Pure breast fat necrosis has distinct imaging characteristics. The imaging presentation depends on the stage of fat necrosis, the degree of inflammatory reaction, the amount of liquefied fat, fibrosis and calcifications, as well as the etiology of the fat necrosis. Therefore, knowledge of imaging appearances of fat necrosis at different stages is essential for a radiologist to make accurate interpretation and avoid unnecessary invasive workup (35). Mammography of fat necrosis often reveals well-defined, low-density oil cysts, which may have coarse, ring-like or ‘eggshell’ calcifications. MRI of fat necrosis often reveals hyperintensity on both T1WI and T2WI, with clear margins. However, fibrosis or inflammation can cause slight spiculation. The ‘black hole’ sign on T2WI fat-saturated sequences is a specific marker for fat necrosis. Enhancement is often absent or rim-like, with low restricted diffusion. In summary, analyzing these imaging features can effectively distinguish fat necrosis from invasive breast cancer and other breast diseases, providing a reliable clinical diagnosis.

In conclusion, the present study reported a relatively uncommon case of massive breast fat necrosis coexisting with invasive breast cancer. Imaging findings reveal several similarities between fat necrosis and breast cancer, often making them difficult to differentiate. Although previous literature has largely focused on the differential diagnosis between the two, the present case highlighted the possibility of their concurrent occurrence, with a minor focus on invasive breast cancer, which is key for the improvement of diagnostic accuracy. Furthermore, the present case provided additional evidence supporting the close association between inflammation and cancer development, which aligns with findings from previous related studies.

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Availability of data and materials

The data generated in the present study are included in the figures of this article.

Authors' contributions

AZ designed the present case report and wrote the manuscript. LS, BT, YL, XY and XC performed all the experiments. GJ provided data and preliminarily interpretated them. LJ performed data analysis, conceptualization and critical review. GJ and LJ confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent for publication was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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