Fat necrosis of the breast—A review


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Summary
Fat necrosis of the breast is a benign condition that most frequently affects peri-menopausal women. It can mimic breast cancer clinically or radiologically. In other cases it can obscure malignant lesions.

The core of this review is derived from a MEDLINE database literature search from 1966–2004. Further references were from lateral search.

In this paper, we review the pathogenesis and pathology clinical and radiological features of fat necrosis of the breast. The implication of fat necrosis in the management of patients with breast lump is also discussed.

Fat necrosis of breast is a complex process. Therefore, a systematic review of this condition will enable surgeons, radiologists and oncologists working in the field of breast disease to understand it better and improve its management.

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Introduction

Fat necrosis is a benign non-suppurative inflammatory process of adipose tissue which was initially described in the breast in 1920.¹⁻² Hadfield described it as "an innocent lesion of the breast presenting itself most often in women between the fourth and fifth decades, frequently as a stony-hard tumour firmly fixed to the skin, often resembling an early cancer so closely that a wide resection of the breast has been performed".³

It is important to diagnose fat necrosis because it often mimics carcinoma of the breast. The aim of this paper is to review the clinical, pathological and radiological features of fat necrosis of the breast which distinguishes it from breast cancer.

Epidemiology

The incidence of the disease is estimated to be 0.6% in the breast, representing 2.75% of all benign lesions.¹⁻⁴ Fat necrosis is found in 0.8% of breast tumours and 1% of breast reduction surgery cases.⁵ The average age of patients is 50 years.¹⁻⁴
Aetiology

The aetiological factors include trauma (21–70%),¹⁻⁴ radiotherapy,⁶⁻⁸ anticoagulation (warfarin),⁹ cyst aspiration, biopsy, lumpectomy, reduction mammoplasty, implant removal, breast reconstruction with tissue transfer,¹⁰ duct ectasia and breast infection. Other rare causes include polyarteritis nodosa, Weber-Christian disease and granulomatous angioanpticulitis. In some patients, the cause is unknown.¹¹

Pathogenesis

Fat necrosis is a sterile, inflammatory process which results from aseptic saponification of fat by means of blood and tissue lipase.¹² It varies in appearance depending on the stage of the process. It is recognised histologically as fat-filled macrophages and foreign body giant cells surrounded by interstitial infiltration of plasma cells.¹³

After trauma to the breast, haemorrhage occurs within a surgical cavity, or extravasates into the parenchyma. Blood dissects along the fibrous planes of breast (contusion). Contusion may also occur secondary to capillary rupture, thrombophelia, allergic reaction, and arterial or venous thromboses.

Extravasation of blood into the parenchyma causes oedema and swelling of the trabecular framework of the breast, with considerable tissue ischaemia and pressure necrosis, with subsequent disruption and fragmentation of fat cells.

This destruction causes formation of intra-cellular vacuoles filled with necrotic lipid material. Fibroblasts, multinucleated giant cells and lipid-laden histiocytes ('fat-filled macrophages' or 'foam cells') accumulate between cyst-like areas.

At a cellular level, apoptosis and necrosis are two forms of cell death with distinctive morphological and biochemical features.¹⁴ Apoptosis is a process of ‘programmed cell death’ while necrosis is a deranged form of cell death. The intensity of the initial insult determines whether apoptosis or necrosis predominates. Various stimuli such as cytokines, ischemia, heat, irradiation and pathogens can trigger both apoptosis and necrosis.¹⁴

Furthermore, signalling pathways such as death receptors, kinase cascades, and mitochondria, participate in both processes.¹⁴

In necrosis, cytosolic constituents spill into the extracellular space through the cell membrane and provoke an inflammatory response. In apoptosis these products are safely isolated by cell mem-

Clinical features

Clinical presentation of fat necrosis can range from an incidental benign finding to a lump highly suggestive of cancer.¹⁶,¹⁸ In most cases it is clinically occult; however, it can present as single or multiple smooth, round, firm nodules or irregular masses. It may be associated with ecchymosis, erythema, inflammation, pain, skin retraction or thickening, nipple retraction and lymphadenopathy simulating carcinoma.¹⁰,¹⁶,¹⁹,²⁰

Hadfield¹ described 66% of lesions as being stony hard. Up to 52% of these lesions are adherent to the skin and 10% are associated with retraction of the nipple. Adair and Munzer² described 64% of patients with skin tethering. Pulleyblank et al.⁴ found clinical signs suggestive of cancer in 45% of cases.

There appears to be little difference in clinical presentations of lesions regardless of whether they are related to trauma.³,⁴ In cases related to trauma, the majority of patients presented with a lump in the breast. The mean time for patients to present with a breast lump from the time of trauma is 68.5 weeks (range 3–208).⁴

Both Hadfield¹ and Adair and Munzer² found that in lesions precipitated by trauma, the lump occurred at the site of the trauma. In cases where there was no history of trauma, Hadfield¹ found the lesion to be most often in the upper outer quadrant of the breast. The fact that most patients with trauma had a lump in the upper inner quadrant is thought to be related to the use of seatbelts. DiPiro et al.²¹ described different patterns of injuries to the inner breast according to whether the patient was the passenger or the driver of the vehicle. Fat necrosis is commonly found in the superficial breast tissues and subareolar regions in obese women with pendulous breasts.¹⁰
Tissue diagnosis

Fine needle aspiration cytology (FNAC)

FNAC is reported to have a high sensitivity and specificity—87% and 99%, respectively.\(^{22,23}\)

Using FNAC as a diagnostic tool enables rapid results particularly in a ‘one-stop’ clinic setting. FNAC can decrease the number of excision biopsies.\(^{22,23}\) However, the diagnosis of fat necrosis using FNAC is limited by inadequate samples\(^{24}\) and repeated attempts may be necessary to achieve a confident result. FNAC is reliable in collaboration with a good history of trauma and close follow-up in diagnosing fat necrosis.\(^{25}\)

Core biopsy

Core biopsy of breast lesions has been shown to be more sensitive than FNAC.\(^{6}\) The diagnostic accuracy between large-core needle biopsy and excision (surgical) biopsy are favourably comparable.\(^{26,27}\) Parker et al.\(^{26}\) report false negative rates of 1.2–1.5% with large-core needle biopsy. However, core biopsy is often inadequate or indeterminate in the investigation of suspected fat necrosis in the breast\(^{11,25}\). Pullyblank et al.\(^{4}\) reported two (4.7%) cases in their series of 42 patients who were found to have malignancy on excision biopsy after a core biopsy diagnosis of fat necrosis. Hence surgical excision biopsy is indicated where there is still suspicion of malignancy following negative core biopsy.

Imaging

Mammography

The mammographic appearance of fat necrosis include normal appearance (9%), discrete round or oval radiolucent oil cyst with thin capsule (27%), thickening and deformity of skin and subcutaneous tissue (16%), focal mass (13%), and ill-defined spiculated mass (4%).\(^{5}\) Oil cysts may be associated with uniform continuous eggshell calcification (27%). There may also be multiple clustered pleomorphic microcalcifications (4%) suspicious of malignancy.\(^{10,19,28}\) The most common mammographic findings are dystrophic calcifications, followed by radiolucent oil cysts.

The variable mammography changes are attributable to the degree of fibrosis in different stages of the disease. During early stages, less extensive fibrosis is associated with a lipid cyst with a thin, fibrous capsule. They have benign looking round or oval, radiolucent shapes (sharply demarcated lucent area) with a thin rim on mammograms. Older lesions appear as radiolucent oil cysts with ring-like dystrophic calcifications in the wall. Fat necrosis may also appear as lipophagic granulomas which are associated with greater degree of fibrosis.

Occasionally fat necrosis may manifest as ill-defined, spiculated dense or focal masses associated with distortion, skin thickening and retraction as commonly seen in breast cancer.\(^{10,16,19,21,29,30}\) Fat necrosis may also be associated with pleomorphic, clustered or branching-type microcalcifications which are indistinguishable from those associated with cancer.

Ultrasound

The ultrasound appearance of fat necrosis range from solid nodules with posterior shadowing, to complex intra-cystic masses that evolve over time.\(^{18,30}\) These features depict the histological evolution of fat necrosis.\(^{11,31}\) Sonographically, fat necrosis may appear as cystic or solid masses. Cystic lesions appear complex with mural nodules or with internal echogenic bands. Solid masses have well-circumscribed or ill-defined margins, and are often associated with distortion of the breast parenchyma.\(^{25}\)

Common features of fat necrosis on ultrasonogram are increased echogenicity of subcutaneous tissue (27%), as an anechoic cyst with posterior acoustic enhancement (17%), hypoechoic mass with posterior acoustic shadowing (16%), solid mass (14%), cyst with internal echoes (11%), normal appearance (11%) or cystic mural nodule (4%).\(^{5,18,30,31}\)

The oil cyst, which shows posterior acoustic shadowing, corresponds to the round radiolucent lesion with curvilinear wall calcification on mammography. Ultrasound can reliably diagnose oil cysts. Soo et al.\(^{18}\) defined an echogenic band that shifted in orientation with changes in patient position as being diagnostic of oil cysts.

Magnetic resonance imaging (MRI)

Fat necrosis produces a wide spectrum of findings on MRI. Magnetic resonance images correlate well with the histology of fat necrosis. The abundant iron-containing siderophages cause a diffuse decrease in signal intensity on both T1- and T2-weighted images. A focal area of oedema is seen as a hyperintense zone on T2-weighted images.
Fat necrosis consists of oil cysts and lipophagic granulomas in varying proportions. Pure oil cysts are fairly well identified as round, well-circumscribed hyperintense areas on T1-weighted images. They may show a faint rim of enhancement along the boundary of the cavity. Lipophagic granulomas are more difficult to distinguish from malignancy on MRI. Hence such lesions require biopsy for confirmation of diagnosis.

MRI may show irregular peripheral enhancement with a non-enhancing central areas in fat necrosis. Histologically the enhancing areas correspond to peripherally developing fibrosis and inflammatory cell infiltration, and the central non-enhancing areas correspond to necrotic fat. However, this MR appearance of fat necrosis may be indistinguishable from malignant lesions which also often have necrosis.42 As the commonest presentation is that of a lump there, an underlying malignancy must be overlooked, as patients' attention may only be drawn to the lump by an episode of trauma. Management may include short-term follow-up with imaging and physical examination, to reduce the number of unnecessary biopsies. In one series on the mammographic follow-up period of 3 years, it was noted that six round opacities decreased in size and density, and in two of them, a radiolucent oil cyst and calcifications developed. Eleven dystrophic calcifications changed to a benign appearance. In ultrasonographic follow-up, the most common finding was normalisation of the subcutaneous tissue echogenicity and formation of small cysts. Solid masses remained solid, whereas complex lesions tended to evolve. Most of the solid masses decreased in size confirming a benign process. None of the complex lesions became more solid, while some became more cystic. No mass enlarged on ultrasound follow-up in this series.

Although the changes in echo texture on ultrasound may be chronologically and morphologically consistent with the diagnosis of fat necrosis, one must be wary of sinister pathology obscured by increased density on mammography. Multiplicity and distribution along the seat-belt line may warrant follow-up rather than a biopsy, particularly in young patients. The recent work of Soo et al. concluded that with the superior quality of current imaging, any abnormality with sufficiently benign characteristics might safely be managed expectantly. A needle core biopsy may be reserved for selected cases where the lesion appears indeterminate or suspicious. Clearly, this strategy involves a period of observation before the lesion can be confirmed as benign which may well exacerbate patient anxiety. Furthermore, 66% of mammographic abnormalities and 74% of ultrasound lesions were classified as indeterminate or suspicious. For best practice, the histological result should be considered in conjunction with the clinical and imaging findings, with involvement of a multidisciplinary team.

Discussion

The management of fat necrosis continues to be challenging in practice. Even with modern diagnostic modalities, fat necrosis of the female breast can still be difficult to diagnose. In patients who have undergone breast conservation surgery or reconstruction for breast cancer, fat necrosis must be distinguished from cancer recurrence. Hence in specific cases, needle core biopsy is required to confirm diagnosis.

Although there is a definite association with trauma, surgery or biopsy of the breast, not all patients present with a clear history for fat necrosis. As the commonest presentation is that of a lump there, an underlying malignancy must be considered. Even with a clear history of previous trauma, the possibility of a malignancy should not be overlooked, as patients' attention may only be drawn to the lump by an episode of trauma.
Investigation and management of fat necrosis does not fit easily into a rigid protocol. Where there is any diagnostic uncertainty we recommend needle core biopsy to obtain definitive diagnosis and that follow-up imaging is performed to confirm resolution. Pitfalls in diagnosis of fat necrosis may arise in cases following radiotherapy and/or surgery for breast carcinoma. Therefore the diagnosis of fat necrosis should only be a diagnosis by exclusion of malignancy.

References


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