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Review Article

Fat in Disguise – Mask Unleashed on Breast Imaging

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Abstract

Fat-containing lesions of the breast are a heterogeneous group of conditions and are predominantly benign tumors. Fat necrosis of the breast is a non-suppurative benign inflammatory condition of the adipose tissue that can be mistaken for cancer during a clinical examination or imaging studies as it progresses through various stages of pathological transformation. Injury to breast tissue is the cause for this condition and the sources include blunt trauma, procedure surgeries, and radiation. The clinical symptoms and radiological findings can mimic malignancy and hence precise history is a key feature that points to the diagnosis. The imaging features of fat necrosis may vary depending on the stage of evolution. Mammogram can either be normal, show asymmetry, malignant features or may present as a straightforward oil cyst. Ultrasound can be normal or show inflammatory changes, dilated ducts, or malignant characteristics. Magnetic resonance imaging is not the modality of choice for fat necrosis unless a diagnostic confusion of malignancy or recurrence occurs. Hence, in-depth knowledge of the various imaging features during different phases can help in diagnosing fat necrosis. However, histopathology remains a necessity to arrive at a final diagnosis.

Key words: Cytology, Fat necrosis, Histopathology, Mammogram, Ultrasound.

INTRODUCTION

Fat-containing lesions of the breast are a heterogeneous group of conditions and are predominantly benign tumors.[1] Fat necrosis is a benign non-suppurative inflammatory process of the adipose tissue.[2] Previously it was said to result from blunt trauma to the breast. In the present day, with the growing number of surgeries, procedures, and radiation therapy, fat necrosis is being encountered often in routine practice. Fat necrosis has varied imaging appearances from benign to suspicious for malignancy during its many stages of evolution.[3] The spectrum of radiologic manifestations of fat necrosis poses a challenge in diagnosing the condition even with the new diagnostic modalities.[4] Hence, it is important for radiologists to know the accurate history and have knowledge of the various imaging findings to achieve the correct diagnosis and avoid unnecessary interventions.[2] In this article, the various presentations of fat necrosis on imaging with histopathological examination (HPE) correlation are discussed.

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DISCUSSION

The incidence of fat necrosis is estimated to be 0.6%, accounting for 2.75% of all benign breast lesions.[5] Fat necrosis of the breast is a benign inflammatory process that may be mistaken for cancer in clinical examination or imaging studies. With the growing number of breast surgeries performed today (e.g., breast-conserving, autologous tissue reconstruction, and mammoplasty), fat necrosis is often encountered in daily practice.[6] The mammary gland is a common site for traumas which often leads to the formation of intraglandular hematomas. The abundance of fat tissue in this gland accounts for

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the relatively high frequency of fat necrosis and the self-digestion of fat by lipases after traumas.[7] Knowledge of its imaging features could improve clinical management, including the avoidance of unnecessary biopsy procedures.[6]

CLINICAL FEATURES

The presentation can vary from being clinically occult to a hard lump with skin changes highly suspicious for malignancy. A history of accidental trauma raises the suspicion of fat necrosis in a breast lump. However, the absence of a history of trauma does not exclude fat necrosis.[5] Fat necrosis presents as a small, painless, ill-defined breast mass when it becomes palpable. Usually, the palpable abnormality is periareolar and superficial in location, rarely can present with bruising and tenderness, skin tethering, and nipple retraction. These lesions may enlarge, remain unchanged, regress, or resolve over a period of time.[8]

PATHOPHYSIOLOGICAL EVOLUTION OF FAT NECROSIS

Fat necrosis is a sterile, inflammatory process that results from aseptic saponification of fat employing blood and tissue lipase.[9]

In the early phase, fat necrosis appears as an area of hemorrhage in fat, resulting in induration and firmness on gross pathology. On cytology, a newly insulted adipose cell will first lose its nucleus accompanied by degenerative changes in adipocytes with hemorrhage.[5]

After several weeks, the affected area becomes demarcated, forming a distinct yellow (due to saponification) and focally reddish mass. In the intermediate stage of fat necrosis, it is replaced by foamy histiocytes, macrophages, and multinucleated giant cells filled with dead adipose cells. Lesions that do not resolve undergo cystic degeneration, resulting in a cavity that contains oily fluid.[5]

In the late stage over months to years of fat necrosis, calcification develops which is seen as a chalky white lesion, and fibrosis presents as a yellow-gray mass. Finally, scar formation develops due to reactive inflammatory components giving rise to fibrosis. Hemosiderin deposition may be seen and indicates remote hemorrhage. At lower magnification, necrotic material is wrapped by a layer of fibrous tissue. Fibrosis gives the appearance of an irregular spiculated mass due to the retraction of nearby vascularized tissue within 2–4 weeks. Calcification develops within 6–12 months around the lesion.[9] Imaging appearances can mimic malignancy at this stage unless the characteristic benign lucent-centered or rim calcifications are seen on a mammogram.[5]

The varied appearances of fat necrosis on imaging studies are attributed to various amounts of histiocytic infiltration, hemorrhage, fibrosis, and calcification.[8]

Immunohistochemistry with CD 68 is helpful in confirmation of the histiocytic nature of the macrophages. Confusion may arise with invasive lobular carcinoma in areas of extensive fibrosis. In invasive lobular carcinoma, discohesive single cells with small monomorphic nuclei that infiltrate the stroma are seen. Pan Cytokeratin is a very useful marker in these situations, and is a helpful problem-solving tool, and shows uptake by the tumor cells.[10]

The diagnosis can be confirmed based on either serial imaging studies that show chronological changes compatible with the evolution of fat necrosis or improvement in clinical symptoms (lump no longer detectable on palpation). Histological confirmation may be reserved for indeterminate or suspicious imaging features.[5]

Imaging

As mentioned earlier, the imaging appearances of fat necrosis depend on its stage of evolution.[5]

Mammography

Mammographic findings in fat necrosis of the breast include lipid cysts, microcalcifications, coarse calcifications, spiculated areas of increased opacity, asymmetry, and/or focal masses. Fat necrosis manifesting as a clinically palpable mass also may demonstrate no appreciable mammographic finding.

Lipid Cyst

Lipid cysts are pathognomonic of benign fat necrosis. A lipid cyst is a round to oval, smooth-bordered, and lucent mass with a thin rim [Figures 1a-c, 12d, and e]. The fibrous rim of the cyst may or may not calcify.[11] Calcifications are usually smooth and round or curvilinear.[12]

Microcalcifications

Fat necrosis uncommonly manifests as branching, rodlike calcifications, angular, or pleomorphic microcalcifications that are mammographically indistinguishable from those of malignancy.[12]

Spiculated Area of Increased Opacity

If the reparative phase fibrosis replaces all of the necrotic fat, it gives the appearance of an irregular, dense, and spiculated mass which makes it difficult for differentiation from malignancy on a mammogram [Figure 4a-c].[12] Hence, fat necrosis should be included in the differential diagnosis

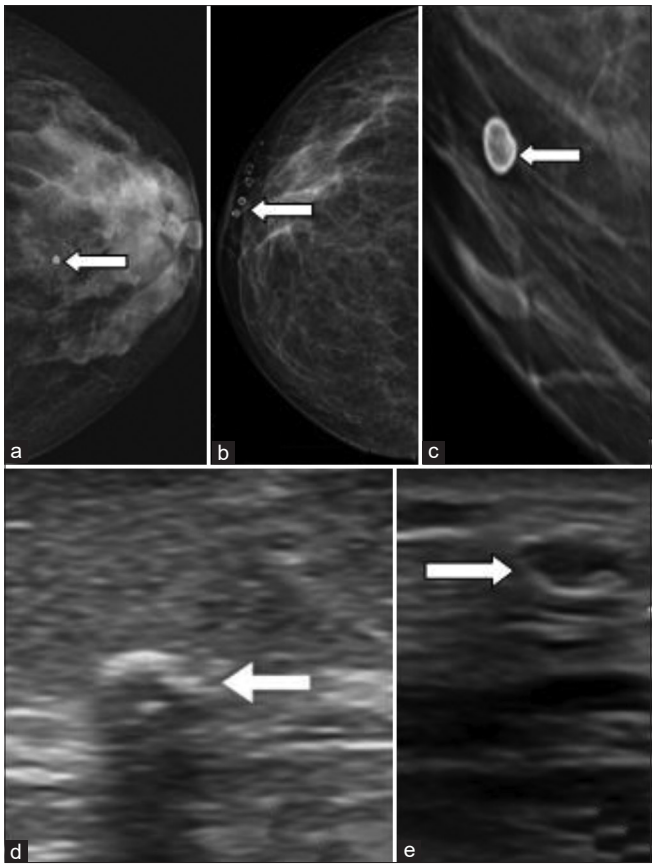

Figure 1: Different patients who came for routine annual checkup. (a and b) X-ray mammogram CC view and (c) zoomed-in view showing oil cysts with rim calcification (arrow). (d and e) Ultrasound images showing oil cyst with peripheral calcification (arrow)

of a spiculated mass in addition to carcinoma, radial scar, and post-biopsy changes.[11]

Focal Mass/Asymmetry

Rarely, fat necrosis manifests as a non-lucent, focal mass [Figures 2b and 7a], or asymmetry [Figure 3b and d] with or without associated macrocalcification. However, the presence of lucent areas within a mass representing fat [Figure 4a-c] suggests that the lesion is almost always benign.

Ultrasound (US)

Similar to mammogram, US of fat necrosis shows a gamut of imaging findings that can appear benign or malignant. Virtually all the cases have findings on US, inclusive of those cases with a normal mammogram. Hence, US plays an important role in excluding malignancy and suggesting fat necrosis as the diagnosis.

US features that are relatively reliable predictors of benignity include hyperechogenicity, well-defined margins, and parallel orientation. Lack of color flow on Doppler is an additional feature; however, it is not a reliable discriminator. Some malignant and indeterminate features in the US constitute an indistinct border with anechoic areas within, irregular shape, taller-than-wide morphology, and posterior acoustic shadowing.

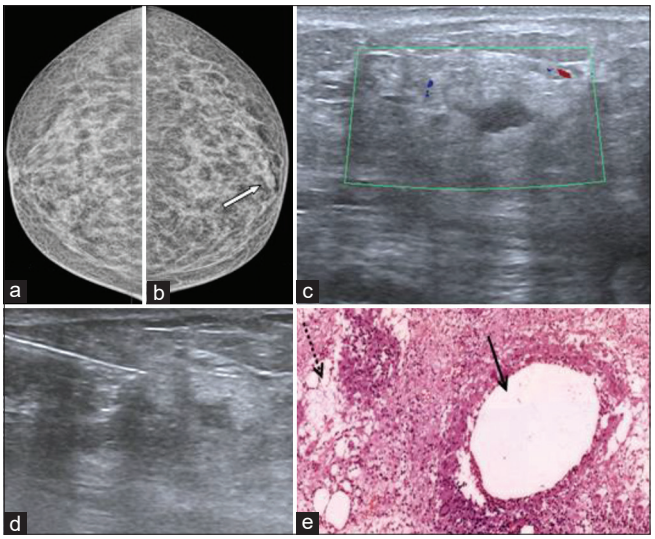

Figure 2: A 65-year-old female with a history of pain in the left retro areolar region breast with no other specific history X-ray mammogram CC view (a) Right breast with no abnormality (b) Left breast shows a subcentimeter irregular high-density nodularity in the subareolar region (arrow) (c) Ultrasound with color Doppler shows an irregular parallelly oriented circumscribed hyperechoic mass with central cystic changes with combined posterior features and absent vascularity. (d) Ultrasound-guided tru-cut biopsy of the mass (e) H & E: Chronic Mastitis with focal cystic change (Black Arrow) and adjacent fat necrosis (Dotted Arrow) ×100

Fat is interspersed in between the fibroglandular tissue in the deeper layer of breast parenchyma. Hence, one needs to be prudent and careful while encountering a hyperechoic nodule in the deeper tissue planes.[5]

The common presentation that we see on a daily routine is a well-defined hypoechoic lesion with peripheral echogenic calcific rim representing an oil cyst [Figures 1d, e and 12f]. An echogenic band within an oil cyst that shifts in orientation with changes in patient position is the most specific feature of fat necrosis.[5]

Other features that we encounter in US include solid hypoechoic [Figures 4a and 10a and b]/isoechoic/hyperechoic masses [Figures 6a and b and 10a] with posterior acoustic shadowing or enhancement, causing architectural distortion of the parenchyma, hyperechoic masses with cystic areas [Figures 2c, 3e, 7b and c] to complex intracystic masses with a mural nodule [Figure 5e], echogenic bands. These features illustrate the histological evolution of fat necrosis.[10]

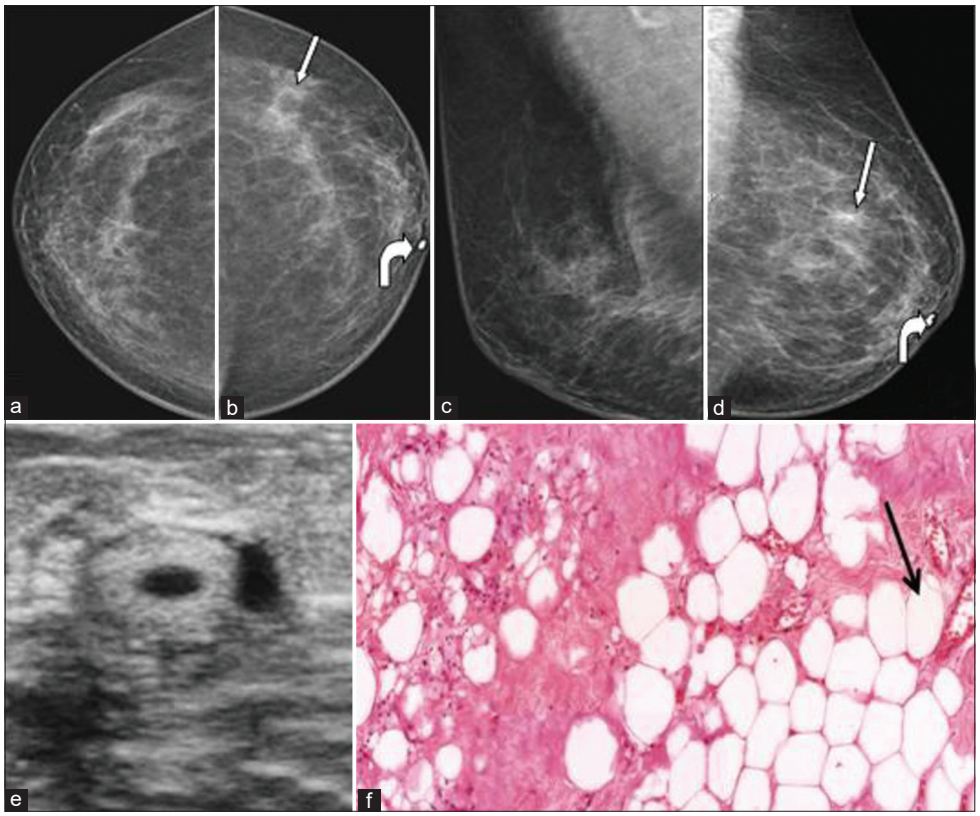

Figure 3: A 48-year-old female with complaints of focal pain in the outer half of the left breast for 1 year, exaggerated for 1 month with no history of trauma. X-ray mammogram (a and c) of the right breast (CC and MLO view) with no abnormality and b&d left breast (CC and MLO view) shows focal asymmetry (straight arrow) in the upper outer quadrant, benign focal round calcification (curved arrows) in the retroareolar region (e) ultrasound image shows an oval parallelly oriented circumscribed hyperechoic mass with central cystic component. (f) H&E: Fibroadipose tissue with focal necrosis of adipocytes (Black Arrow) ×200

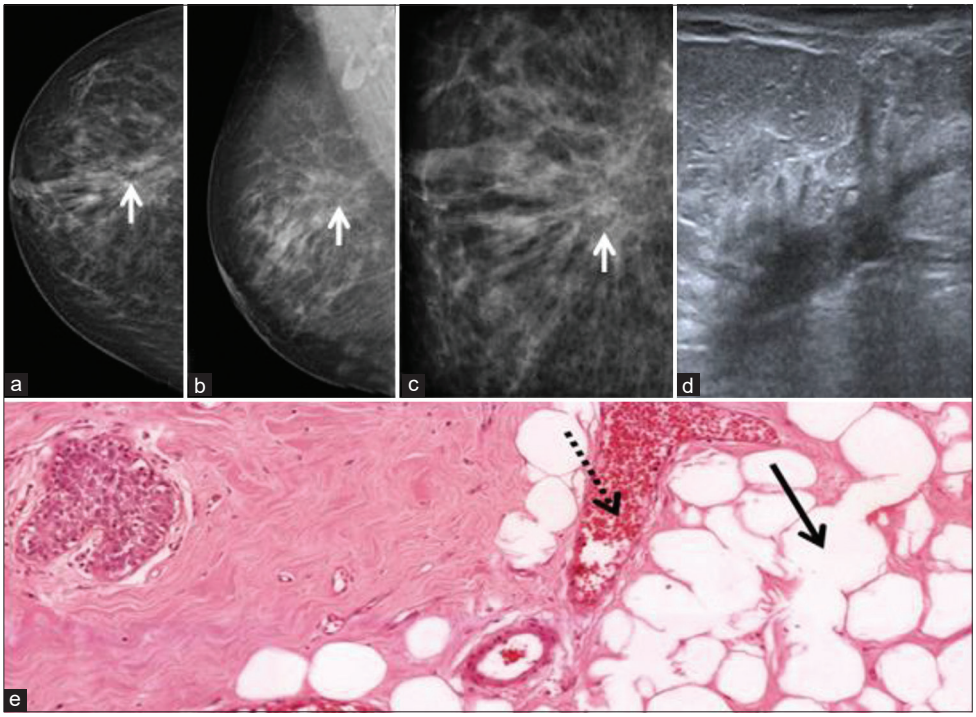

Figure 4: A 58-year-old female with complaints of pain in the right breast for 1 year, history of surgery in the same breast 3 years before for a benign condition. X-ray mammogram of right breast (a) CC view showing speculations and architectural distortion with fat lucencies (white arrow) suggestive of post-operative scaring and (b) MLO view and (c) Spot magnification view shows the speculations are spread out with interspersed fat lucencies (white arrow). (d) Ultrasound image showing an irregular, spiculated, hypoechoic mass with combined posterior features. (e) H&E: Fat necrosis (solid arrow) with adjacent congested vessels (Dotted Arrow) - ×200

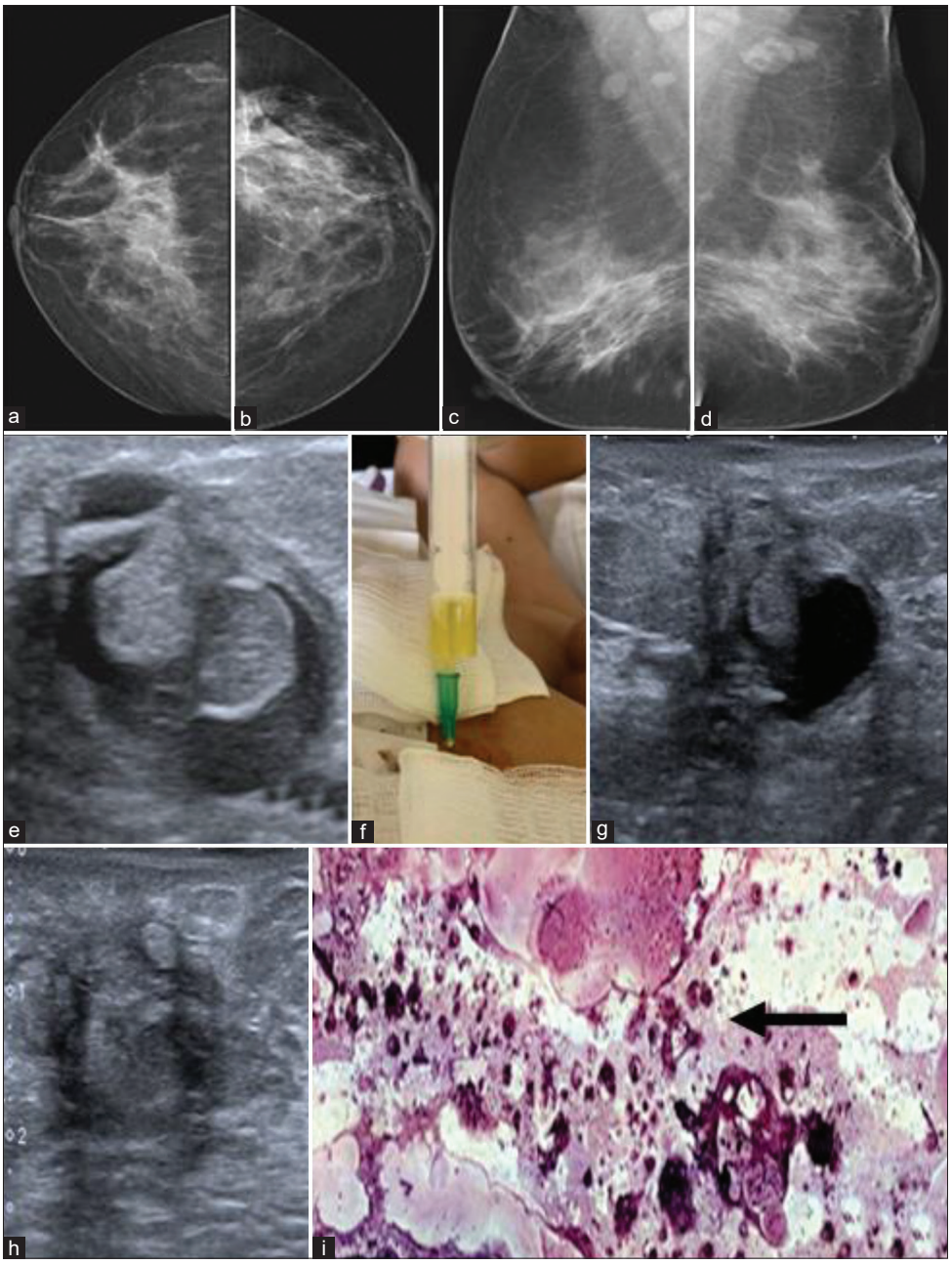

Figure 5: A 46-year-old female post-operative case of phyllodes tumor – 18 months, came for a routine check-up with no specific complaints. X-ray mammogram (a and c) CC and MLO view of the right breast shows no abnormality and (b and d) CC and MLO view of the left breast shows architectural distortion involving the upper outer quadrant with adjacent skin retraction (e) ultrasound image shows an oval parallel oriented circumscribed anechoic mass with few hyperechoic areas within (g) shows image of fine-needle aspiration of the mass with thick yellow oily fluid being aspirated. (h) Post-aspiration image showing complete resolution of the cystic mass. (i) Cytology: H & E: Showing fat necrosis (Black Arrow) ×200

Hyperechoic masses very rarely personify a malignancy and are reported in <0.8% of tumors.[12] Although rare, malignant hyperechoic lesions include invasive ductal and lobular carcinoma, lymphoma, angiosarcoma, and liposarcoma.[10]

In our article, we present few cases of fat necrosis that have a unique presentation of multiple irregularly dilated ducts showing thick internal echoes with surrounding inflammation [Figures 8a and b, 9b]. Some cases had associated features of skin thickening. Most of these cases demonstrated normal X-ray mammogram except for focal skin thickening [Figure 9a] in one case. HPE correlation of these cases unveiled the appearance of fat necrosis.

A case report by Coyne shows that intraductal fat necrosis can occur due to the displacement of fatty tissue into the ducts following prior needling. This form of fat necrosis is termed as membranous intraductal fat necrosis. Although this is a rare entity, we need to keep this into consideration

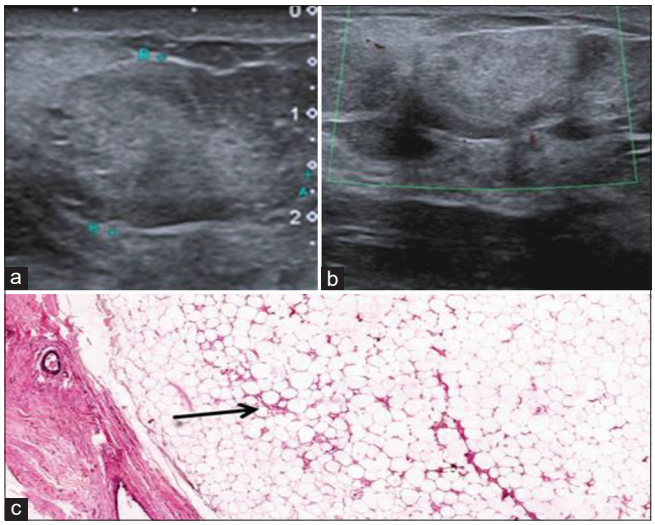

Figure 6: A 37-year-old female with complaints of a lump in the breast for 8 months. (a and b) Ultrasound and color Doppler image show an oval, parallel oriented, circumscribed, hyperechoic mass with few cystic changes at the periphery (arrows) with no posterior features or vascularity. (c) H & E: Well circumscribed mass with adipocytes showing fat necrosis (Black Arrow) ×100

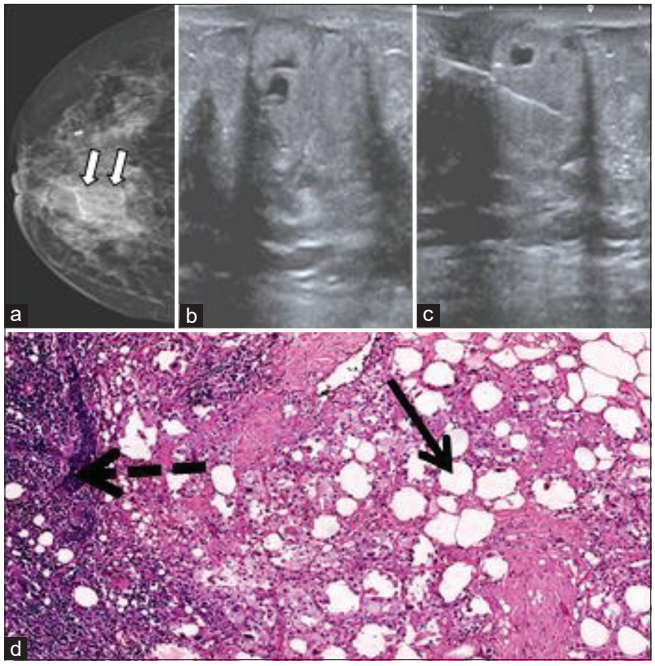

Figure 7: A 43-year-old female with a history of a lump in the right breast for 6 months. (a) X-ray mammogram CC view shows an irregular indistinct equal density mass (arrows). Two specks of benign round calcification noted in outer quadrant. (b) Ultrasound image shows an oval parallel oriented circumscribed predominantly hyperechoic mass with cystic changes and no obvious posterior features. (c) Ultrasound-guided biopsy image of the same mass (d) H&E: Lymphocytic mastopathy (Dotted Arrow) with adjacent fat necrosis (black arrow) ×200

when fat necrosis within a dilated duct is seen and ask for a history of the previous procedure.[13]

The proposed follow-up of probably benign USG lesions is to do a diagnostic mammogram and/or US

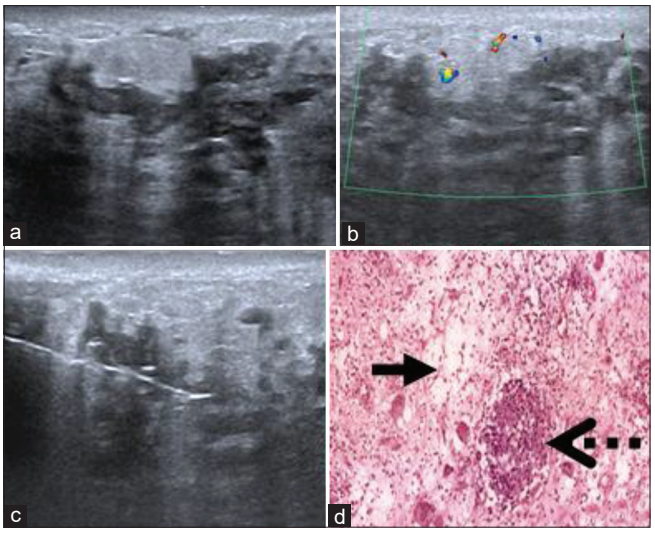

Figure 8: A 31-year-old female with a history of skin changes 1 week and progressive hardness of breast 4 months. (a) Ultrasound image shows multiple dilated ducts with thick internal echoes seen within. (b) Color Doppler image shows vascularity within the adjacent parenchyma- probable diagnosis of idiopathic granulomatous mastitis was made. (c) Ultrasound-guided biopsy of the mass. Multiple biopsy cores were obtained from within and periphery of the abnormal ducts. (d) H &E: Granulomatous lesion (Dotted Arrow) with adjacent fat necrosis (Black Arrow) ×200

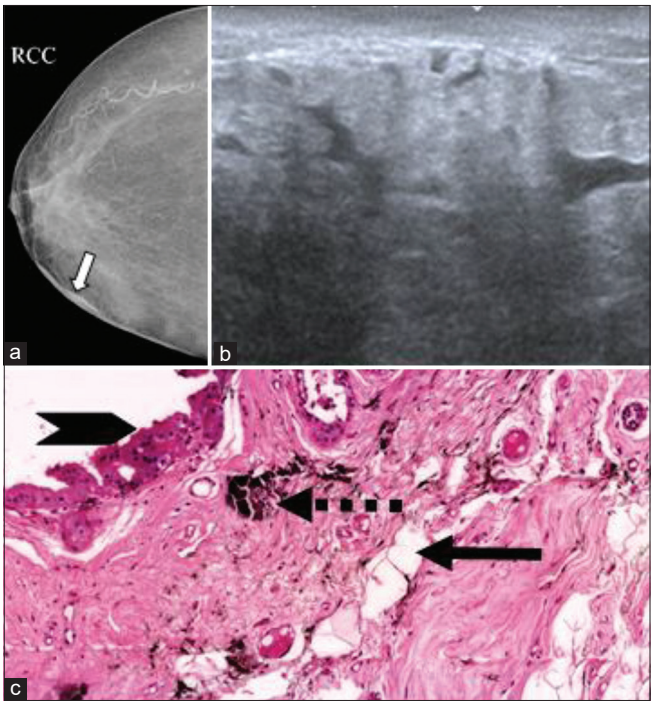

Figure 9: A 48-year-old female with bilateral non-cyclical mastalgia and a vague history of domestic accident 3 months back. Family history of breast cancer positive. (a) X-ray mammogram CC view of the right breast shows focal skin thickening (arrow) and benign vascular calcification in the outer quadrant. b. Ultrasound image shows prominent ducts with surrounding edematous parenchyma, focal skin thickening, and no definitive mass. (c) H & E: Benign calcification (dotted arrow) with apocrine metaplasia (arrowhead) of ducts and adjacent fat necrosis (black arrow) ×200

at a 6-monthly interval for a year and annually for either 1 or 2 years. The usual findings in follow-up US's include normalization of the subcutaneous reflectivity, progression into anechoic areas, and solid and complex lesions becoming more cystic.

In doubtful cases, especially with a complex nodule at initial presentation, fluid aspiration is recommended. If the aspirate is oily material [Figure 5f], the diagnosis of malignant complex mass is excluded and fat necrosis is confirmed. Other findings include flattening of the lesion and resorption of the pure oily fat and an increase in the serosanguinous fluid.[5]

COMPUTED TOMOGRAPHY

In the early stages, fat demonstrates low density [Figure 11b and c] and in later stages with the development of fibrosis linear densities of fibrous bands are seen. In cases of inflammation, enhancement is seen after contrast.[10]

Computed tomography is not the modality of choice in diagnosing fat necrosis in the breast.[10]

Magnetic Resonance Imaging (MRI) Mammogram

Similar to other imaging modalities, MRI appearance of fat necrosis varies depending on the amount of inflammatory

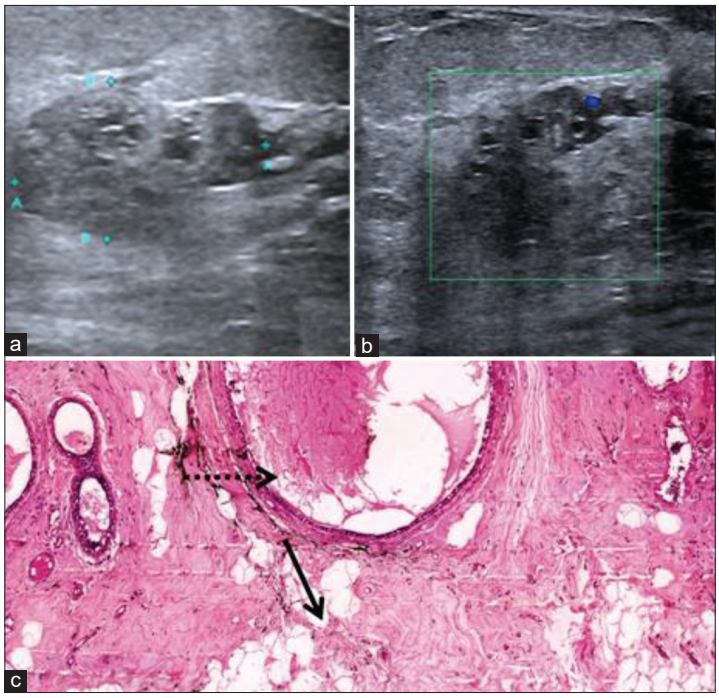

Figure 10: A 35-year-old female with no complaints came for a regular checkup. No history of trauma. (a and b) Ultrasound and color Doppler image shows an irregular hypoechoic mass with tiny cystic changes with absent vascularity and no obvious posterior features (arrow). (c) H & E: Dilated ducts (dotted arrow) and adjacent fat necrosis (black arrow) ×200

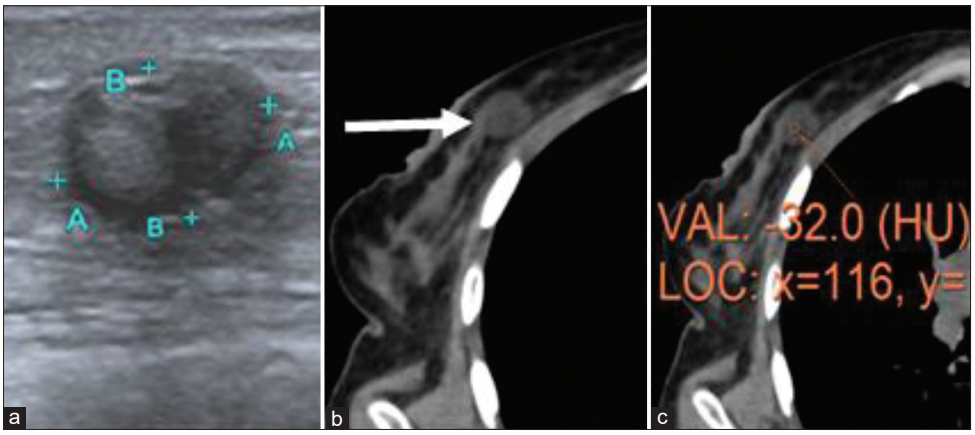

Figure 11: (a) 49-year-old female with no specific complaints. Ultrasound image shows an oval, parallel oriented, circumscribed heterogeneous mass predominantly hyperechoic with no posterior features. Axial section of plain computed tomography in soft tissue window (b) shows a well-defined hypodense mass in the medial quadrant of the breast (arrow). (c) Showing fat density (–32 HU) within the mass

reaction, liquefied fat, and degree of fibrosis. It can have a benign appearance and at times mimic carcinoma, especially postoperatively, as more fibrotic lesions can enhance irregularly or appear spiculated, which are key characteristics of malignancy.[14] The most common appearance of a lipid cyst is a round or oval non-enhancing central mass with an enhancing edge. The immature granulation tissue at the edges of the lesion may enhance after contrast injection due to poor vessel wall integrity. It is hyperintense on T1-weighted imaging and hypointense on T2-weighted imaging – can be used to differentiate fat necrosis from a malignancy, which would not generally contain a central region of fat. Furthermore, the mass becomes hypointense on T1-weighted signal on fat saturation[14] [Figure 12h]. In instances where fat necrosis presents as fibrosis, the appearance is that of a spiculated or irregular mass. On contrast, administration, thin, thick, irregular, or spiculated enhancement may be seen.

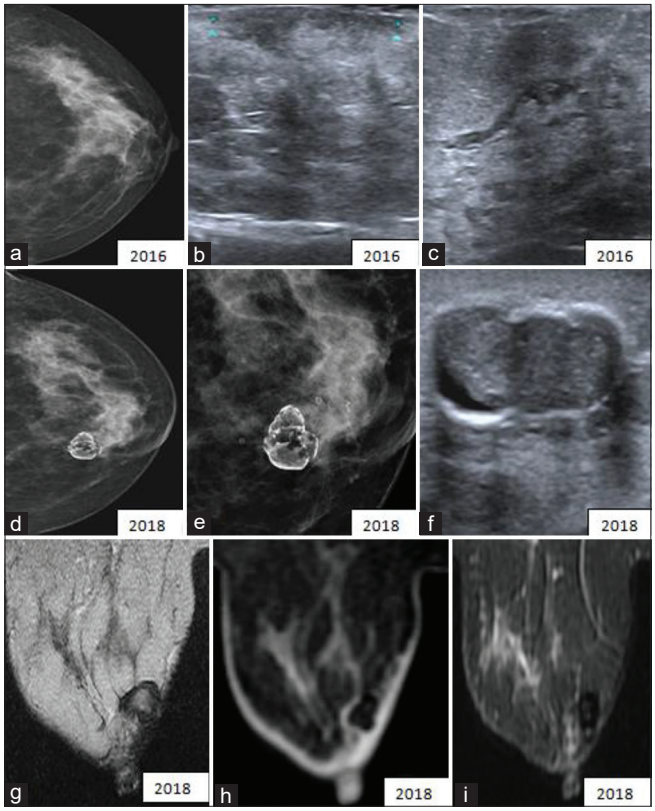

Figure 12: A 43-year-old female with a history of surgery for malignancy in 2015. November 2016 imaging for a routine checkup – (a) X-ray mammogram CC view of the left breast appears normal. (b and c) Ultrasound image shows ill-defined areas of heterogeneity at the operative site corresponding to post-operative inflammatory changes. November 2018 imaging for a routine checkup –X-ray Mammogram of the left breast (d) CC view and (e) zoomed-in view shows a circumscribed radiolucent mass with rim calcification suggestive of fat necrosis. Few other small oil cysts with rim calcification are noted adjacent to the larger lesion. (f) Ultrasound image shows an oval parallel oriented circumscribed hypodense mass with peripheral calcification in the mass and combined posterior features. (g) Axial sections of T2 weighted magnetic resonance imaging (MRI) shows a circumscribed isointense mass compared to adjacent parenchyma with peripheral hypointenserim. (h) Axial T2 FS images show hypointense mass, with fat being suppressed within the mass. (i) Axial contrast-enhanced MRI shows a non-enhancing mass

A recently identified characteristic of fat necrosis on MRI is the "black hole" sign in which there is marked hypointensity on STIR images when compared with surrounding fat.[10]

Prognosis and Complications

Fat necrosis has a good prognosis with no risk of developing cancer in the future. However, the similarity in the clinical and radiological presentation of mimicking a malignancy warrants histopathological correlation. There are no major complications related to fat necrosis; however, pain, infection, and breast deformity are a few of the minor issues.

Few differentials that need to be considered during imaging evaluation include breast carcinoma, breast cyst, fibroadenoma, and granulomatous mastitis.[9]

CONCLUSION

The varied spectrum of clinical presentation and imaging findings of fat necrosis puts the clinician and radiologist in a diagnostic dilemma. Proper history with an insight into the imaging features makes it easier in differentiating fat necrosis from other conditions. Therefore, it is mandatory to have a clear history, assess risk factors, and consider the age of the patient. In high-risk patients, namely, those who had primary oncologic surgery, patients older than 40 years of age, and those with very delayed presentation of fat necrosis, a more extensive workup is necessary. Mammography is a better modality of choice for fat necrosis than US especially in diagnosing a lipid cyst. However, in the late stages, there is an overlap in features with malignancy resembling a spiculated mass due to the fibrotic reaction. All these factors pose a challenge to arrive at the diagnosis and hence an in-depth knowledge of the spectrum of imaging findings will help in arriving at a diagnosis and can avoid unnecessary procedures and the anxiety caused to the patient. However, biopsy remains the gold standard where the diagnostic dilemma lingers on.

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