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A Review on Fat Necrosis of the Breast: The Dilemma of Differential Diagnosis with Cancer

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ABSTRACT

Fat necrosis is a benign inflammatory process which can involve adipose tissue anywhere in the body. A previous history of trauma or surgery may or may not be present. Information about the clinical and radiological appearance of this lesion is very important because it can mimic breast cancer.

In this article, we review the features of fat necrosis in different imaging modalities including mammography, ultrasound, and magnetic resonance imaging (MRI), and compare them with histopathologic findings; then, we try to provide a logical approach for fat necrosis management.

The appearance of fat necrosis at imaging is variable from definitely benign type to highly suspicious for malignancy. The specificity of mammography is higher than that of ultrasonography; therefore, for a definite diagnosis of fat necrosis, emphasis should be mainly based on mammography rather than ultrasonography.

Finally, fat necrosis is not a common disease; however, regarding unusual and atypical findings in different imaging modalities, differentiation from a cancer may be difficult, especially in patients with a previous history of malignancy. Therefore, a multimodality approach is required for a definite diagnosis.

Introduction

Fat necrosis is a benign inflammatory process which can involve the adipose tissue anywhere in the body. This entity was first explained in the breast in 1920. A previous history of trauma or surgery may or may not be present. Information about the clinical and radiological appearance of this lesion is very important because.[1-6]

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In this article, we review the literature on fat necrosis based on the associated histopathological findings, and clarify the spectrum of its manifestations on mammography, ultrasonography and MRI. Then, we propose an algorithm for fat necrosis management.

Methods

A literature review was performed using information websites such as PubMed, Cochrane, and Springer from 1990 to 2013. A total of 550 articles were found using the following key words: fat necrosis, breast, mammography, sonography, and MRI. Twenty four papers that were more relevant to fat necrosis imaging were selected. Their results in terms of clinical and histopathologic findings and imaging appearances including mammography, ultrasonography, and MRI were summarized. At the end, a standardized approach is proposed for the diagnosis of fat necrosis through a multimodality approach.

Results

Epidemiology

The reported incidence of fat necrosis is 0.6% representing 2.75% of all benign masses. The mean age of fat necrosis is 50 years. Fat necrosis is observed in 8% of breast masses and 1% of reconstructive surgeries.[2] This condition is becoming more frequently encountered in daily practice because of the growing number of autologous tissue reconstruction surgery. Improved knowledge of its imaging features is required to avoid unnecessary biopsy procedures.[1,3,4]

Etiology

Fat necrosis is a benign inflammatory process that is usually secondary to trauma but is sometimes idiopathic. Trauma can be accidental or iatrogenic. One example of accidental injury is seatbelt trauma. Iatrogenic events include breast surgery (lumpectomy, reduction, or augmentation). Reconstruction techniques are deep inferior epigastric perforators (DIEP) and transverse rectus abdominis musculocutaneous (TRAM). Other less common causes are percutaneous procedures (fine needle aspiration, core needle, vacuum-assisted biopsy), or fine chemical irritation by anticoagulant agents, radiotherapy, and infection.[2,3,7] Other causes of fat necrosis are collagen vascular diseases such as giant arteritis, Wegener granulomatosis, poly arteritis nodosa, Weber-Christian disease, granulomatous angiopaniculitis, and SLE.[5] Most of inflam-matory fat necrosis are in patients with a breast conserving treatment of breast cancer and inflam-mation is related to the adjuvant radiotherapy.

Histopathology

A cascade of cellular events begins with the initial injury and results in different imaging appearances. Initially, fat cells and hemorrhage are infiltrated by inflammatory cells, including histiocytes. Subsequently, fat cells undergo liquefaction necrosis. There is also increased vascularization and infiltration of fibroblasts, lymphocytes, and histiocytes that wall off the focus of necrotic cellular debris.[1] All the above-mentioned factors lead to the accumulation of fluid in the interstitial space and cause the edema which is a characteristic of the hyperacute inflammatory phase.[1] Afterwards, fibrinogen is released in the interstitial space by the damaged vessels, and is converted to active fibrin by the enzyme thrombin. Fibrin combines with the platelets and forms a mesh which can control bleeding. A fat-containing granulation tissue is formed by the combination of free fat from adipocytes, macrophages, leukocytes (mainly neutrophils), fibrin, fibroblasts, and angioblasts and is recognized as an oil cyst.[2] With time, the oil cyst can either calcify or can be reabsorbed and replaced with connective tissue.[2] Proliferation of foreign body giant cells with fibrosis eventually occurs. Ultimately, the focus of fat necrosis may be replaced with a scar or may persist as an oil cyst walled off by fibrous tissue.[6] The stage of development and the form of fat necrosis at the time of imaging affect the appearance on imaging.[4,6]

Clinical findings

Fat necrosis of the breast is usually a mammographic finding in asymptomatic patients.[1,4] Clinical features of fat necrosis can be variable from benign findings to highly suspicious for malignancy. It is sometimes clinically occult.[2] When a clinical abnormality is present, it frequently manifests as a lump with smooth margins or an irregular, painless, indurated, fixed and ill-defined breast lump.[1,2] Associated findings are echymosis, erythema, inflammation, skin or nipple retraction, skin dimpling, and lymphadenopathy.[1,2] Some of these findings mimic breast cancer. The mean time from trauma to referring with clinically palpable abnormality is 6-8 weeks. There is no difference in clinical findings according to the etiology. If there is no previous history of trauma, the typical location will be in the upper outer quadrant.

Tissue diagnosis

Sensitivity and specificity of fine needle aspiration (FNA) is 88-99% and core needle biopsy (CNB) are more sensitive and comparable to surgical biopsy. False negative is 1.2 to 1.5%; however, CNB can be suspicious or borderline. Therefore, if there is still clinical suspicion for malignancy, excisional biopsy is recommended.[2]

Mammographic features

The appearance of fat necrosis in mammography depends on the stage of evolution.[8] The hemorrhage occurring in the early phases causes edema of the breast trabeculae, or asymmetry at mammography. If this process remains unresolved, oil-containing cavities which are seen on gross pathology are in fact the results of cystic degeneration.[8,9] If they are large enough, the corresponding imaging finding at this stage would appear as an oil cyst on mammograms. In the absence of fibrotic reaction, a classical oil cyst may be present.[10,11] As described by Evers and Troupin and Hogge *et al.*, this latter appears as an entirely radiolucent mass representing macroscopic fat necrosis surrounded by a thin fibrotic membrane.[3,4] This feature is pathogonomic of fat necrosis. When the fibrotic reaction is more intense but the radiolucent necrotic fat is not completely replaced, the oil cyst may have thickened irregular, speculated, or ill-defined walls.[8] The imaging appearance of calcification and fibrotic reaction, which develop after several months or years, can resemble malignancy. During these phases, the diagnosis of benign lesion can be made through visualization of the characteristic benign lucent-centered or coarse rim calcifications.[8,10] The reparative fibrotic reaction may eventually replace all the radiolucent necrotic fat, making it appear as an irregular speculated distortion or mass, a focal dense, or a focal asymmetry suspicious for breast cancer.[7-10,12-14]

Calcifications are sometimes the only mammographic findings. They usually have typical benign features and appear as thin–walled egg shaped calcifications in oil cysts or as coarse irregular calcification with radiolucent areas interspersed between them.[8,14] Less frequently, a cluster of pleomorphic calcifications similar to ductal or amorphous calcifications representing early-stage cancer may be observed.[2,8] Calcifications appear in various combinations associated to typical or atypical oil cysts with or without fibrotic scar. The appearance of these combinations allows a correct diagnosis.[8] The prevalence of mammographic findings are as below: normal (9%), oval or round radiolucent oil cysts with well- defined margins and a thin capsule (27%), skin thickening and deformity in the subcutaneous fat (16%), focal masses (13%), and spiculated masses (4%).[2] The most common mammographic findings are dystrophic calcifications followed by radiolucent oil cysts.[2]

As a typical and pathognomonic finding of fat necrosis in mammography is an oil cyst with or without dystrophic calcification, no more investigations with other imaging modalities are needed. Atypical findings regarding the amount of fibrosis in the initial oil cyst which might need further assessments are focal dense mass, irregular or speculate mass or distortion focal asymmetry and a group of pleomorphic calcification similar to ductal and amorphous calcification.

The diagnosis of fat necrosis can be made based on a personal history of trauma or breast surgery, typical changes in serial radiologic assessments of a suspicious mass or reduction in the size of the mass during follow-up visits. In case of suspicious imaging findings, histologic confirmation might be necessary to rule out malignancy.

Ultrasonography findings

Echogenic internal bands which are considered the hallmark of fat necrosis in ultrasonography represent the interface between the lipid and sero-hemorrhagic components of the lesion.[12] Other features of fat necrosis at ultrasonography without a specific pattern are posterior acoustic shadow by dystrophic calci-fication, distortion of the normal parenchymal architecture, or a heterogeneous halo surrounding tissue.[8,12,14,15] Soo *et al.* found that most of the oil cysts identified on mammography appeared solid on ultrasonography.[16] Solid masses, complex cystic masses with internal mural nodules, anechoic masses with posterior acoustic enhancement, and anechoic masses with posterior shadowing are other findings.[17]

The most common finding at ultrasonography is increased echogenicity in the subcutaneous fat which is a reliable predictor of benignity.[8] Other findings with less frequency are: an echoic cyst with posterior through transmission, a hypoechoic mass with posterior shadowing, a cyst with internal echoes or a normal appearance and a cyst with mural nodules.[18]

While in the anterior superficial plane, subcutaneous fat is dispersed within connective tissue, on deep parenchymal levels it is often scattered within the fibroglandular tissue.[8,11] Therefore, caution should be exercised when hyperechoic nodules in the deeper tissue planes are detectable, and findings such as 'taller-than-wide' orientation, irregular shape, posterior acoustic shadowing are encountered.[8] The location of fat necrosis is not specially important for diagnosis, since oil cyst is considered as a specific sign of fat necrosis. Parallel orientation, an ultrasonography feature of benignity, is very important in cases with solid abnormality. Lack of flow on Doppler suggests the presence of fat necrosis.[8,17] Nevertheless, according to the available literature, this sign cannot reliably distinguish benign from malignant nodules.[8,19]

Magnetic resonance imaging

Histologic bases of the MRI features of the fat necrosis are the inflammatory reaction, the amount of visible liquefied fat, and the degree of fibrosis in the tissue at the time of study.[6] Diagnostic keys are characteristics of internal signal and mass enhancement.

Unenhanced non-fat-saturated T1-weighted imaging is the best sequence in diagnosis of fat necrosis and discriminating between a necrotic tumor and fat necrosis. Fat necrosis exhibits an isosignal with fat.[6,9] The oil cyst as a typical finding is detected as a round or oval mass with a well-defined margin which does not enhance.[2,20] It is hyper-intense on T1Wsequences and can be either hypo or hyper-intense on T2Wsequences. Depending on whether granulation tissue surrounds the cyst, the typical rim enhancement may or may not be observed. Depending on the degree of calcification of the cyst, a signal void may be present, while edema is hypersignal on T2-weighted images.[2,21,22]

Calcifications associated with fat necrosis are rarely seen on MRI in which they appear as signal voids. Fibrosis is mainly responsible for architectural distortion and spiculated margins associated to fat necrosis on MRI. Fibrosis usually appears as high, intermediate, or low signal on T1-weighted images depending on the stage of the process.

Fat necrosis can be enhanced after injection of paramagnetic contrast. The main cause of increased uptake of the contrast media is presence of granulation tissue. Since the granulation tissue is often peripherally distributed around the oil cyst, rim enhancement (a characteristic of malignant lesions) might be a common finding. However, the MRI findings of oil cysts are generally unequivocal due to the benign nature of this enhancement.[2,23]

However, in some cases that the distribution of the granulation tissue is not well-defined, the signal intensity of T1-wighted sequences should be taken into consideration. Presence of fat, which is typically hyper-intense signal intensity on T1-weighted sequences, together with the patient's clinical history, can aid in ruling out malignancy.[2,21,24] The presence and degree of this enhancement depend on the intensity of the associated inflammatory process. Enhancement is more frequent and intense during the initial stages of fat necrosis when the inflammatory component is most significant. During the later stages of fat necrosis, enhancement seems to be less frequent and weaker with gradual resolution of this process. The enhancement pattern can be diffuse or focal homogenous or heterogeneous. In addition, focal enhancement can be predominantly peripheral. The enhancement pattern may be similar to those seen in malignant lesions. Kinetic patterns of contrast enhancement observed in some cases can present slowly and gradually or abruptly with an intense enhancement pattern and sometimes even a washout sign.[6]

MRI can play an essential role in diagnosis of a fibrous scar. The greater the fibrotic content of the scar is, the scar enhancement would be less likely. However, the persistence of granulation tissue can cause scar enhancement On T1W, due to persistence of fat, hyperintense foci may be visible within the region of the scar tissue.[2,24]

Among patients with a history of breast cancer surgery, the negative predictive value of MRI approximates 100%. In such instances, it is imperative to determine the morphokinetics of the contrast media in the scar tissue. Lack of enhancement is suggestive of a process other that malignancy. Yet, in cases where increased uptake in the scare tissue is detected, the possibility of relapse should be borne in mind.[2] Complementary MRI techniques might be of help in distinguishing the correct diagnosis in these cases. For instance, a highly apparent diffusion coefficient value in the lesion detected on diffusion-weighted MRI suggests that the tumor recurrence has not occurred. On the other hand, choline peaks in MR spectroscopy are suggestive of local relapse.[2]

Discussion

Fat necrosis is a complex entity from both the clinical and diagnostic aspects. On one hand, it is extremely easy to diagnose fat necrosis in patients with a clear history of breast trauma and the typical findings on imaging. However, the diagnosis could be challenging in patients with suspicious findings on imaging, with or without a prior history of trauma. On the other hand, it can be very difficult to be diagnosed in patients with suspicious imaging findings

A systematic approach using the American College of Radiology (ACR) guidelines will aid in avoiding misdiagnosis and ruling out the possibility of malignancy, thus preventing unnecessary biopsies.[8]

If mammography revealed the oil cyst with typical findings, no further imaging would be necessary. This is while in case of a soft tissue mass density presenting with partial halo or focal asymmetry with or without architectural distortion on mammography at the site of palpable abnormality, ultrasonography is needed to confirm the diagnosis of fat necrosis. When any suspicious features for malignancy such as irregularity, spiculated mass, architectural distortion or suspicious group calcifications is found on mammography, BIRADS category would be 4 or 5 and biopsy should be considered according to the ACR recommendation. It is important to categorize the BIRADS for mammography first before performing ultrasound to minimize the chance of overlooking malignancy, as ultrasound is less specific than mammography. If the BIRADS category according to sonography is 3 but 4 on mammography, the final category would be 4 rather than 3 and a biopsy is recommended.[8] Adding MRI to standard imaging could be useful in some cases.

To avoid false negative and false positive findings, it can be suggested that for the management of such patients three fundamental components need to be taken into account: clinical manifestations of the patient, personal risk of breast cancer, and results of imaging studies.[2] If clinical and imaging findings are compatible with fat necrosis and the patient is at high risk for malignancy, the next step should be MRI. If fat necrosis is confirmed on MRI, follow-up by mammography and MRI for 1 year is recommended. If fat necrosis is not confirmed on MRI, percutaneous biopsy is recommended by means of core needle biopsy (CNB) or vacuum-assisted breast biopsy (VABB).[2]

If there are abnormal clinical or imaging findings in favor of fat necrosis, but the patient is not at high risk for breast cancer, MRI is not required. In these circumstances, if clinical and imaging findings are concordant, follow-up with mammography and sonography for 1 year is recommended. In case of discordant clinical and imaging findings, tissue diagnosis with CNB or VABB should be performed.[2]

Fat necrosis is not a common finding at imaging; however, because of variable and atypical features at clinical examination and/or at imaging, it can be misdiagnosed as a cancer, especially in patients previously treated for a breast cancer. Therefore, familiarity with different manifestations of fat necrosis on mammography, ultrasonography, and MRI is fundamental for avoiding misdiagnosis. Interpretation of imaging findings with various diagnostic modalities should be performed in sight of potentially different stages of histopathologic evolution of fat necrosis. Thus, a multimodality approach based on the patient's risk profile may enhance the accuracy of fat necrosis diagnosis.

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