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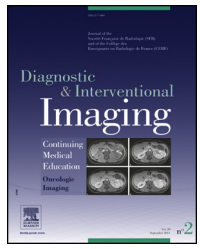

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Inflammatory breast disease: The radiologist's role

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KEYWORDS
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Abstract Mastitis is the inflammation of breast tissue. From a pathophysiological point of view, mastitis reflects a variety of underlying etiologies. It can be due to non-infectious inflammation, infection (generally of bacterial origin) but can also be caused by inflammation resulting from malignant tumor growth. Mastitis always manifests clinically by three cardinal signs of inflammation, which are redness, heat and pain. Breast specialists examining women with mastitis should proceed as follows: first, it is important to distinguish between cancer-related and non-cancer-related breast inflammation, since their clinical presentation can be misleading. Cancer-related mastitis reflecting the presence of aggressive cancer is less commonly observed than other forms of mastitis but its diagnosis, which can sometimes be difficult, needs to be made, or excluded, without delay. Once cancer-related mastitis has been excluded, the causes of inflammation should be elucidated to enable rapid treatment and patient recovery.

Radiological presentation of inflammation

The breast is a superficial organ. The clinical signs of breast inflammation are therefore obvious. They include redness, heat and pain. The patient should be questioned as to how inflammation appeared, and notably whether it occurred suddenly or not. Any cases of inflammation that occurred progressively should be regarded as atypical. As is the case in the rest of the body, breast inflammation may be of infectious or non-infectious origin, but it can also be caused by breast cancer.

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Skin thickening is one of the signs that should be sought. Although clinical examination can often evidence skin thickening, radiological imaging enables detailed analysis of the thickness of the dermis and comparison between the affected and contralateral sides. Clinical examination alone is insufficient to adequately assess the extent of skin thickening or detect limited skin thickening. Mammograms reproducibly highlight cases of dermal thickening. Focal skin lesions are better visualized by digital tomosynthesis which provides images of cross-sections of breast tissue. The thickness of the skin can also be estimated adequately by ultrasound examination using a high frequency transducer (Fig. 1).

MRI also provides precise measurements of skin thickness. Radiological imaging highlights the changes to adipose tissue instigated by inflammation, as well as other signs of inflammation. Such changes are only very rarely detected using mammography or MRI. Ultrasound is very effective for detecting hyperechoic fat lobules that are typical findings [1] to look for inflammatory breast tissue (Fig. 2). The extent of the hyperechoic zones is variable and depends on the degree of inflammation.

Subcutaneous dilatation of lymphatic vessels is another cardinal sign of breast inflammation. Ultrasound performs well for visualizing this sign and reveals anechoic slits located at the interface between the dermis, which is generally thickened, and subcutaneous fat. Doppler ultrasound, which evidences the absence of flow (even low flow) within these structures, helps distinguish them from hyperemic blood vessels that are often associated with lymphatic vessel dilatation (Fig. 3).

Breast hyperemia, defined as increased vascularization of breast tissue, is also associated with inflammation [2]. Hyperemia can be evidenced by Doppler ultrasound which reveals an increased number of arterial and especially venous structures. Hyperemia is most visible in the superficial regions of the breast. Such hypervascularization can also be evidenced by MR angiography by comparing the vascular structures of both breasts (Fig. 4).

The possibility of lactiferous duct abnormalities should be investigated in patients with breast inflammation, because some inflammatory conditions are related to lactiferous duct involvement. Ultrasound images can reveal dilated, ectatic ducts with thickened walls and/or echoic contents. Ultrasound should be performed from the nipple towards peripheral zones following a radial pattern to detect possible abnormalities within each breast segment. Mammography is generally not of much help when examining lactiferous ducts, because the latter are not visible on mammograms. Sometimes however, the lactiferous ducts can be visualized by mammography in very dense or very fatty breasts and lactiferous duct abnormalities can be observed. MRI is an appropriate imaging modality for examining the lactiferous duct system due to its high spatial resolution and use of contrast. Indeed, the inflammatory involvement of lactiferous ducts can be determined by injection of contrast medium and assessing wall thickening (Fig. 5).

Radiologists examining patients with breast inflammation should take particular care to detect possible fluid collections. Initial fluid collections within the breast can be small and difficult to detect as they are only very slightly more hypoechoic than the neighboring breast tissue. They are practically always accompanied by hyperechoic changes to the surrounding fat. If a fluid collection is evidenced, its contents are generally found to be hypoechoic, but remain heterogeneous. Typically, it features a fluid-fluid level. The walls of fluid collections can appear as thickened or irregular and tend to spread to and dissect neighboring fat lobules (Fig. 6). Radiologists should search for possible fistula paths towards the skin or lactiferous ducts.

The axilla of patients with breast inflammation should be examined to determine possible lymph node involvement. Lymphadenopathy can be a reaction to inflammation or secondary to metastasis in patients with inflammatory breast cancer. Lymph nodes with regular cortical thickening, smooth borders and a visible central hilum generally reflect a benign condition. On the contrary, malignancy is characterized by focal or off-center cortical thickening combined with abnormalities of lymph node borders with infiltration of the adipose tissue and disappearance of the central hilum (Fig. 7).

Imaging techniques

As discussed hereafter, breast inflammation can arise from a variety of etiologies, some of which can be difficult to diagnose. Full use of breast imaging techniques is therefore crucial to ensure diagnosis is as precise as possible and subsequently to provide the patient with the most efficient treatment. To do this, it is advisable to make use of the whole range of diagnostic methods, without trying to cut expenses. Technically, the choice of modalities should depend on available human and technical expertise and the clinical setting that should take into account the patient's age.

Mammography

Mammography should be proposed to patients aged over 30 years presenting with breast inflammation. The imaging procedure should be adapted in each case to accommodate the pain experienced by patients with breast inflammation. An acceptable compromise must be found between the need for sufficient image quality and the pain caused to the patient by breast compression. Although mammogram quality can sometimes be suboptimal due to issues related to breast compression, the images obtained can provide crucial information for diagnosing and managing the patient's condition. Bilateral mammography should be performed in order to compare the healthy and affected breast. Indeed, the detection of specific details on the affected side involves comparison with the contralateral side and the unaffected side also needs to be screened for clinically undetected disease. Careful examination of mammograms is required to detect possible nodular zones, architectural distortion or microcalcifications. Even discreet details that do not generally raise suspicion may prove decisive for the diagnosis and management of breast inflammation. It can therefore be helpful to use enlarged images and digital tomosynthesis to visualize such details [3].

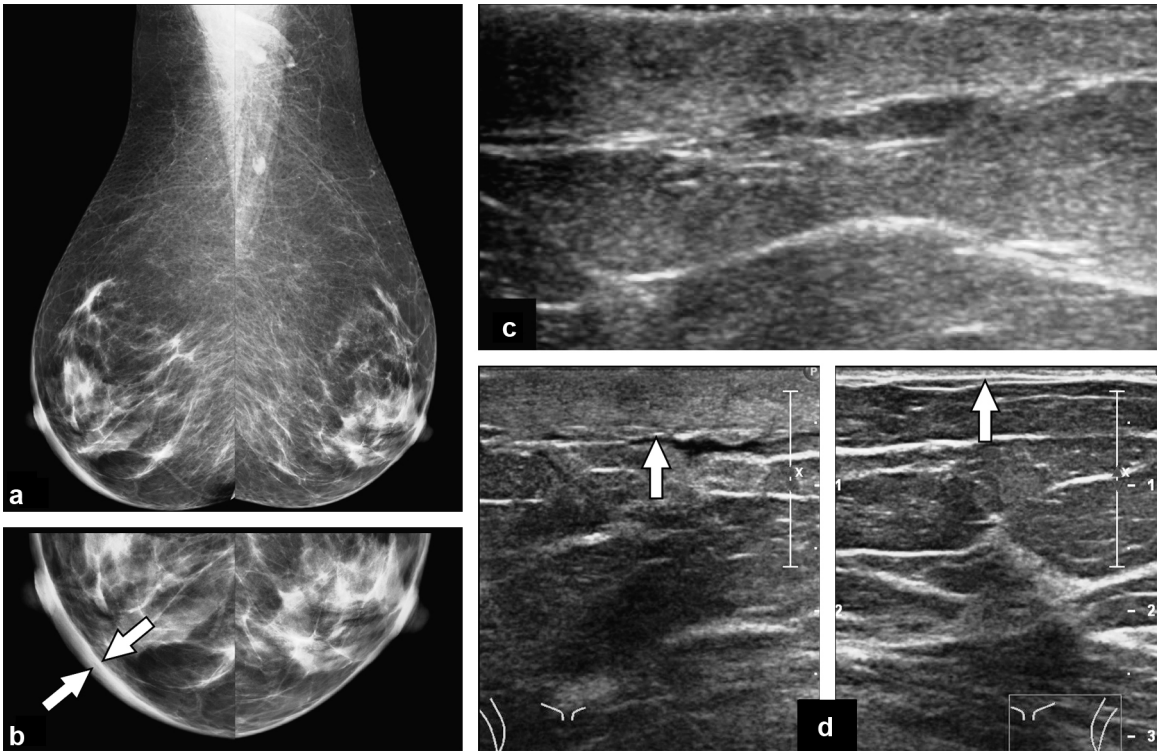

Figure 1. Skin thickening. a: mammogram (MLO view) shows thickening of the skin of the right breast; b: enlarged image of 1a shows asymmetric skin thickness, particularly visible in the lower quadrant (white arrow); c: ultrasound examination shows thickening of the dermal layer; d: ultrasound images of right and left breasts show thickening of the skin and normal skin thickness, respectively (white arrow).

Ultrasound

Ultrasound examination is crucial for assessing patients with breast inflammation. Ultrasound should be performed on a systematic basis, should be bilateral and include examination of axillary lymph nodes. The radiologist should always search for signs of inflammation and attempt to clearly identify the area affected by the inflammatory process. In patients with inflammatory breast cancer, ultrasound helps to locate fluid collections and provides images that suggest the presence of tumor growth. Finally, ultrasound can be used to plan and guide percutaneous sampling procedures which are an essential part of the diagnostic- and treatment-planning process. Ultrasound can also be used to guide tissue biopsies of lymph nodes in patients with suspected lymph node involvement.

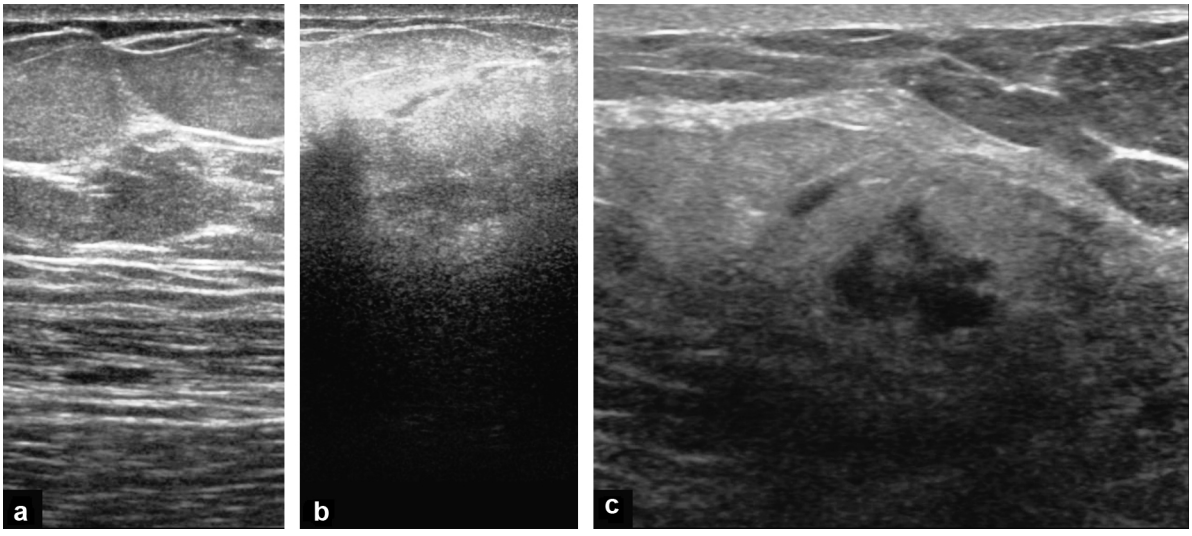

Figure 2. Hyperechoic fat. a: normal right breast; b: left breast with diffuse hyperechoic fat and reduced penetration depth of the ultrasound beam due to attenuation; c: fat hyperechogenicity is focused around a central hypoechoic collection.

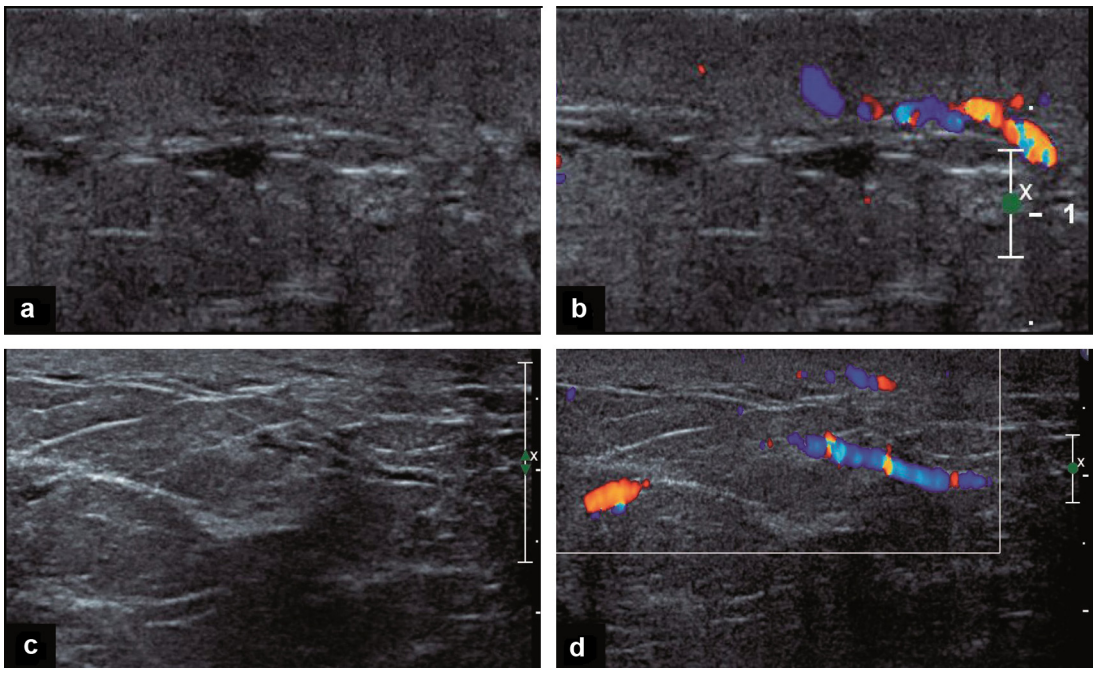

Figure 3. Visibility of subcutaneous lymphatic vessels. a: ultrasound examination reveals thickening of the skin and hypoechoic slits between the dermal and hypodermal layers; b: same image as (a) in Doppler mode. Detection of a Doppler signal within the vascular structures. The slits remain hypoechoic and unvascularized, and reflect lymph vessel ectasia; c: ultrasound examination allows distinguishing between increased blood vessels and distended lymph vessels that respectively show up as vascular slits with or without a Doppler signal; d: Doppler ultrasound can be used to distinguish between blood vessels and distended lymph vessels.

Breast MRI

Breast MRI, which requires the injection of contrast medium, should only performed in specific circumstances. It is often performed once an inflammatory carcinoma has been diagnosed and is aimed at providing more detailed information on tumor development. MRI provides more detail on possible deep involvement and can reveal signs of inflammation of

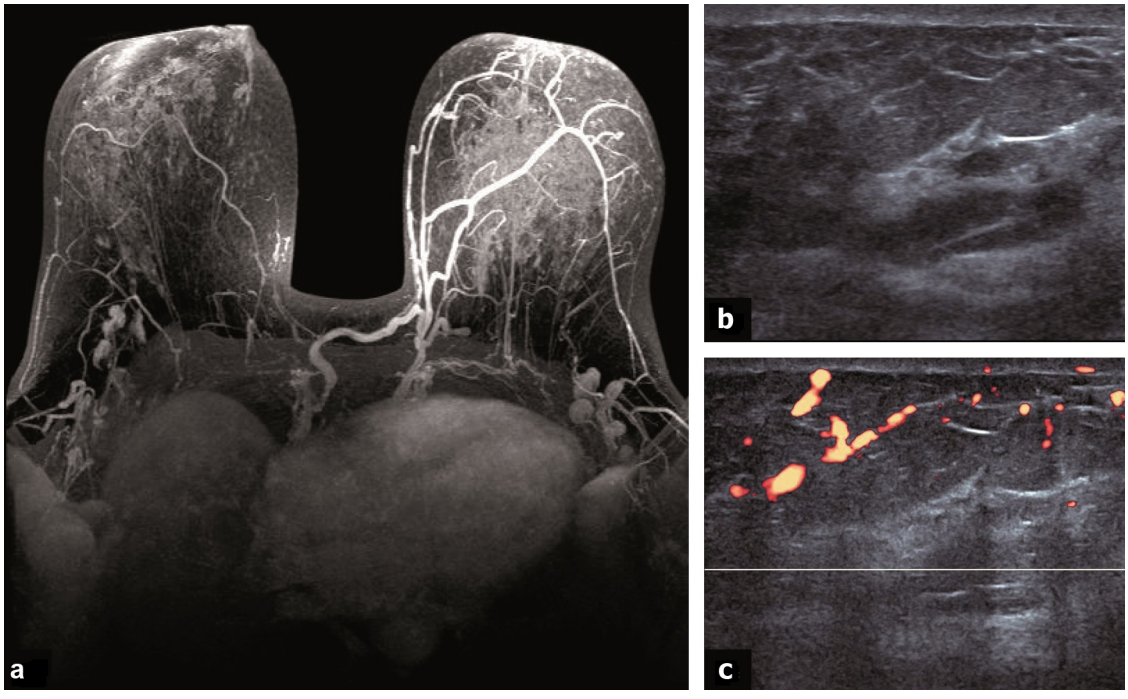

Figure 4. Increased vascularization. MR image of a woman with left breast inflammation shows increased vascularization that is particularly visible on this fat-saturated T1-weighted image with MIP reconstruction following intravenous administration of a gadolinium chelate. Ultrasound examination of mastitis. Same image as (b) using Doppler ultrasound reveals increased vascularization of breast tissue.

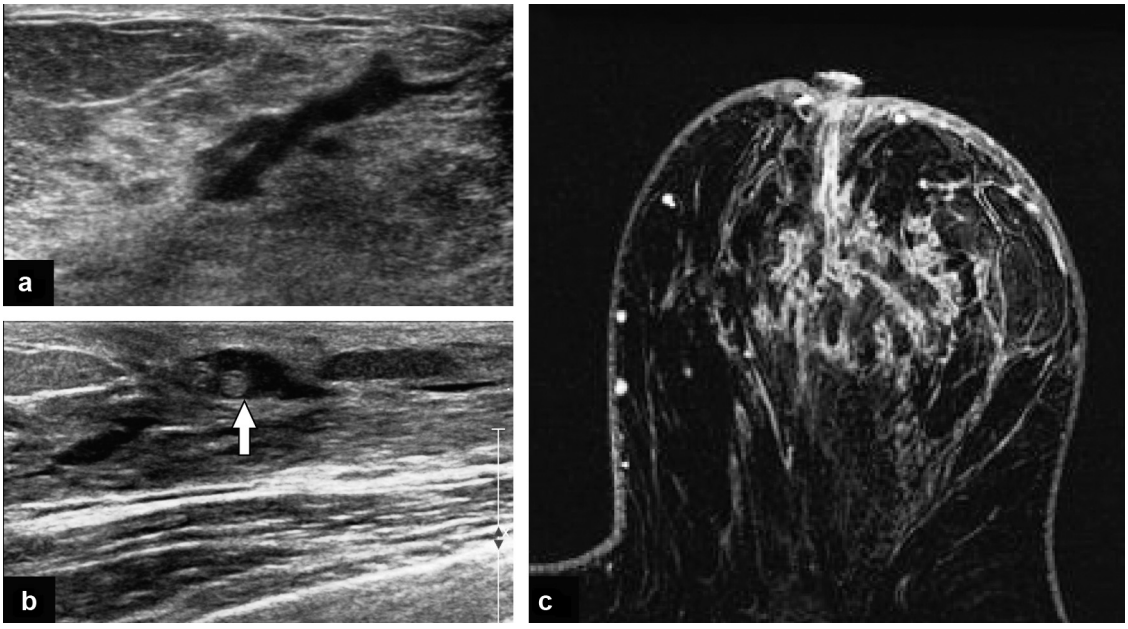

Figure 5. Lactiferous duct changes. Ultrasound examination showing an ectatic lactiferous structure with regular borders in the retroareolar region. Ultrasound examination showing lactiferous duct ectasia with intraductal hyperechoic nodular changes that reflect the presence of thick inflammatory secretions (arrow). Fat-saturated T1-weighted MR images in the axial plane following intravenous administration of a gadolinium chelate shows distended lactiferous ducts with parietal enhancement.

underlying muscles and chest structures. It is used to detect lymphadenopathy of the internal mammary lymph nodes that is difficult to detect via ultrasound. It also performs better for evaluating the involvement of axillary and apical lymph nodes. If malignancy is detected, the contralateral breast should be examined using a high sensitivity modality, such as MRI, to exclude tumor development on the contralateral side. Patients with inflammatory carcinoma generally receive neoadjuvant chemotherapy before surgical management is considered. In these cases, MRI is the best modality for monitoring disease progression and patient response to chemotherapy. MRI can also be performed in patients presenting with ostensibly non tumor-related inflammation but that seems atypical or progresses in an unusual way, as well as in patients for who neither mammography, ultrasound nor percutaneous sampling has led to diagnosis. In such circumstances, MRI can reveal breast tumors that remain undetectable using conventional techniques.

Percutaneous samples should be collected rapidly from patients with breast inflammation. Percutaneous sampling procedures are in principle guided by ultrasound that reveals presence of the abnormality(ies) (generally collections or hypoechoic zones that may reflect developing fluid collections or tumor masses). Due to the broad spectrum of possible diseases that can cause breast inflammation, histological analysis of pathological samples seems advisable. Cytological and bacteriological analysis of the fluid collected during these procedures is also mandatory. When performed in a timely manner (if possible during the first visit), such histocytological and bacteriological samples help to move quickly through the diagnostic process.

If breast cancer is suspected, even if a clear target lesion has not been identified, samples should be obtained from areas of minor change detected using ultrasound. This often enables diagnosis based on histological results because inflammatory cancers show diffuse tissue involvement with lymphangitic carcinomatosis throughout the breast. Samples from even seemingly unaffected zones can therefore often lead to diagnosis. In patients with proven fluid collection(s), immediate puncture aspiration of the collection reduces necrotic abscess volume and promotes efficient anti-inflammatory and anti-infective treatment. In rare cases, mammography data is sufficient to guide stereotactic sample collection, particularly in patients with microcalcification clusters.

MRI-guided biopsies are generally only considered when no clear target can be seen on mammograms or ultrasound images and MRI reveals the presence of a suspicious focal target.

Diagnostic approaches and management of breast inflammation

Inflammatory cancer

In the great majority of cases, breast inflammation is caused by an inflammatory or infectious disease of breast tissue; however sometimes it can be due to inflammatory cancer. Although inflammatory breast cancer is clinically quite rare, radiologists specializing in breast disease must be familiar with its signs and be able to diagnose it without delay [4,5]. Inflammatory cancer is an aggressive form of invasive cancer characterized by diffuse infiltration of breast tissue and the sudden onset of symptoms. Typically, inflammatory breast cancer is diagnosed within 3 months of the onset of clinical symptoms. Patients present with diffuse breast edema

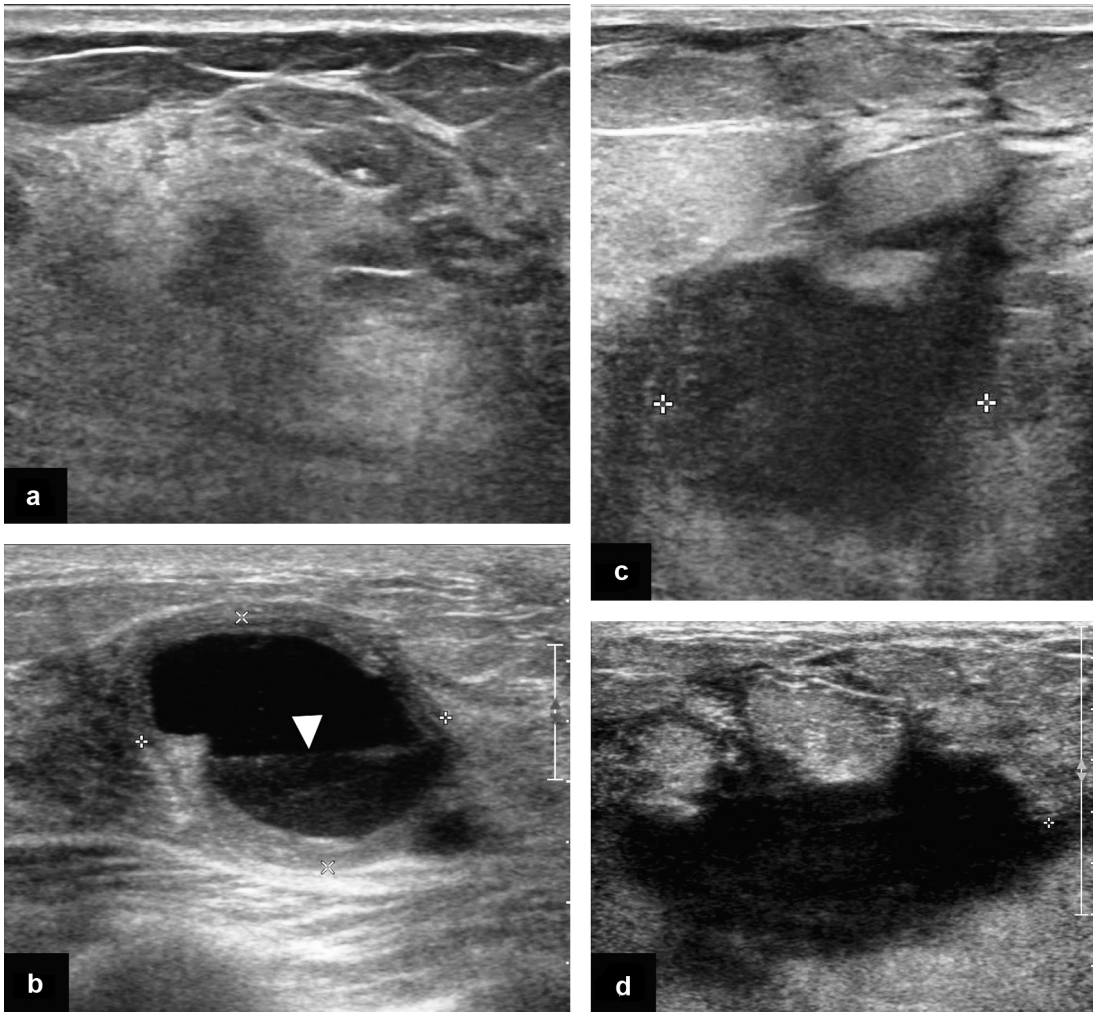

Figure 6. Fluid collection. Ultrasound examination shows a hypoechoic area of approximately 1 cm, surrounded by highly hyperechoic fat. The central hypoechoic zone is a developing fluid collection. Ultrasound examination shows a fluid collection measuring 2.2 cm in diameter, with a horizontal fluid level (arrowhead) as well as wall thickening. Ultrasound examination shows a fluid collection (diameter 2.5 cm) within the breast with poorly defined borders and tending to infiltrate neighboring tissues. Ultrasound examination shows fluid collection > 3 cm within the breast with relatively well-defined borders and extending along fat lobules.

visible by clinical examination with ''orange peel'' skin or erythema. The entire breast is usually swollen and no real palpable masses are detected. It is estimated that 3 to 10% of invasive cancers show the clinical signs of inflammatory cancer.

Minimum criteria for diagnosing inflammatory carcinoma include: skin changes (erythema, edema, orange peel, redness and heat); clinical history of less than 6 months; erythema covering at least one third of the breast; histopathological evidence of invasive carcinoma [6].

The typical clinical presentation of skin inflammation is a consequence of tumor cell emboli within the lymphatic vessels that are mainly subcutaneous in the breast. Lymphangitic carcinomatosis of the skin therefore characterizes inflammatory cancers, but it is neither indispensable nor sufficient to diagnose inflammatory carcinoma.

Inflammatory cancer must be distinguished from late-stage localized cancer with skin involvement. Inflammatory cancer is generally characterized by the recent history of symptoms (< 3 months) in relatively young women (average age: 58 years), diffuse cutaneous signs, the presence of a relatively fast-developing growth as well as a relatively high rate of metastasis at diagnosis (estimated at 20—40%). These cancers are generally of poor prognosis and the survival rate at 2 years is 84%.

Late-stage localized cancers are usually characterized by a long clinical history and a mass that has been present for more than 6 months. Skin involvement is often localized to a specific part of breast. The inflammatory form of such cancers generally occurs in older women (average age: 66 years). Tumor growth is slow and only 10% of women have metastases at diagnosis. The prognosis of these cancers is more favorable with a survival rate at 2 years of 91%.

Imaging techniques often enable radiologists to evidence and diagnose breast cancer. Mammographic findings often reveal significant asymmetry with skin thickening and diffuse edema of the breast. Although sometimes easy to see, breast cancer is often reflected by only subtle mammographic details so mammograms should be reviewed meticulously. Image enlargement can help to evidence

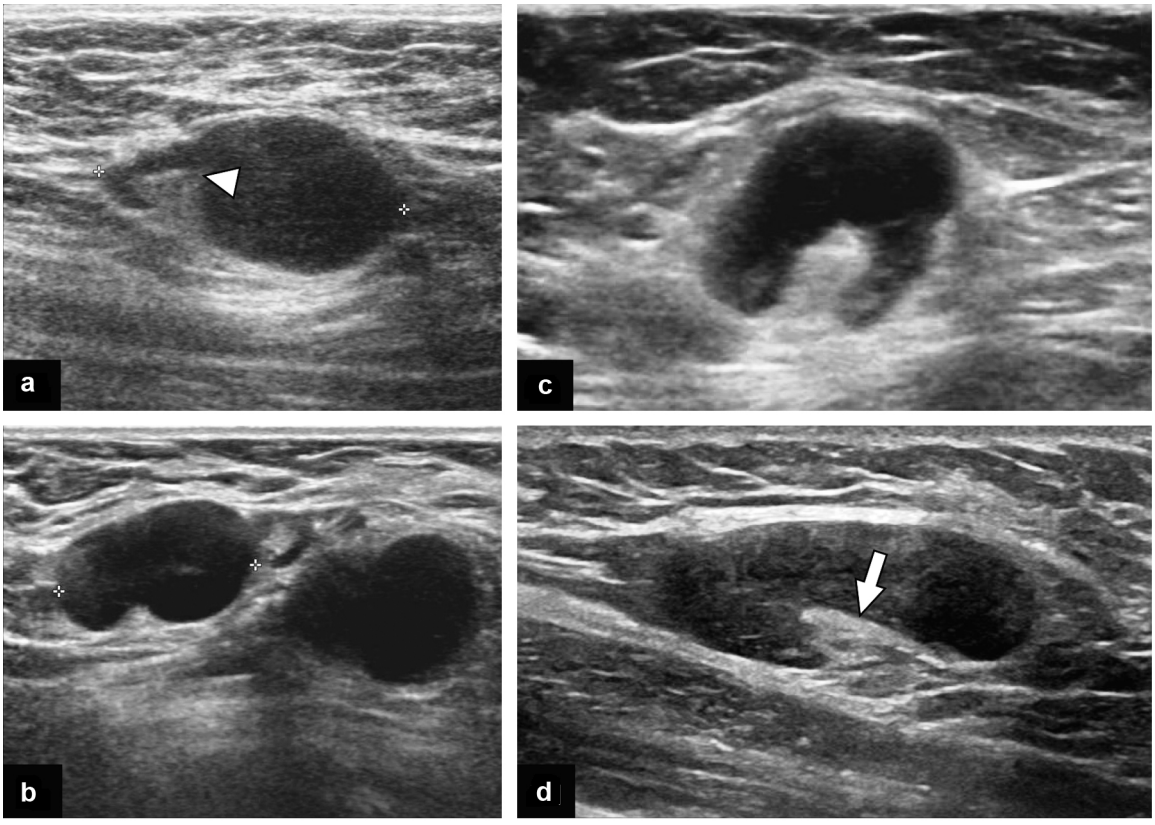

Figure 7. Lymphadenopathies. Lymph node enlargement in a patient with malignant disease (1.6 cm). Off-center hilum (arrowhead) and significant asymmetric, cortical thickening. Lymph node enlargement in a patient with malignant disease (1.8 cm) in association with complete disappearance of the hilum. Ultrasound examination of lymphadenopathy in a patient with inflammatory disease. The hilum is still visible and associated with regular cortical thickening. Adenomegaly. Longitudinal diameter: 2 cm. In patients with inflammatory disease, the lymph node hilum remains visible (arrow) and cortical thickening is regular.

microcalcifications, the presence of which is always highly suspicious in these circumstances. Localized compression or digital tomosynthesis images can reveal opacities (generally spiculated) or asymmetric density that are also highly suspicious in patients with breast inflammation (Fig. 8).

Ultrasound examination shows the previously described inflammatory signs, but should be used to detect possible breast tumors (masses) or attenuated or hypoechoic zones from which percutaneous samples can be collected for histological diagnostic techniques. Investigation of the lymph nodes of the axillary region can provide information pointing towards breast cancer; possible lymph node involvement should spur radiologists to collect tissue or cell samples for further analysis.

Breast MRI is generally performed in patients with inflammatory cancer. It provides detailed information on the spread of cancer cells within the breast tissue and lymph node involvement (especially apical and internal mammary groups). MRI is also used to detect possible contralateral lesions that might not have been detected during the initial mammographic and ultrasound examinations in patients with patent homolateral breast cancer. MRI guidance helps radiologists collect percutaneous biopsies by subsequently targeting a zone delimited by MRI using ultrasound guidance [7]. In patients for whom such ultrasound-guided biopsy techniques do not provide adequate tissue samples, real-time MRI-guided biopsies should be considered. The first-line treatment of inflammatory cancers is generally neoadjuvant chemotherapy. In such cases, pretreatment MRI allows radiologists to subsequently and reliably assess the efficacy of therapy. From time to time, radiologists strongly suspect inflammatory carcinoma without being able to identify a clear target for percutaneous sampling by mammography, ultrasound or MRI. Such cases generally reflect very diffuse breast cancer (Fig. 9) and percutaneous samples should be taken, without proper radiological guidance, from the areas that clinically seem to be most affected. By proceeding this way, reliable diagnostic results can be obtained for patients with inflammatory breast cancer. If despite all these diagnostic procedures, inflammatory cancer is still clinically suspected but cannot be evidenced histologically based on the different percutaneous samples obtained, a multidisciplinary case assessment meeting should be scheduled to determine the appropriate diagnostic approach (which is often based on excisional biopsy).

Puerperal mastitis

The diagnosis of puerperal mastitis is frequently quite easy due to the clinical circumstances in which it arises [8,9]. This form of mastitis occurs in breast-feeding women. During its initial stages, puerperal mastitis results in milk stasis which is often due to a poor anatomical drainage of part of the breast. At this stage, leukocyte and bacterial counts in

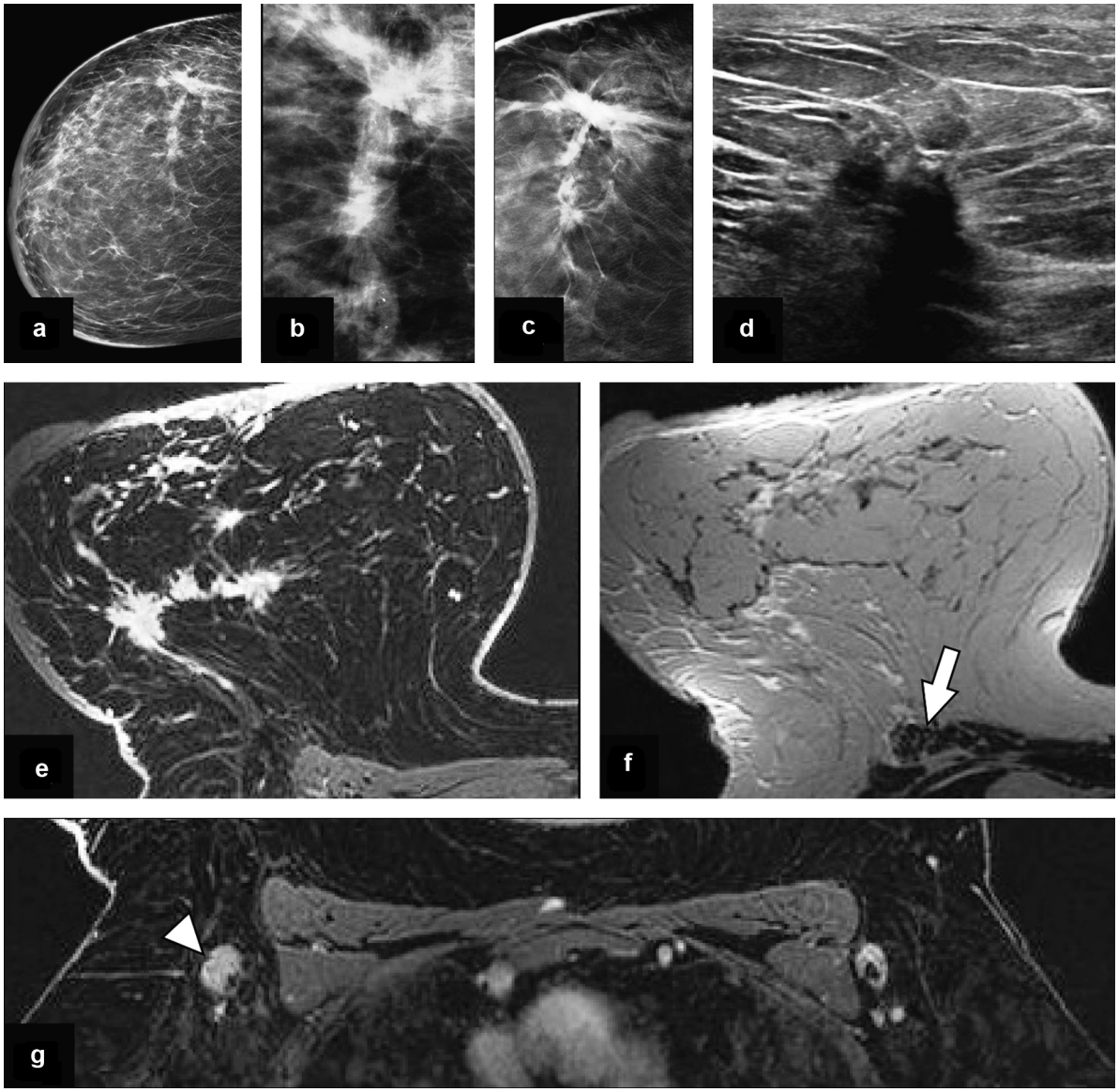

Figure 8. Inflammatory carcinoma of the right breast. Mammogram of the right breast shows substantial thickening of the skin of the breast and diffuse edema of the right breast tissue. Magnified craniocaudal (CC) view mammogram shows a few calcifications categorized as BI-RADS 4. Tomosynthesis images shows a mass with complex shape and irregular borders. Breast ultrasound shows an irregularly shaped nodular structure with poorly defined borders which is a tumor. Fat-saturated T1-weighted MR images in the axial plane following intravenous administration of a gadolinium chelate show spiculated tumor masses with multiple areas of enhancements as well as thickening of the skin. Fat-saturated T2-weighted MR images show hyperintensity of the cutaneous tumor masses, as well as an extended pectoralis major muscle with high signal intensity zones (arrow). Fat-saturated T1-weighted MR images in the axial plane of the axilla region following intravenous administration of a gadolinium chelate show asymmetry of both lymph node size and appearance. Metastatic involvement of some of the lymph nodes of the right axilla region is probable (arrowhead).

the milk are low. Most cases of milk stasis do not require therapeutic management and resolve spontaneously. However, if milk stasis persists, non-infectious inflammation appears. It is associated with an increased milk leukocyte count, although the bacterial count does not change significantly. Fifty percent of cases of non-infectious inflammation eventually result in infectious mastitis, characterized an increased milk leukocyte count, as well as a significant increase in the number of bacteria in the milk. In 90% of cases, patients with infectious mastitis recover following anti-inflammatory and antibacterial treatment. In 10% of cases, the patients develop a breast abscess which tends to complicate treatment.

In breast-feeding women with breast inflammation, ultrasound should be performed to search for fluid collection. If ultrasound evidences fluid collection, percutaneous sampling and drainage of the fluid collection should be considered and performed in a timely manner (Fig. 10). This will allow more accurate diagnosis and above all targeted antibiotic treatment against the bacteria detected

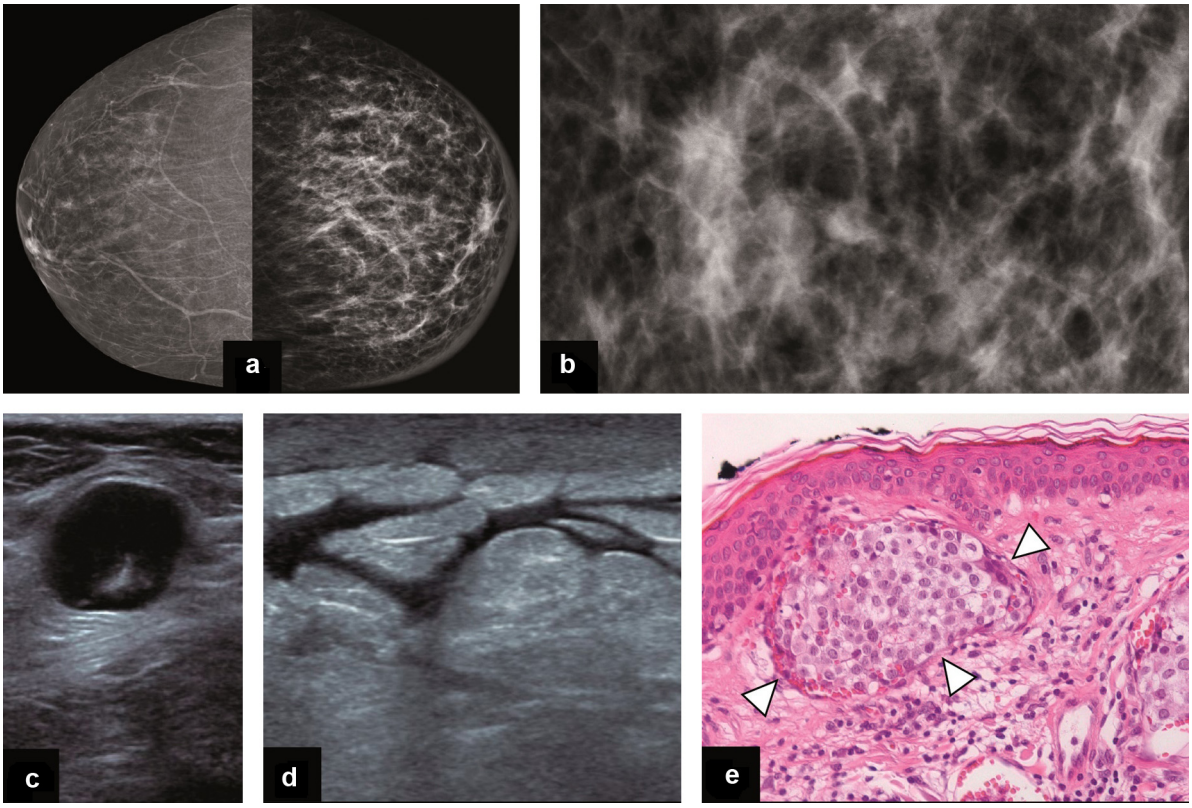

Figure 9. Inflammatory cancer. Comparison of right (normal) and left (pathological) mammograms in a patient with inflammatory carcinoma. CC view. Left breast: diffuse cutaneous edema and breast edema. Discreet architectural distortion, but no unequivocal mass observed on mammography. Ultrasound examination of the left axilla region shows enlarged lymph node, the hilum of which has practically completely disappeared. Ultrasound examination of the left breast shows a thickening of the skin and significant dilation of lymphatic vessels within the subcutaneous fat. Skin histology showing tumor cells within distended lymphatic vessels in the dermis, a hallmark of lymphangitic carcinomatosis (arrowhead). The lymphatic nature of the vessel was established by immunohistochemistry.

in the collection. In patients with a recurrent fluid collection, drainage may be repeated but if the collection persists or recurs again, and especially if sized > 3 cm, the placement of a percutaneous drainage catheter should be considered and discussed with the treating physician [10—13] (Fig. 11). Only in the event of recurrent fluid collections, and inconclusive percutaneous drainage and placement of a percutaneous drainage catheter, the possibility of referring the patient to a surgeon for surgical drainage should be considered. Although previously used in cases of puerperal abscess, surgical drainage is now rarely performed due to the effectiveness of percutaneous procedures and antibiotics. The possibility of carcinoma should not be neglected in breast-feeding women with breast inflammation. In these patients, cancer can sometimes develop rapidly with signs of breast inflammation consistent with mastitis.

If clinical examination seems suspicious or ultrasound images appear unusual, then mammography can sometimes reveal suspicious abnormalities that allow more accurate diagnosis. Percutaneous sampling in breast-feeding women with atypical imaging findings can prevent misdiagnosing cancer which, although rare, is difficult to diagnose (Fig. 12).

Inflammation of the nipple-areola complex

The nipple and the nipple-areolar complex (NAC) form a specific, complicated anatomical entity within the breast. Anatomically, they form a hub into which flow the lactiferous ducts that drain the breast tissue. In addition, numerous apocrine glands such as sebaceous and sweat glands, as well as Montgomery glands are located in the NAC [14]. Montgomery glands are small glandular units that are located just beneath the surface of the skin on the edge of the areola. Montgomery glands communicate directly with the external environment and can therefore become contaminated by bacteria. For these reasons, breast inflammation of infectious origin often begins and spreads from the NAC.

Radiological investigation of the NAC and neighboring tissue is challenging due to its small anatomical size and its superficial position. The usefulness of mammography for investigating the NAC is quite poor and ultrasound examination is difficult because of the acoustic shadow cast by the anatomy of the nipple due to diffraction of ultrasound waves. Clinical examination is therefore of utmost importance for this region of the breast. Most nipple conditions are caused by inflammation or infection of Montgomery glands. They are associated with lesions located within the

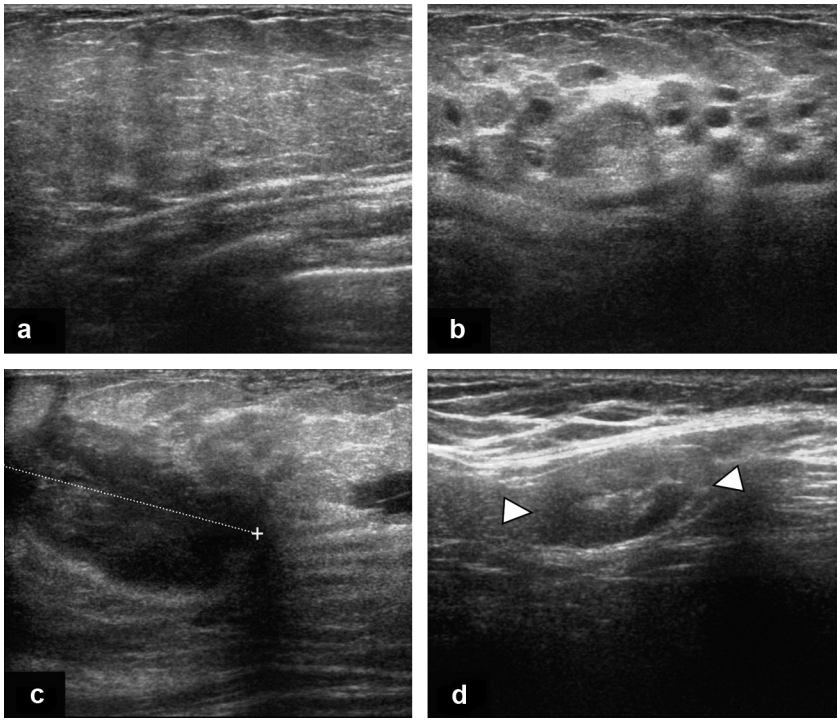

Figure 10. Puerperal mastitis of the left breast. Ultrasound examination of the right breast reveals hyperechoic breast tissue that typically characterizes hypertrophic glandular tissue in nursing women. Left breast: substantial duct ectasia near to the zone clinically affected by mastitis. Echoic, poorly delimited fluid collection infiltrating the breast tissue. Ultrasound examination of the left axilla region shows an enlarged lymph node (arrow).

dermis (dermoid or epidermoid cysts) and inflammation of neighboring tissue, or direct suppuration from sebaceous or sweat glands. Radiological examination reveals an intradermal lesion with inflammatory signs that can spread into the subcutaneous layer and the superficial portion of the breast (Fig. 13). In such situations, diagnostic and therapeutic interventional procedures are of little help. Percutaneous sampling is difficult because of the very superficial location of the lesions and, by their very nature (dense structures), they cannot be drained adequately using percutaneous procedures. NAC lesions should therefore, in the first instance, be treated by drug therapy. Should resistance to drug therapy or recurrence be observed, surgical excision should be considered.

Radiologists should be familiar with a specific clinical condition called Zuska's disease [15] and also known as lactiferous fistula or subareolar abscess, and be able to diagnose it in patients with NAC inflammation. It is a largely unknown disease characterized by repeated and recurrent episodes with a specific clinical presentation. Patients present with inflammatory abscesses and a fistula that generally opens on the edge of the areola or in the breast tissue close to the NAC. The pathophysiological mechanism underlying this disease is based on changes of the epithelium lining the lactiferous ducts where they drain into the nipple. The epithelium, which usually consists of a double layer of cuboidal cells, becomes squamous and thickens causing lactiferous duct obstruction. Duct obstruction leads to secretory stasis of the distal part of the lactiferous duct and appearance of an abscess in the retroareolar region. The continuing inflammatory process results in the formation of a fistula in the periareolar region. Because it is relatively unknown, Zuska's disease (duct obstruction, abscess and fistula) is often managed by surgical ablation of the fistula and the abscess. In these cases, the lactiferous duct causing the disease remains in place, and leads inevitably to recurrent local outbreaks of the condition. Only appropriate surgical management removing the fistula path, the abscess and the obstructed lactiferous duct allows complete recovery from this disease (Figs. 14 and 15).

Galactophoritis and peripheral breast abscess

Even if initially located in the nipple region, lactiferous duct infection can spread in a retrograde manner to the entire lactiferous system and cause widespread lactiferous and breast inflammation. In such cases, the breast shows significant diffuse inflammation and differential diagnosis between inflammation of infectious origin and inflammatory carcinoma can be difficult. Radiological investigation of these patients shows abnormalities of both the central and peripheral lactiferous system. Ultrasound examination reveals significant duct ectasia and duct contents are sometimes visualized as a dense fluid but are often solid (Fig. 16). Mammography is usually not very helpful and mostly shows signs of edema without substantial fluid collection. MRI, however evidences widespread lactiferous involvement with diffuse signs of inflammation and no suspicious tumor masses suggesting the diagnosis of galactophoritis.

Peripheral breast abscesses generally occur in women with preexisting cystic lesions (Fig. 17). Such patients have a long history of cystic breast disease with a painful palpable

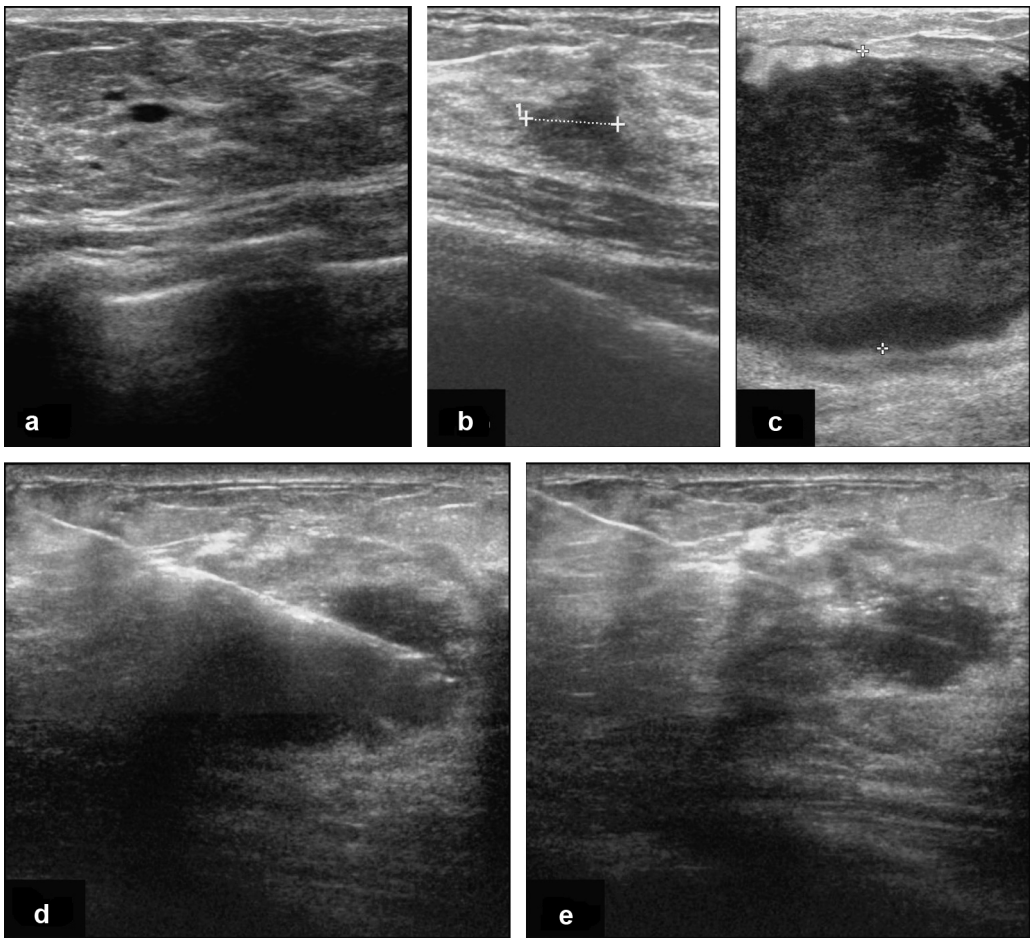

Figure 11. Fluid collection in patients with puerperal mastitis and percutaneous drainage. Slight duct ectasia without fluid collection in a patient with puerperal mastitis. One-centimeter fluid collection in a patient with puerperal mastitis. Substantial fluid collection (> 5 cm), a patient with puerperal mastitis. Ultrasound-guided drainage of the collection shown in (c); needle located inside the fluid collection. Subtotal drainage of the collection shown in (c) after withdrawal of 8 mL of pus.

nodule and signs of localized inflammation. The diagnosis of peripheral abscesses using ultrasound can sometimes be challenging due to the difficulty of visualizing an abscess in the middle of numerous other cystic lesions. A lesion is suspected to be inflammatory based on subtle signs of the cystic wall, notably thickening, wall fragmentation or abnormal contents (Fig. 18). Percutaneous puncture can lead to diagnosis while allowing collections to be drained and therefore faster recovery.

Granulomatous mastitis

Granulomatous mastitis is an inflammatory condition of non-infectious origin that specifically affects breast tissue. From a histopathological point of view, it is caused by a granulomatous inflammatory response containing giant cells [16—18]. Its etiology is unknown. Granulomatous mastitis generally occurs in young women, often after a breast-feeding period, and within a period of 5 years following childbirth. Clinically it is characterized either by a localized palpable mass with lymph node enlargement, or by a more diffuse condition (Figs. 19—21). In the majority of cases, it is not associated with the clinical signs of inflammation, but sometimes such signs can predominate. When the inflammatory component is significant, aseptic abscesses are frequently observed with formation of a fistula between the abscess and the skin. The presentation of granulomatous mastitis is very variable and all the different signs of inflammation can be observed including fluid collections, cutaneous symptoms and lymph node enlargement. The presence of multiple lesions and lymph node enlargement mimics multifocal breast cancer with lymph node involvement. The diagnosis can be made by histological analysis of percutaneous samples; it is indeed rarely made simply on the basis of clinical signs and radiological findings. In the initial stages of the disease, before histological analysis is performed and due to the absence of positive results following bacteriological testing, patients with granulomatous mastitis are often first treated to no avail with anti-inflammatory drugs and the standard antibiotics used for infectious mastitis. Some patients are wrongly referred to cancer centers for probable inflammatory cancer. Such erroneous diagnoses can be corrected by obtaining percutaneous tissue samples and histological results showing a granulomatous response

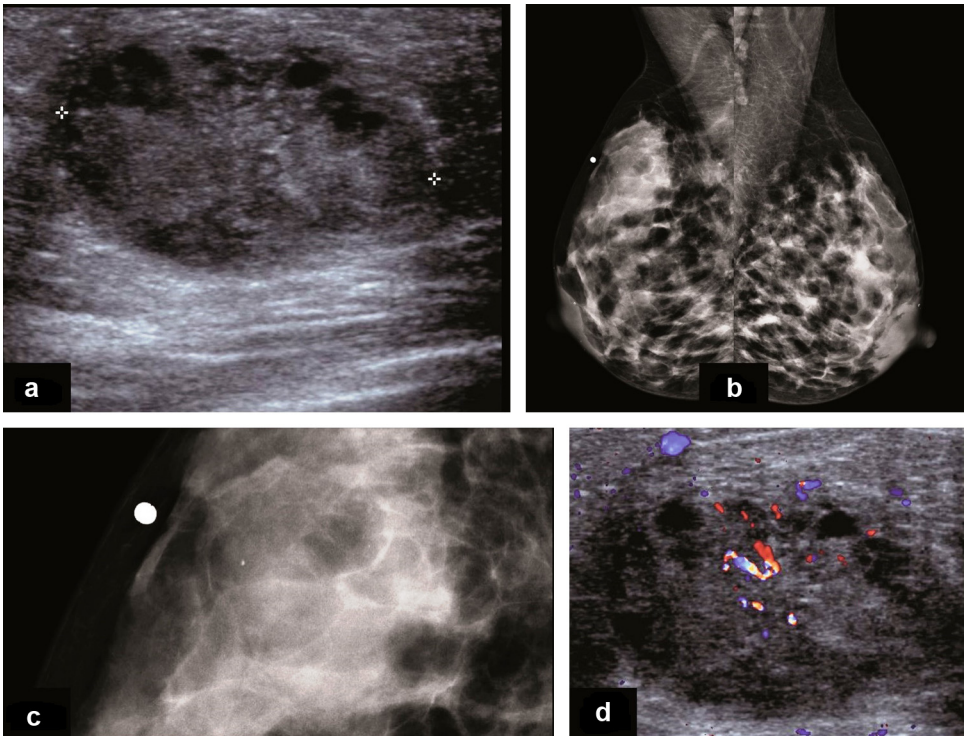

Figure 12. Invasive carcinoma of the right breast in a nursing patient. Ultrasound examination shows a 3-cm, hypoechoic structure with heterogeneous content and poorly defined borders. MLO mammograms of the right and left breast show an asymmetric tissue mass consistent with the palpable lump found on the right side but not on the left. Enlargement of mammogram (b) shows a few rare calcifications within the mass. Doppler ultrasound shows that the lesion is vascularized and that it is a solid mass and not a collection of fluid.

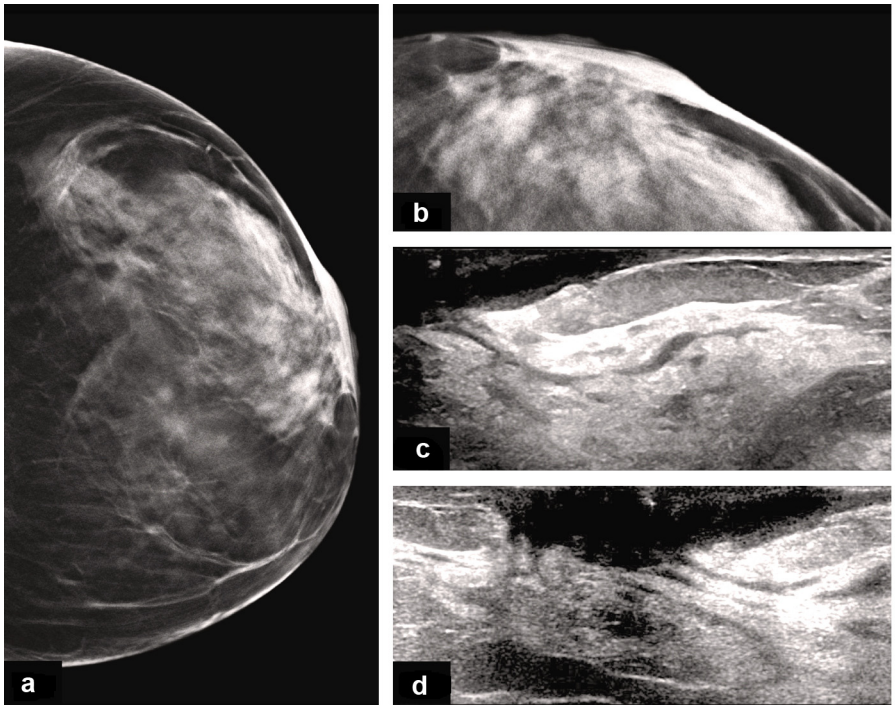

Figure 13. Left periareolar inflammatory lesion due to an infected dermoid cyst. Left tomosynthesis CC view shows thickening of the skin in the periareolar region. Enlargement of tomosynthesis image (a) shows a thickening of the left nipple-areola complex. Ultrasound examination of the left nipple-areola complex shows thickening of the dermis (arrowhead). Intradermal fluid collection (width: 1 cm) in contact with underlying lactiferous ducts.

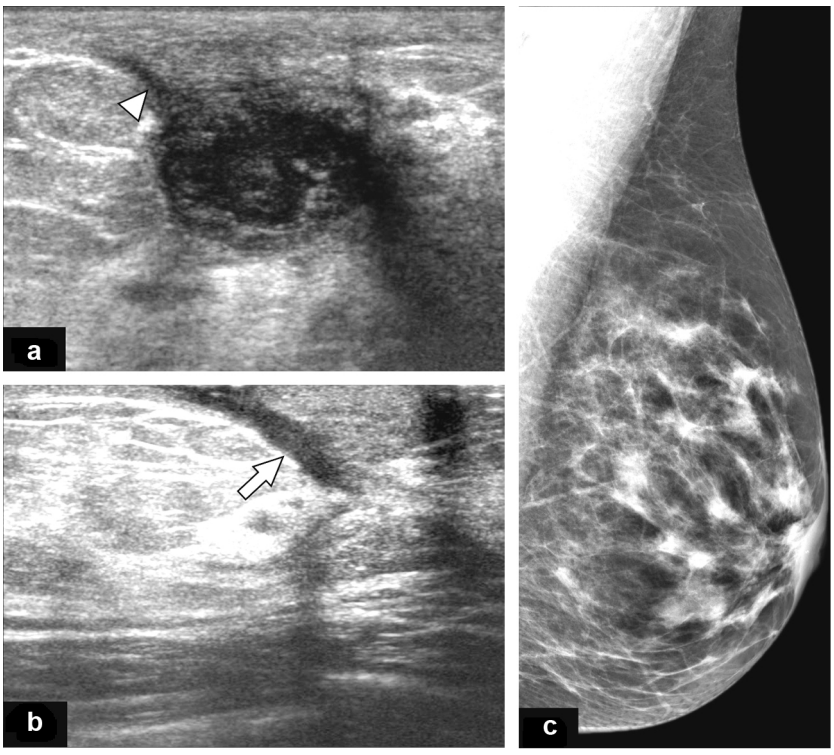

Figure 14. Non-puerperal subareolar mastitis (Zuska's disease) of the left breast. Ultrasound examination of the periareolar region of left breast performed in 2008 shows a hypoechoic collection with a duct-like structure extending towards the nipple (arrowhead). Left periareolar breast ultrasound performed in 2012. Clinical examination reveals a periareolar fistula. Ultrasound examination shows a dilated lactiferous duct draining into the area of the cutaneous fistula (arrow). Mammogram performed in 2012 shows areolar thickening without a detectable breast mass.

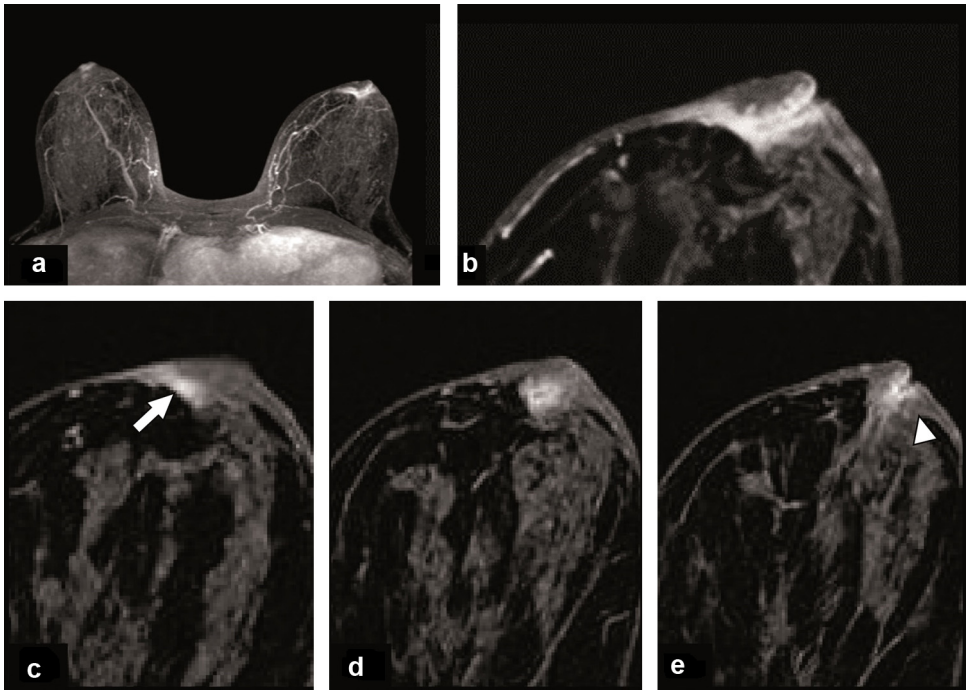

Figure 15. Non-puerperal subareolar mastitis (Zuska's disease) of the left breast (same patient as Fig. 14). a: breast MRI shows enhancement of the lactiferous ducts of the left retroareolar region (arrow) after intravenous administration of a gadolinium chelate; b: reconstruction of thick T1-weighted fat-saturated MR images after intravenous administration of a gadolinium chelate shows an enhanced lactiferous duct that extends towards a skin fistula; c, d and e: three enlarged T1-weighted fat-saturated images after intravenous administration of a gadolinium chelate show the path of the fistula in the periareolar region (arrow) and the opening of the thickened and widened lactiferous duct on the nipple (arrowhead).

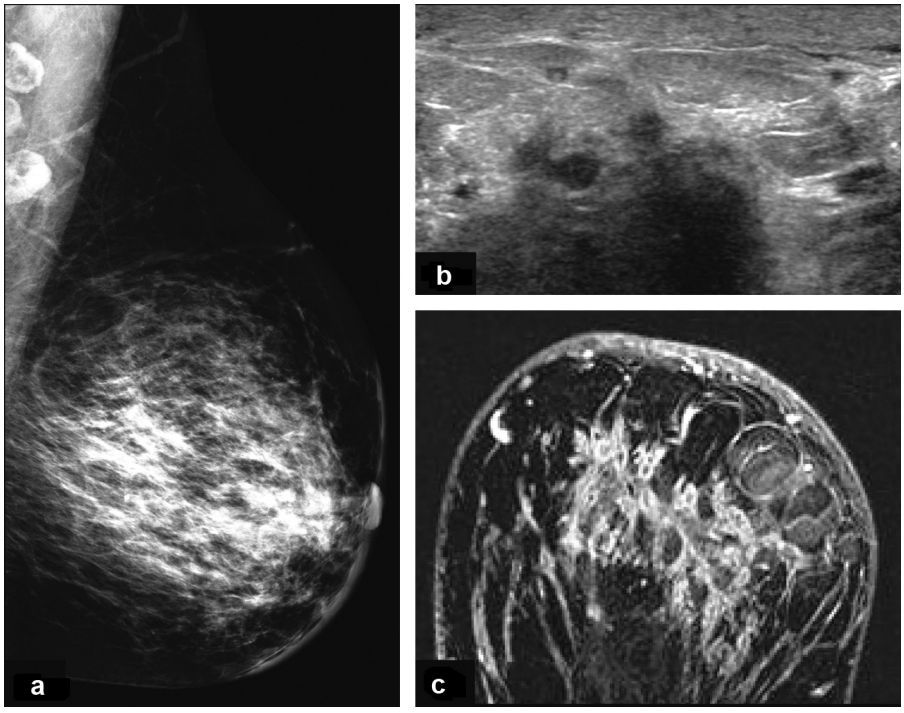

Figure 16. Extensive mastitis of the lactiferous ducts of the left breast. Mammogram, left breast, MLO view, shows breast and cutaneous edema as well as increased tissue density for the whole breast. Breast ultrasound shows widened lactiferous ducts, seen here on transverse images of the central portion of the breast. Fat-saturated T1-weighted MR images in the transverse plane after intravenous administration of a gadolinium chelate show widened lactiferous ducts with enhanced walls, skin thickening and changes to subcutaneous fat.

containing typical giant cells. In particular circumstances, specific infectious diseases (for example tuberculosis) that can lead to formation of granuloma need to be excluded.

Once histological evidence of granulomatous mastitis has been obtained, patients should receive systemic oral steroids which lead to full recovery from this disease. Surgery is rarely called for due to the efficacy of systemic steroid treatment and should only be used in patients with recurrent episodes or who do not respond to steroid treatment.

Rare forms of mastitis

Rare forms of mastitis caused by exposure to specific organisms should be considered in special conditions [19]. In patients with penetrating wounds by thorns associated with traumatic exposure of the wound, it is advised to search for micro-organisms of the Nocardia family, nontuberculous mycobacteria and fungal infection. Patients having traveled to tropical countries should be screened for *Burkholderia pseudomallei*, chromoblastomycosis and *Chromobacterium*. *Mycobacterium marinum* should be screened for in cases of trauma in contaminated water (sea, lake, aquarium or swimming pool). In the same way, patients having wounded themselves in a spa swimming pool or bath should be screened for *Pseudomonas aeruginosa*.

If patients have been in contact with animals such as pigs, sea fish and poultry, they should be tested for *Erysipelothrix rhusiopathiae* which causes erysipeloid-like lesions. Patients having been bitten, especially by dogs or cats, should be screened for bacteria such as *Pasteurella multocida* and *Capnocytophaga*. Human bite wounds can lead to inflammation due to *Eikenella corrodens*. Patients treated with immunosuppressant drugs, such as HIV-positive and transplant patients, should be tested for Gram-negative bacteria such as Nocardia and *Crytococcus neoformans*.

Iatrogenic infections

Post-invasive procedure infections following breast surgery or interventional radiology procedures account for a substantial proportion of breast infections [11]. In these cases, patient questioning generally provides clear information and diagnosis is usually not a problem.

Practical measures, diagnostic approach and core therapy for breast inflammation

Radiologists examining women consulting for breast inflammation should first question the patient to obtain any information that might help diagnose the condition [19]. The circumstances of the onset of inflammation, for example during breast-feeding, after breast surgery or biopsy, will obviously help to orientate the diagnostic approach. It is important to obtain information about the duration of the patient's breast inflammation. Recent and sudden onset of inflammation is generally not caused by inflammatory carcinoma. However in cases with symptoms that appeared subtly and progressed quite slowly, the diagnosis of breast cancer must be suspected and excluded with certainty.

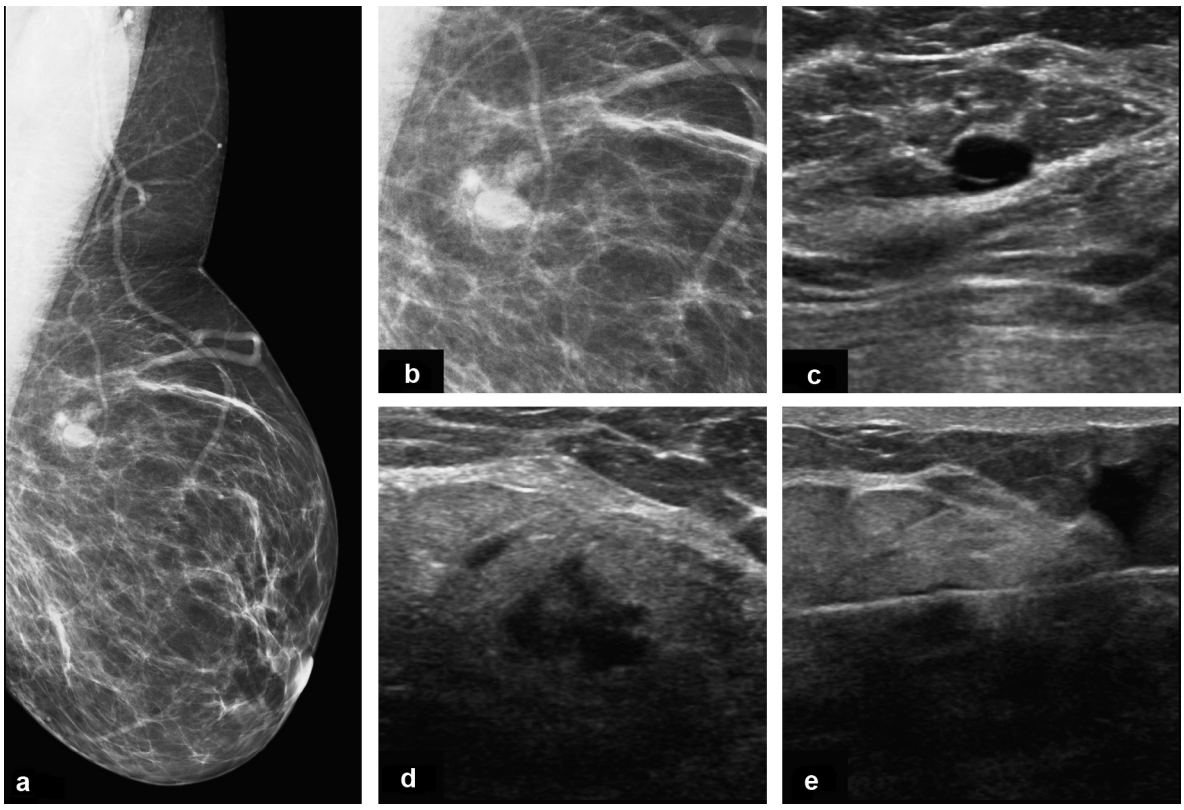

Figure 17. Infection of a breast cyst. a: mammogram, MLO view, shows an opaque area with well-defined borders in the upper quadrant (arrow); b: enlargement of image (a) shows an opacity with well-defined borders measuring approximately 1 cm; c: ultrasound of the upper part of the left breast shows a cystic lesion consistent with the opacity on the mammogram; d: ultrasound of the upper part of the left breast of the same patient as in images (a, b, c), performed 4 months after the onset of left mastitis. Ultrasound images show that cystic lesions have disappeared, but a poorly defined hypoechoic area has appeared and is associated with hyperechogenicity of breast fat; e: percutaneous puncture performed to obtain histological and bacteriological specimens evidenced breast abscess.

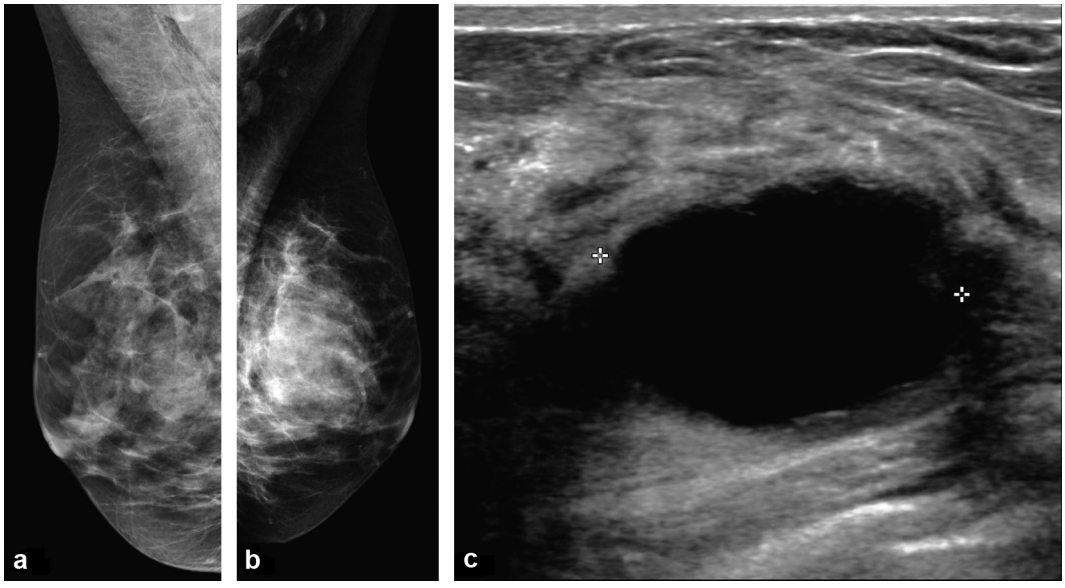

Figure 18. Infected cyst. Normal right mammogram. Left mammogram reveals signs of breast inflammation with a centrally-located mass. Three-centimeter hypoechoic nodule with thick walls consistent with the inflamed region. Puncture evidenced a superinfected cyst.

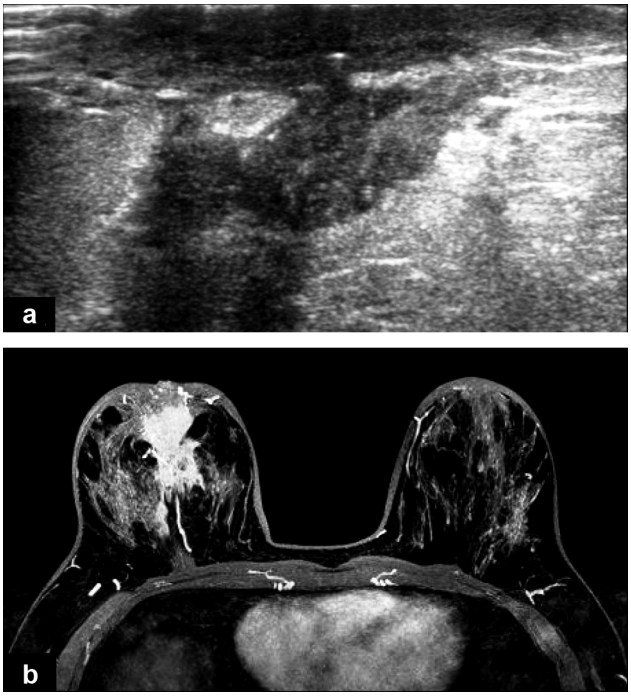

Figure 19. Localized granulomatous mastitis. Fifty-two-year-old patient treated for 4 months for inflammatory episodes, patient status after 3 inefficacious antibiotic therapies. Breast ultrasound shows marked skin thickening and hypoechoic fluid collection with poorly defined borders in the subcutaneous breast tissue. Fat-saturated T1-weighted MR image after intravenous administration of a gadolinium chelate shows extensive tissue enhancement in the right breast.

Next, the patient should be examined as thoroughly as possible using the appropriate imaging techniques that depend on the patient and the circumstances. Mammography should be proposed to all women aged over 30 years with breast inflammation and should be combined with ultrasound examination of both breasts and lymph node stations.

Taken together with the patient's history and clinical examination, imaging findings generally spur the clinician's suspicion in cases of inflammatory carcinoma. When inflammatory carcinoma is suspected, tissue samples should rapidly be taken from suspicious zones. Once the diagnosis is confirmed, breast MRI is indicated to determine the extent of cancer spread and possible lymph node and/or contralateral involvement.

If initial radiological assessment does not reveal clear signs of carcinoma, radiologists should search for possible fluid collections. If detected by initial ultrasound examination, samples of breast fluid collections should be taken for bacteriological testing and, if possible, tissue samples should also be collected. In patients with significant fluid build-up, collections should be drained during this interventional procedure. Drug treatment as outlined below may thus be initiated rapidly. Such treatment may be prescribed by the radiologist, with the attending physician's consent. Both the treatment and diagnostic approach should be reviewed and possibly adjusted when the bacteriological/histological results become available. The patient is instructed to consult her doctor again in the event of rapid clinical deterioration.

She should be seen again about 1 week after the start of treatment to determine whether symptoms have improved.

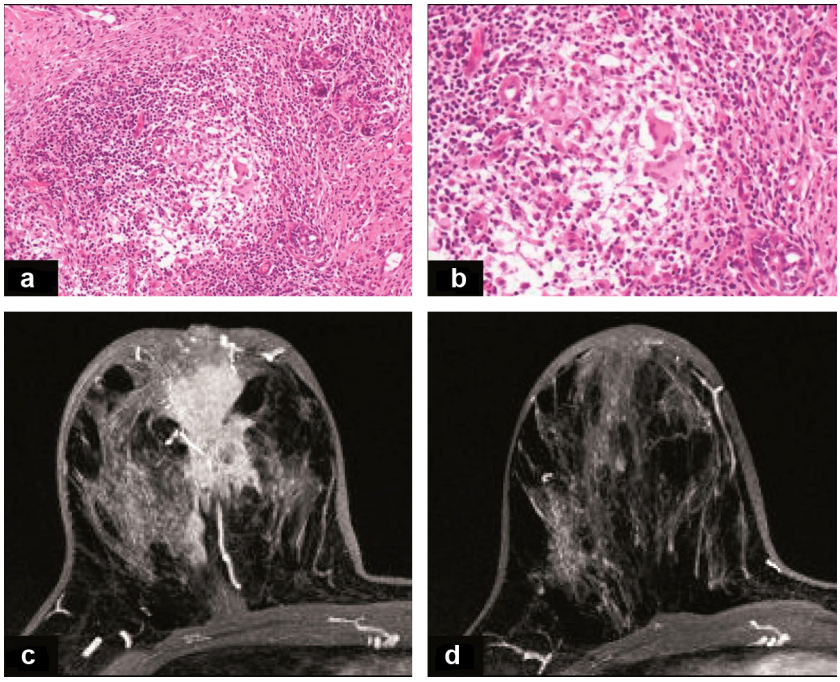

Figure 20. Granulomatous mastitis: same patient as Fig. 19. Histological sections of a sample collected by percutaneous puncture shows inflammatory infiltration with developing granulomatous lesions. Enlargement of image (a) reveals presence of giant cells within the granuloma. Fat-saturated T1-weighted MR image obtained after intravenous administration of a gadolinium chelate prior to corticosteroid therapy. Fat-saturated T1-weighted MR image obtained after intravenous administration of a gadolinium chelate of the same zone as image (c), 3 months after systemic corticosteroid therapy shows complete disappearance of inflammatory lesions.

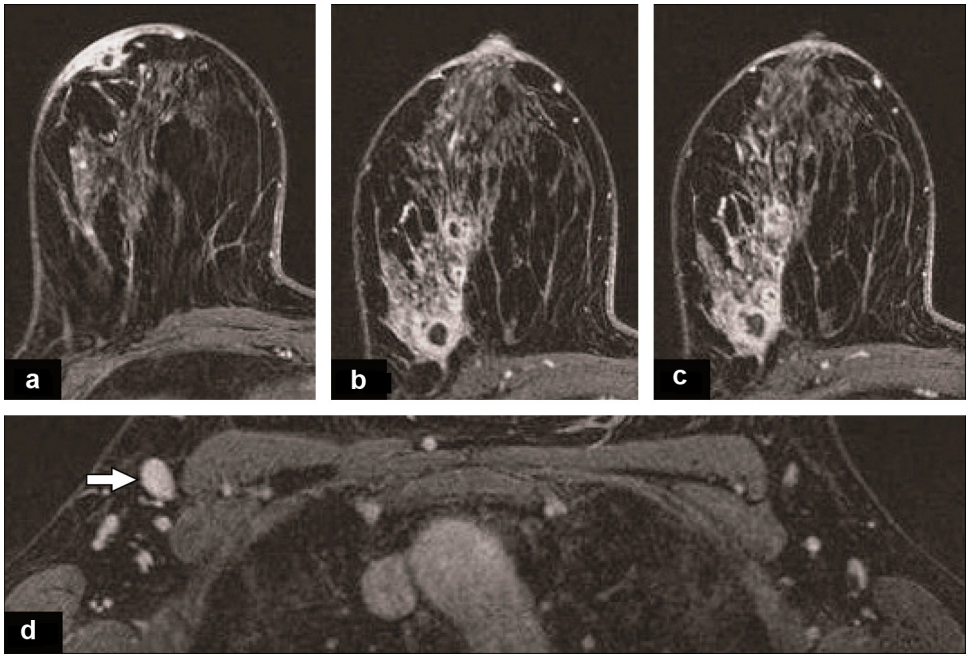

Figure 21. Pseudotumoral granulomatous mastitis in a 55-year-old patient with palpable masses of the right breast. Ultrasound examination shows multiple breast lesions with axillary lymphadenopathy. Patient was referred for breast MRI and puncture biopsy for suspected multicentric breast cancer. Fat-saturated T1-weighted MR image obtained after intravenous administration of a gadolinium chelate shows enhancement of the dermis and subcutaneous layer. b: fat-saturated T1-weighted MR image obtained after intravenous administration of a gadolinium chelate shows extensive enhancement of breast tissue with small nodular areas consistent with multiple microabscesses; c: fat-saturated T1-weighted MR image obtained after intravenous administration of a gadolinium chelate shows the spread of zones of contrast enhancement; d: fat-saturated T1-weighted MR image obtained after intravenous administration of a gadolinium chelate shows right axillary lymph node enlargement (arrowhead).

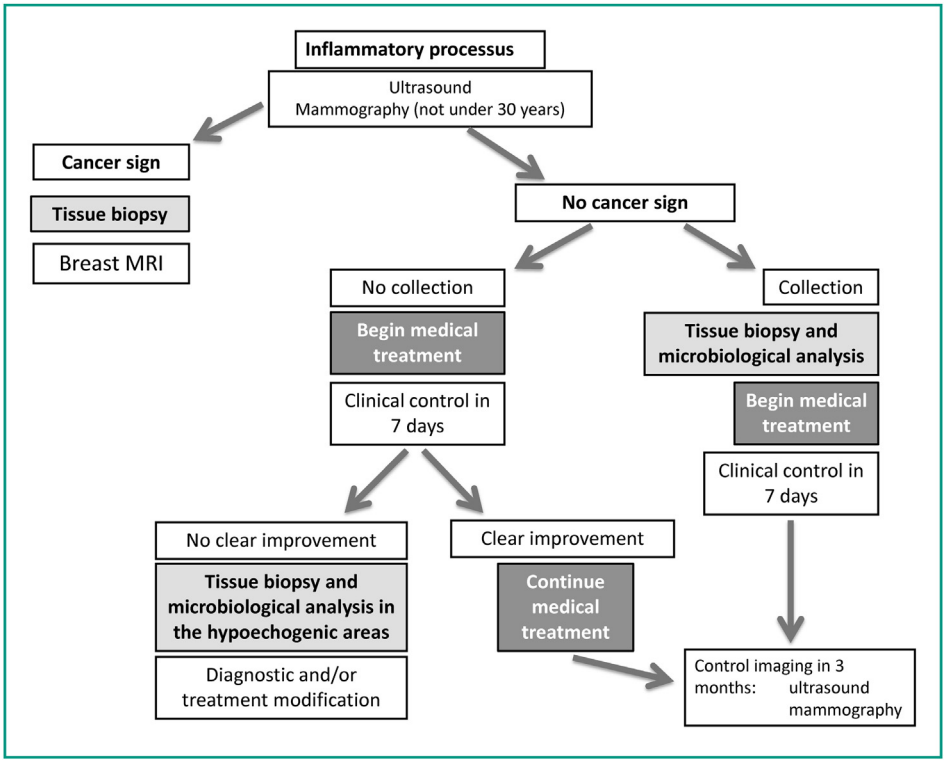

Figure 22. Practical procedure for investigating and treating inflammatory breast disease.

If so, drug treatment should be continued. Imaging should be performed again about 3 months after the onset of symptoms; the aim of it being to examine the patient outside of the clinically acute phase, obtain quality images of the formerly inflamed breast and confirm the absence of suspicious radiological findings that could reflect breast cancer. Indeed, the initial acute phase assessment might not have been of optimal quality or sensitivity, notably due to lesser breast compression because of the pain it causes to patients with an inflamed breast.

If the radiologist cannot evidence fluid collection during the initial acute phase examination but visualizes only signs of inflammation, targeted percutaneous sampling is in principle not possible or recommended. In such cases, empiric drug treatment should be initiated according to the recommendations provided below. The patient should be seen again 7 days later and drug treatment continued if clear clinical improvement is observed. Follow-up imaging should be carried out for all patients about 3 months after the onset of symptoms.

If, at the time of the first early follow-up visit (7 days), no clear signs of clinical improvement are observed, then the patient should be referred again to the radiologist in order to collect samples from zones of tissue showing inflammation. These samples should allow for more accurate diagnosis and adjustment of treatment if necessary.

It is essential that both the radiologist and the attending physician inform the patient that any changes in the progress of her condition, such as a rapid worsening or recurrence after discontinuation of treatment, should incite her to consult again as soon as possible (Fig. 22).

Proposed drug regimen

The radiologist should be able, with the attending clinician's consent, to propose and implement drug treatment. Drug treatment is usually based on antibiotic therapy and treatment with systemic and local anti-inflammatory drugs [19,20].

Antibiotic therapy should bear in mind the patient's history, in particular an allergy to penicillin. One gram of amoxicillin/clavulanate orally 2 times/day is the first choice antibiotic therapy. Patients with known allergy to penicillin should receive 600 mg of clindamycin 3 times/day. Treatment should be continued for about 2 weeks even if the symptoms disappear quickly after initiation of treatment. This prolonged period of treatment is justified by the relatively poor penetration of antibiotics in breast tissue.

Systemic anti-inflammatory treatment is based on non-steroidal anti-inflammatory drugs, such as ibuprofen, at a dose of 400 mg, 3 times/day. Gastric protection can be prescribed depending on the patient's history of use of anti-inflammatory drugs.

Local anti-inflammatory treatment may also be implemented either via creams or gels containing non-steroidal anti-inflammatory drugs, or via patches containing the same substances that are applied to the skin where the inflammation is most pronounced. Local anti-inflammatory application should be renewed 2 times/day. Local cooling can also help.

Take-home messages

- The radiologist must be familiar with the radiological signs of breast inflammation:
  - thickening of the skin,
  - hyperechoic fat,
  - visibility of subcutaneous lymphatic vessels,
  - increased vascularization,
  - lactiferous duct changes,
  - fluid collections and lymphadenopathies.
- Inflammatory cancer must be recognized and diagnosed without fail:
  - frequent significant skin edema,
  - gradual progression of the condition,
  - lesions that are sometimes difficult to identify.
- Radiologists should search for specific forms of inflammation:
  - inflammation of the nipple-areola region, including Zuska's disease,
  - granulomatous mastitis,
  - infections due to specific micro-organisms.
- Percutaneous sampling should be implemented on a regular basis:
  - diagnosis of various forms of breast cancer,
  - diagnostic bacteriological testing, including unusual species,
  - drainage of fluid collections.
- Appropriate drug treatment should be initiated by the radiologist.

Clinical case

Clinical history

A healthy 46-year-old woman with no noteworthy history of breast disease consulted her gynecologist for a painful, palpable, nodule in the right periareolar region that appeared 5 days before. She had no family history of breast cancer. Clinical examination revealed localized skin thickening of the areola over an area of 3 cm^2 next to a palpable plaque. Signs of inflammation in the form of red and locally hot skin were detected. No nipple discharge or fistula was visible. No axillary lymph node enlargement was present (Fig. 23).

Questions

1. Do the patient's clinical history and imaging findings suggest inflammatory carcinoma?
2. What do you think the linear structure within the hypoechoic collection is?
3. What is your diagnosis?

Answers

1. The patient's clinical history, together with the rapid onset of localized symptoms with clear inflammatory signs suggest that this is not a case of breast cancer but rather an inflammatory lesion, perhaps of infectious origin. Imaging also shows localized findings. Neither mammography nor ultrasound detected the typical lesions associated with breast cancer. The

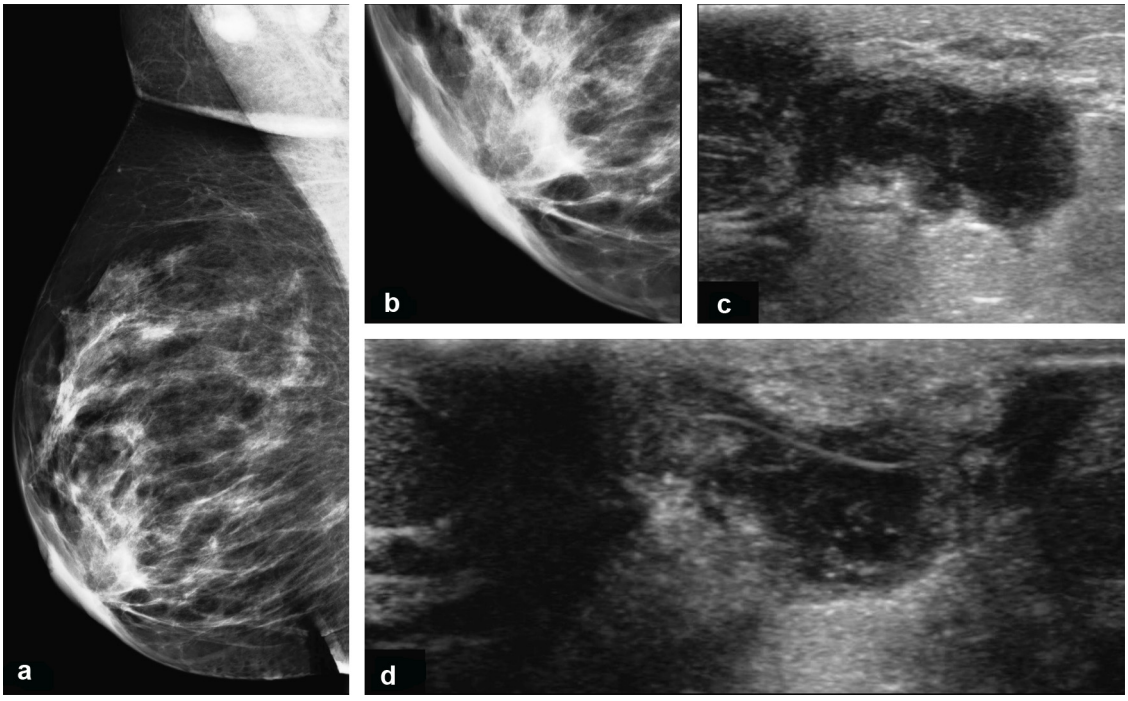

Figure 23. Clinical case: 43-year-old patient with no history of medical problems or breast disease. No family history. Mammogram of the right breast (MLO view) shows no mammographic abnormalities but a thickening of the skin in the periareolar region. Enlarged view of image (a) shows skin thickening in the periareolar region. Ultrasound examination shows skin thickening and hypoechoic fluid collection with poorly defined borders. A linear hyperechoic structure can be seen within the fluid collection.

presence of a fluid collection suggests an inflammatory condition.

2. The linear structure within a fluid collection suggests the presence of a foreign body. Due to the absence of previous breast conditions, the structure cannot be a foreign body introduced during biopsy or surgery. Owing to its proximity with the areolar region, it could be a hair.
3. Diagnosis can be made by questioning the patient further. Indeed, the patient is a hairdresser and hairdressers using clippers when cutting hair have been known to develop pilonidal breast sinuses following penetration of sharp fragments of hair. The patient's condition is due to reaction to a foreign body that may have become superinfected [21,22]. Such sinuses are usually reported in the cleavage region, typically in the internal breast quadrants.

Diagnosis

Superinfected pilonidal breast sinus. It is a condition observed sometimes in hairdressers.

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Disclosure of interest

The author declares that he has no conflicts of interest concerning this article.

References

[1] Adrada B, Wu Y, Yang W. Hyperechoic lesions of the breast: radiologic-histopathologic correlation. AJR Am J Roentgenol 2013;200:W518—30.
[2] Jesinger RA, Lattin Jr GE, Ballard EA, Zelasko SM, Glassman LM. Vascular abnormalities of the breast: arterial and venous disorders, vascular masses, and mimic lesions with radiologic-pathologic correlation. Radiographics 2011;31:E117—36.
[3] Plantade R. Interventional radiology: the corner-stone of breast management. Diagn Interv Imaging 2013;94:575—91.
[4] Yeh ED, Jacene HA, Bellon JR, Nakhlis F, Birdwell RL, Georgian-Smith D, et al. What radiologists need to know about diagnosis and treatment of inflammatory breast cancer: a multidisciplinary approach. Radiographics 2013;33:2003—17.
[5] Scott BG, Silberfein EJ, Pham HQ, Feanny MA, Lassinger BK, Welsh FJ, et al. Rate of malignancies in breast abscesses and argument for ultrasound drainage. Am J Surg 2006;192:869—72.
[6] Dawood S, Merajver SD, Viens P, Vermeulen PB, Swain SM, Buchholz TA, et al. International expert panel on inflammatory breast cancer: consensus statement for standardized diagnosis and treatment. Ann Oncol 2011;22:515—23.
[7] Plantade R, Thomassin-Naggara I. MRI vacuum-assisted breast biopsies. Diagn Interv Imaging 2014;95:779—801.

[8] Vashi R, Hooley R, Butler R, Geisel J, Philpotts L. Breast imaging of the pregnant and lactating patient: imaging modalities and pregnancy-associated breast cancer. AJR Am J Roentgenol 2013;200:321—8.
[9] Eryilmaz R, Sahin M, Hakan Tekelioglu M, Daldal E. Management of lactational breast abscesses. Breast 2005;14:375—9.
[10] Trop I, Dugas A, David J, El Khoury M, Boileau JF, Larouche N, et al. Breast abscesses: evidence-based algorithms for diagnosis, management, and follow-up. Radiographics 2011;31:1683—99.
[11] Ingram AD, Mahoney MC. An overview of breast emergencies and guide to management by interventional radiologists. Tech Vasc Interv Radiol 2014;17:55—63.
[12] Berna-Serna JD, Madrigal M. Percutaneous management of breast abscesses. An experience of 39 cases. Ultrasound Med Biol 2004;30:1—6.
[13] Schwarz RJ, Shrestha R. Needle aspiration of breast abscesses. Am J Surg 2001;182:117—9.
[14] Giess CS, Raza S, Birdwell RL. Distinguishing breast skin lesions from superficial breast parenchymal lesions: diagnostic criteria, imaging characteristics, and pitfalls. Radiographics 2011;31:1959—72.
[15] Kasales CJ, Han B, Smith Jr JS, Chetlen AL, Kaneda HJ, Shereef S. Nonpuerperal mastitis and subareolar abscess of the breast. AJR Am J Roentgenol 2014;202:W133—9.
[16] Altintoprak F, Kivilcim T, Ozkan OV. Aetiology of idiopathic granulomatous mastitis. World J Clin Cases 2014;2:852—8.
[17] Cao MM, Hoyt AC, Bassett LW. Mammographic signs of systemic disease. Radiographics 2011;31:1085—100.
[18] Ocal K, Dag A, Turkmenoglu O, Kara T, Seyit H, Konca K. Granulomatous mastitis: clinical, pathological features, and management. Breast J 2010;16:176—82.
[19] Merz L, De Courten C, Orasch C. Infections du sein. Rev Med Suisse 2014;10:925—6.
[20] Dixon JM, Khan LR. Treatment of breast infection. BMJ 2011;342:d396.
[21] Crepy MN. Dermatoses professionnelles des coiffeurs (http://www.rst-sante-travail.fr/rst/dms/rst/PDF/dmt126.pdf).
[22] Gannon MX, Crowson MC, Fielding JW. Periareolar pilonidal abscesses in a hairdresser. BMJ 1988;297:1641—2.