

CONTINUING EDUCATION PROGRAM: FOCUS...

Imaging benign inflammatory syndromes

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KEYWORDS

Breast; Inflammation; Mammography; Ultrasonography **Abstract** Benign mastitis is a rare disease and its management is difficult. The diagnostic challenge is to distinguish it from carcinomatous mastitis. We make a distinction between acute mastitis secondary to an infection, to inflammation around a benign structure or to superficial thrombophlebitis, and chronic, principally plasma cell and idiopathic granulomatous mastitis. Imaging is often non-specific but we need to know and look for certain ultrasound, mammogram or magnetic resonance imaging (MRI) signs to give a pointer as early as possible towards a benign aetiology. A biopsy should be undertaken systematically where there is the slightest diagnostic doubt, to avoid failing to recognise a carcinomatous mastitis.

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Mastitis is defined as inflammation of the breast. It is most important to differentiate benign acute mastitis from carcinomatous mastitis as early as possible, since the latter is a real diagnostic and therapeutic emergency with an unfavourable prognosis. The clinical and radiological appearance of the two types can be close, and a biopsy should always be undertaken where there is the slightest doubt as to the diagnosis.

Benign mastitis is rare, representing less than 1% of the activity in a breast centre [1]. It may be acute or chronic and can be very difficult to manage.

Aetiology of benign mastitis

Acute mastitis

Benign mastitis of infectious origin

Non-specific infections: acute abscesses

The prevalence of lactational abscesses has decreased. They do not pose a diagnostic problem and their treatment is well documented. They generally occur deep in the central area of the breast.

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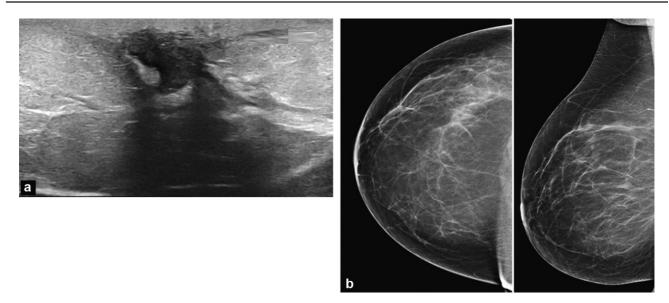


Figure 1. 34-year-old patient. Acute mastitis of the right breast; a: ultrasound shows a heterogeneous hypoechoic mass, without posterior echo strengthening, with a superficial, subareolar location, associated with clear cutaneous thickening. Subareolar abscess; b: mammogram normal, particularly on the right.

Non-puerperal abscesses require more complex management, easily becoming recurrent and chronic.

They occur irrespective of age, favoured by local (ductal ectasia, nipple inversion, malpighian metaplasia of the lactiferous sinus) and general factors (smoking, obesity, diabetes) [2,3].

Their aetiopathogenesis is debated. These abscesses may be secondary to infection of the subareolar lactiferous ducts, distended by *Staphylococcus aureus* or anaerobic microorganisms [3,4], or more rarely, due to the spread of a bacterial infection via the blood [4]. They are often superficial and subareolar [5].

Clinically acute abscesses manifest the classic triad of symptoms, heat, redness and pain, usually without any associated general symptoms [3].

The first course of action should be an ultrasound examination. It may reveal non-specific signs such as thickening of the skin (more than 3 mm), hyperechogenicity of the fatty lobules related to the oedema, or dilatation of ducts (more than 3 mm). At a more advanced stage, intramammary collections may be seen as round or oval masses with thick walls and a vascularised hyperechoic corona. They are anechoic or heterogeneous, possibly with posterior strengthening of the echoes [4,5] (Fig. 1a). Fistulae may be visible as anechoic tubular structures in contact with the abscess. Adenopathy is frequently to be found in the axillae. It is sometimes difficult to differentiate an abscess from a carcinomatous lesion if the margins of the masses are irregular. A 15-day trial treatment should be initiated, with careful clinical monitoring. Biopsy should be performed where there is the slightest diagnostic doubt.

Mammography is difficult given the sensitivity of the breast. Its main aim is to eliminate a tumoural lesion (microcalcifications or a suspect mass) [5] (Fig. 1b), but it is often difficult to interpret, given the oedema and insufficient compression. It may reveal non-specific signs, such as subcutaneous oedema, density asymmetry, or even, in the abscess stage, a highly dense oval or round mass with more or less circumscribed margins [4,5].

Specific infections

This essentially implies mammary tuberculosis. Parasitic and fungal infections are extremely rare [4,6].

The tuberculosis is secondary to infection by a bacterium belonging to the Mycobacteriaceae family. Its location in the breast is rare since it represents less than 0.1% of cases of tuberculosis [7]. Young women during the period of reproductive activity are those most frequently affected [7,8]. It is favoured by pregnancy, lactation and multiparity [7].

Primary mammary tuberculosis initially located in the breast is differentiated from secondary forms which occur after prior infection of an organ other than the breast, the latter being contaminated via the lymphatic system, the blood, the nipple or from a neighbouring organ (rib, shoulder, sternum) [9].

The most evocative clinical symptom is a slowly evolving swelling of the breast, associated with fistulated axillary adenopathy. Mammary tuberculosis should also be considered when confronted with a mammary abscess which persists, despite well-managed treatment, or with a recurring fistula [7].

There is no specific imaging sign for mammary tuberculosis. The most common appearance is of an irregular mass which can easily be taken for neoplasia [6,7]. Mammography also shows well-circumscribed masses (nodular form), focal asymmetric densities (diffuse form) or architectural disorganisation with density asymmetry and retraction of the nipple (fibrous form) [6].

Ultrasonography shows poorly defined hypoechoic areas, with discrete posterior strengthening of the echoes, liquid collections or duct dilatations.

A biopsy is often essential and allows granulomatous lesions to be found with non-pathognomonic epithelialgiant-cell follicles, the certainty of the diagnosis depending on the presence being demonstrated of acid-alcohol resistant bacilli [7].

Non-infectious benign mastitis

Inflammatory cysts

These cysts are secondary to a cyst fissuring under tension with a peripheral inflammatory reaction. They are diagnosed using ultrasound when a typical cyst with a more or less echogenic content is seen, or when there is a more or less vascularised thick-walled collection with echogenic contents, sometimes with a fluid level [5,10] (Fig. 2). The appearance may be atypical and require monitoring or needle aspiration biopsy.

Sebaceous and epidermal cysts

Sebaceous and epidermal cysts are present in the form of rounded, resistant, superficial masses which develop at the expense of pilosebaceous follicles. They may become inflamed in the event of secondary infection, and an epidermal cyst easily becomes inflamed on taking a biopsy [11]. They must be differentiated histologically: unlike an epidermal cyst, a sebaceous cyst does not contain keratin but sebaceous glands.

In a mammogram, these cysts are seen as high-density, circular or oval masses, with well-defined margins and superficial topography (Fig. 3a). In the ultrasound, these masses are seen as superficially located, hypoechoic, oval masses with circumscribed margins (Fig. 3b and c). A

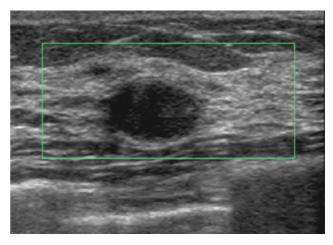


Figure 2. Inflammatory cyst, round mass with finely echogenic content, with no clear posterior strengthening.

typical epidermal cyst is like an onion, formed of concentric hypo- and hyperechoic layers [11].

Asymptomatic lesions should not be treated. Cysts which have repeated inflammatory phases should be treated surgically [11].

Mondor's disease

Mondor's disease is superficial thrombophlebitis usually of the thoracoepigastric vein, affecting young women during the period of reproductive activity. It is a rare condition [6].

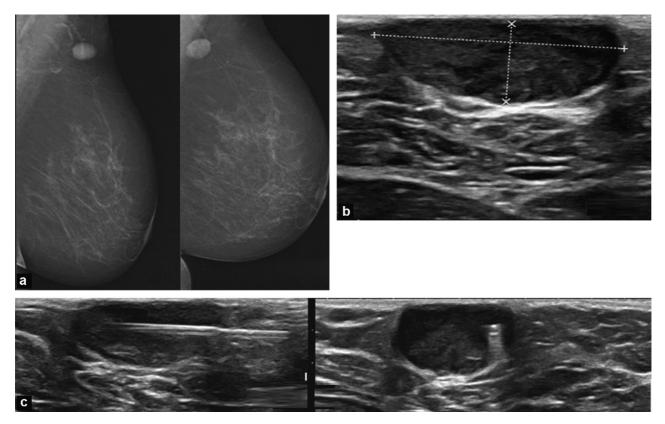


Figure 3. 60-year-old patient, with no noteworthy history. Clinical mass in the left superior lateral quadrant, known for 20 years, but has increased in size recently; a: dense oval mass on the mammogram with circumscribed margins; b: under ultrasound, oval hypoechoic mass with circumscribed margins, with superficial topography and discrete posterior echo strengthening; c: ultrasound-guided microbiopsy: epidermal cyst.

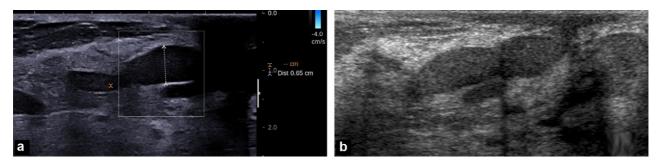


Figure 4. a and b: typical appearance of duct dilatations: tubular structures dilated by more than 3 mm in diameter, with anechoic or finely echoic content, sometimes mobile (thick secretions).

It may be idiopathic or secondary to a local cause such as surgery, trauma, radiotherapy, or breast cancer [6,12].

It presents clinically as a painful indurated cord, embedded in the dermis [12].

The mammogram is normal or shows a dense, rarely calcified, tubular structure in place of the thrombosed vein [6]. Doppler ultrasound shows the usual signs of thrombosis with the presence of echogenic endovascular content and the absence of compressibility of the vessel [6,12].

Recovery is spontaneous, and hastened by taking non-steroidal anti-inflammatory drugs [12].

Chronic mastitis

Duct ectasia and plasma cell mastitis

These are different stages of the same disease, marked in the first instance by dilatation of more than 3 mm of the ducts, which contain a more or less thick substance. The dilatation is usually bilateral and predominantly in the subareolar ducts. At this stage, the clinical manifestation of an intermittent yellowish or brownish mammary discharge is present in a quarter of all cases [13,14]. Fibrosis, lymphocyte infiltration and epithelial atrophy appear later, the association of which leads clinically to retraction of the nipple. In the end the ducts burst, releasing their lipid rich content, which induces an inflammatory reaction and the formation of a foreign body granuloma, corresponding to plasma cell mastitis, responsible for the appearance of a palpable mass and inflammatory symptoms. The association with nipple retraction may wrongly evoke an inflammatory carcinomatous lesion [13].

A mammogram of duct ectasia may be normal or show retroareolar, liquid-density, tubular structures. Ultrasound shows dilated ducts with more or less echogenic content [14] (Fig. 4a and b).

The appearance in a mammogram of plasma cell mastitis is non-specific with skin thickening and density asymmetry (Fig. 5a and Fig. 6a). Smooth-sided, rod-like calcifications, which may be discontinuous and generally greater than 1 mm in diameter, may be associated with this condition and may be solid if they are intraductal, or with a clear centre if they are periductal (Fig. 7). They are frequently bilateral. Ultrasound shows duct dilatations, thickening of the skin and non-specific attenuating hypoechoic areas, rarely a true mass [14] (Fig. 5b and Fig. 6b).

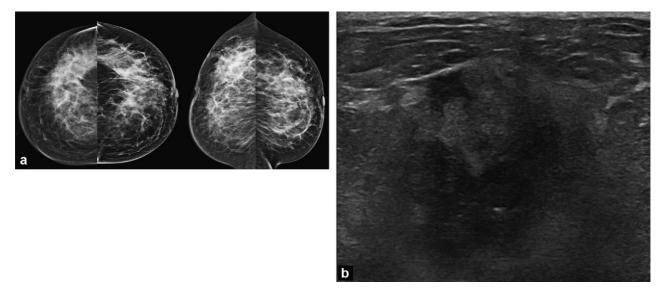


Figure 5. 29-year-old patient. Acute mastitis of the right breast. On clinical examination, 10-cm suspect mass in the superior quadrants; a: on the mammogram, focal asymmetric density and architectural disorganisation of the right lat. sup. quadrant, with no visible real mass; b: ultrasound showed BI-RADS 4 attenuating areas, associated with clear skin thickening of the right sup. lat. quadrant. Percutaneous biopsy: plasma cell mastitis.

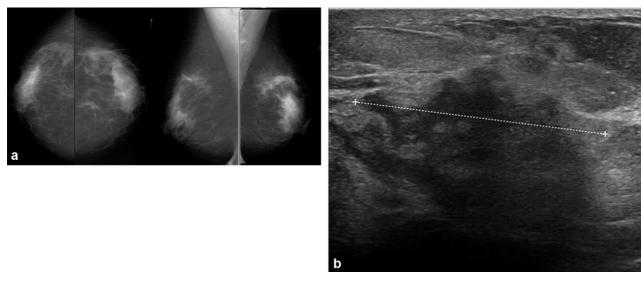


Figure 6. 55-year-old patient. Acute mastitis with clinical induration of the left sup. lat. quadrant. Mammography (a) and ultrasound (b) signs similar to Fig. 5 (a and b).

Idiopathic granulomatous mastitis

This is a rare condition with poorly understood aetiology, characterised by the presence of aseptic inflammatory lesions in the lobules [6,15-17]. It affects young women during the period of reproductive activity [15]. Pregnancy, breast-feeding and taking an oral contraceptive are the factors that promote it [6,18].

Clinically, it presents as a poorly delineated unilateral induration sometimes fixed to the deeper layers and mimicking an inflammatory cancer [15–17]. Adenopathy is present in 15% of cases (Fig. 8a).

The retroareolar region is generally not affected.

As far as imaging is concerned, it is classically seen in a mammogram as a unilateral focal asymmetric density and in the ultrasound scan as a hypervascularised, attenuating, hypoechoic area with non-circumscribed margins, linked to ducts [16,17] (Fig. 8b, c and d).

Magnetic resonance imaging (MRI) is not systematically indicated but if performed, the appearance most frequently described is of a hyposignal mass in T1- and T2-weighted images, with spiculated margins which cannot be differentiated from a cancer [17,19,20] (Fig. 8e and f).

A biopsy must be performed to eliminate a neoplastic condition. Histology will find a lobular inflammatory infiltrate with the presence of giant cell nodules with no caseous necrosis [6,18] (Fig. 8g and h).

Once an infectious origin has been formally eliminated, treatment is based on corticosteroid therapy [6,18]. Long-term monitoring is indicated since the condition recurs in 25% of all cases [20,21].

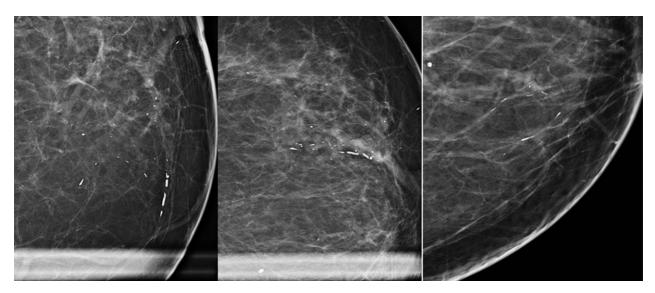


Figure 7. Typical discontinuous micro-calcification in duct ectasia in the form of solid, smooth-sided rods with a clear centre.

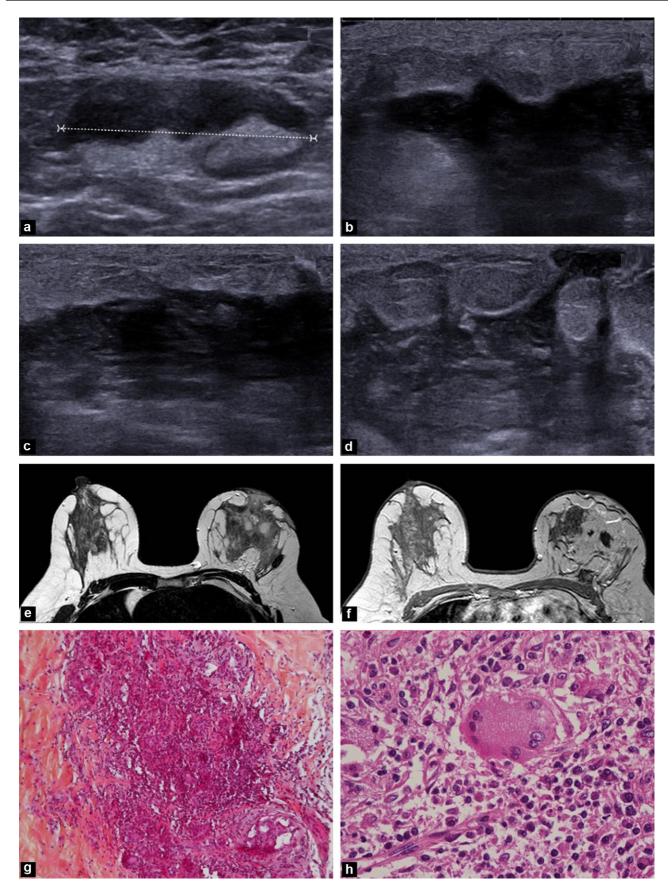


Figure 8. 36-year-old patient. Acute mastitis of the left breast; a: suspect, 7 cm, clinical mass in the sup. lat. quadrant with axillary adenomegaly. Ultrasound shows a 3-cm voluminous left axillary adenomegaly with clear thickening of the cortex; b, c and d: ultrasound

Benign mastitis: hierarchy and imaging methods

Mammography and ultrasonography

Mammography and an ultrasound examination should be performed as the first course of action for any mastitis. The abnormalities which appear are often non-specific (focal asymmetric density, a poorly defined hypoechoic mass, etc.) and do not permit an aetiological diagnosis to be made with certainty [22]. However, a number of signs should be carefully sought to provide an early pointer towards a benign aetiology or carcinomatous mastitis.

A normal mammogram, even if it does not eliminate an inflammatory cancer, leans towards benign mastitis. The presence of duct dilatations, the absence of skin thickening, suspect micro-calcification or masses, particularly large ones, also plead in favour of the benign nature of the mastitis [22,23].

With ultrasound, the existence of duct dilatations and collections, and finding non-suspect axillary lymph nodes are the features pointing towards a benign condition [22,23]. The absence of a large tissue mass, of marked skin thickening or of interstitial oedema also weighs in favour of a benign condition [22,23].

Magnetic resonance imaging (MRI)

MRI is an examination to be used as a second course of action. It should not be performed until at least 15 days after starting well-managed anti-inflammatory and antibiotic treatment.

It seems to be better able to differentiate benign from carcinomatous mastitis. T2-weighted and dynamic sequences are the most discriminating and should be carefully analysed [22]. Masses are found less frequently in non-tumoural aetiologies. A benign nature can be inferred from a T2 isosignal or hypersignal (cancers are collagenrich and appear as a T2 hyposignal), a moderate size and a subareolar location or one remote from the pectoral plane [22,24,25] (Fig. 9 and Fig. 10). The shape and margins of masses are not elements that can be used for differentiation.

After injection, there is often progressive or plateau enhancement, the presence of washout being suspect (Figs. 11, 12 and 13). This also applies to the ''blooming sign'' which corresponds to good early definition of delineation of the mass, the margins gradually becoming more indistinct later with increase in the diameter of the lesion.

The associated signs of the presence of bilateral oedema and the existence of oval lymph nodes, with a long axis of less than one centimetre with retention of a fatty hilum, are reassuring. We must also check that there is no "hook



Figure 9. T2-weighted magnetic resonance imaging (MRI): abscess: medium-sized mass in clear hypersignal with a subareolar location, associated with skin thickening.

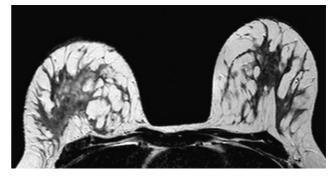


Figure 10. T2-weighted magnetic resonance imaging (MRI). Plasma cell mastitis: hypersignal mass, associated with skin thickening and architectural disorganisation. Pectoral plane intact and prepectoral fatty line conserved.

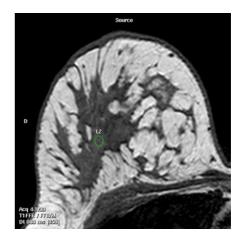


Figure 11. T1-weighted magnetic resonance imaging (MRI) without injection. Plasma cell mastitis: hyposignal mass, associated with skin thickening and architectural disorganisation.

shows a poorly defined BI-RADS 4 attenuating hypoechoic area associated with clear skin thickening; e: T2-weighted magnetic resonance imaging (MRI): hypersignal mass, associated with skin thickening and architectural disorganisation; f: T1-weighted MRI after injection of gadolinium; g and h: progressively enhanced, heterogeneous mass with irregular shape and margins, with no washout. Diagnosis: idiopathic granulomatous mastitis. Histology of ultrasound-guided samples: abscessed lobular granulomatous mastitis. The lobule is effaced by chronic lymphoplasmacytic inflammation rich in neutrophilic granulocytes. Granuloma: fibro-inflammatory reaction rich in lymphocytes, plasma cells and Langhans type multinucleate giant cells.

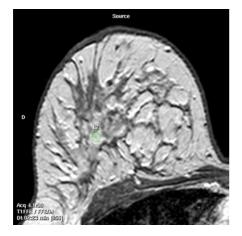


Figure 12. T1-weighted magnetic resonance imaging (MRI) after injection of gadolinium. Plasma cell mastitis: progressively enhanced, heterogeneous, irregular mass. No enhancement of the pectoral muscle.

TAKE-HOME MESSAGES

- Benign mastitis is rare.
- Imaging of chronic benign mastitis is often nonspecific.
- Differentiating between benign and carcinomatous mastitis can be difficult.
- You need to look for certain specific imaging signs that point towards a benign aetiology.
- Mammary MRI is not indicated as a first course of action.
- Benign mastitis must be monitored over the long term since it frequently recurs.
- A percutaneous biopsy should be systematically performed where there is the slightest diagnostic doubt.

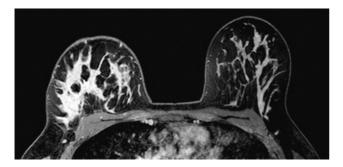


Figure 13. T1-weighted magnetic resonance imaging (MRI) after late injection of gadolinium. Plasma cell mastitis: clear asymmetric uptake of contrast medium, with skin thickening and architectural disorganisation.

sign'' (a T2 hyposignal band joining the mass to the pectoral muscle), no focal uptake of contrast by the skin, no enhancement of the pectoral muscle and no change to the prepectoral fat, all factors helping confirm the benign nature of mastitis [22,24] (Fig. 10).

Non-mass enhancement is not a specific criterion directing diagnosis towards a benign or malignant aetiology [22].

Conclusion

The diagnosis of benign mastitis is still a difficult exercise holding the constant dread of failing to recognise an inflammatory cancer. It is based on multidisciplinary management by the clinician, the radiologist and the histologist. At the slightest doubt in the diagnosis and in the absence of any improvement in the clinical and radiological symptoms after appropriate treatment, a biopsy must be systematically performed. Careful clinical and radiological monitoring is essential both because of the risk of recurrence and to avoid missing an associated non-inflammatory cancer.

Clinical case

A 42-year-old patient with no personal or family history of breast cancer.

Untreated acute mastitis of the left breast, which appeared five days ago. No fever.

Patient seen by a multidisciplinary committee consisting of a medical oncologist, a surgeon, a radiotherapist and a radiologist.

Clinical examination: painful, red, hot, indurated left breast, without any real mass being palpated.

Question 1

What imaging examination(s) would you request?

- 1. Bilateral mammogram;
- 2. Ultrasound examination;
- 3. Mammary MRI;
- 4. No immediate imaging; only to be performed after 15 days of trial medical treatment.

Answer

1 and 2. These examinations must be performed as a matter of urgency to look for features indicating a carcinomatous mastitis (micro-calcifications or suspect masses) and to guide a possible biopsy. MRI should not be performed as a first course of action but should be discussed after 15 days of appropriate medical treatment if there is no improvement in the clinical symptoms or if histological results have been received that conflict.

Question 2

What are the features in favour of a benign nature (Fig. 14)?

- 1. The presence of thickened skin;
- 2. The absence of a mass;
- 3. The absence of suspect calcification;
- 4. The fact that the abnormalities are unilateral.

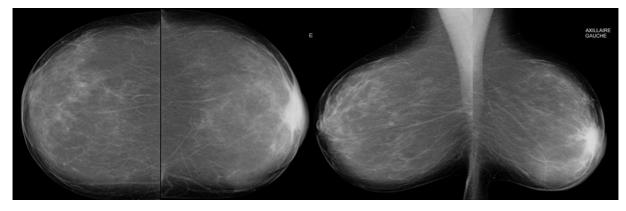


Figure 14. Density asymmetry and clear skin thickening on contact with the left areola-nipple complex.

Answer

2 and 3. Skin thickening is more frequently found in carcinomatous mastitis. The unilateral character is not a discriminating factor.

Question 3

Ultrasound found a medial 3 cm para-areolar mass in the left breast (Fig. 15). What would you do?

- 1. Microbiopsy under ultrasound;
- 2. A needle aspiration biopsy;
- Ultrasound monitoring 15 days after antibiotic treatment;
- 4. Clinical monitoring at 15 days and another ultrasound examination after 4 months.

Answer

1. Presence of an ultrasound object, without a particular feature permitting carcinomatous mastitis to be eliminated. An aetiological diagnosis must be obtained urgently to avoid missing a tumoural lesion and so that the treatment can be modified. Microbiopsy samples should be taken under ultrasound.

Figure 15. 3-cm medial para-areolar oval tissue mass, with strengthened posterior echoes. BI-RADS 4.

Question 4

The histological results indicate plasma cell mastitis. What would you do?

- 1. Perform MRI;
- 2. Give anti-inflammatory treatment;
- 3. Take macrobiopsies under ultrasound;
- 4. Undertake careful clinical and ultrasound monitoring.

Answer

2 and 4. The histological results are benign and may explain the clinical symptoms. MRI is not indicated because it will not change management of the patient in any way. Careful clinical and ultrasound monitoring is essential with suitable medical treatment to ensure rapid regression of the symptoms and the ultrasound abnormalities.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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