CONTINUING EDUCATION PROGRAM: FOCUS...

Complex cystic breast masses in ultrasound examination

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KEYWORDS
Breast; Breast ultrasound; Complex cystic masses

Abstract

Complex cystic masses are defined as lesions composed of anechoic (cystic) and echogenic (solid) components, unlike complicated cysts, the echogenic fluid content of which imitates a solid lesion. Complex masses are classified as ACR4 and require histological verification by percutaneous biopsy and/or surgical ablation. The etiology is diverse, and can be benign or high risk (an abscess, hematoma, fat necrosis, fibrocystic mastopathy, a phyllodes tumor, papilloma) as much as malignant (papillary cancer, necrotic cancer, a ductal carcinoma in situ, metastases). The biopsy technique must be adapted to each case and it is often necessary to insert a coil during the procedure. Histopathological correlation is essential to ensure that the samples are representative and concur with the ultrasound appearance, so as not to fail to recognize high risk or malignant lesions requiring appropriate management.

Cysts are by far the most frequently encountered breast condition and are usually asymptomatic and found accidentally while performing an ultrasound examination. Cystic lesions need to be described and classed according to the BIRADS lexicon [1,2] (Table 1):
• typically benign, simple cysts (ACR2): strictly anechoic content, imperceptible wall, posterior acoustic enhancement;
• probably benign, complicated cysts (ACR3): homogeneous hyperechoic content or with more or less sloping fluid/fluid levels, imperceptible wall, with or without posterior enhancement;
• complex cysts of indeterminate nature (ACR4): association of cystic and solid components, thick wall or internal septum/septa.

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The challenge for the radiologist is differentiating between a complicated cyst and a complex cystic mass. When a solid component is revealed, even if discreet, the lesion comes into the category ACR4 (PPV between 2–95%) with a biopsy indicated for diagnostic purposes. Indeed, the rates of malignancy reported in the literature vary between 23% and 31% depending on the paper [3–5]. The aim of this article is to describe how to optimize the ultrasound technique, the signs of complex masses, the place of the different techniques of percutaneous biopsy and to examine the diagnostic range of complex masses.

Examination techniques

As for any imaging examination, it is essential to have available all the clinical and radiological data before performing and interpreting a breast ultrasound examination. The ultrasound technique (B mode) should meet the following criteria:

• linear probes of frequencies between 7.5 and 20 MHz (more often 12–14 MHz) should be used. The frequency must be adapted to the breast volume and the location of the lesion in the breast (lower frequency for deep lesions, high frequency for superficial lesions);
• total gain and TGC should be used to obtain an adequate and homogeneous signal from the skin to the depth of the pectoral muscle;
• the focal zone must be adjusted in depth relative to the lesion;
• the lesion must be analyzed in at least two planes: transverse and longitudinal or radial (according to the major axis of the lactiferous ducts) and anti-radial.

The use of additional modes helps characterize the lesion; the radiologist needs to know their main characteristics as well as their respective advantages and disadvantages in order to make the best use of them.

Harmonic mode

Harmonic mode improves spatial resolution and contrast of the lesion and reduces artefacts (e.g. reverberation artefacts from cyst walls), so that posterior ultrasound modifications are seen better [6].

Compound mode

Compound mode improves the signal/noise ratio by reducing background noise and speckle artifact, optimizes analysis of the margin of the lesion and the internal echostucture of masses. It also enables better detection of intralesional calcifications [7]. On the other hand, posterior ultrasound modifications are attenuated [8].

Doppler mode

Doppler mode (color and/or power) ought to be systematic. It provides elements guiding diagnosis: perilesional hyperemia if lesions are inflammatory (cysts, abscesses) versus intralesional vascularization indicating the solid nature of the lesion. In order to obtain a good Doppler map, it will be necessary to:

• work with PRF values of around 1000 Hz;
• set amplification just above the noise threshold;
• adjust the size of the Doppler box in order to increase sensitivity and decrease flow artifacts [9].

Power Doppler is more sensitive to slow flows but is also more sensitive to artifacts [10]. It should be remembered that the absence of a Doppler signal does not mean that the solid nature of a lesion can be excluded.

Elastography

This can help characterize complicated cysts by revealing the fluid component (trilaminar or bull’s eye appearance in static mode, signal void appearance in shear mode). In the same way, if the lesion is found to be very hard, this will help confirm diagnosis of complex masses and guide percutaneous biopsies (improving the histological characterization of the lesion) [11,12].

Ultrasound signs of complicated cysts

Complicated cysts show all the aspects of simple cysts except for the content, which is finely echogenic. They may have a fluid level or internal echoes that correspond to debris and which are displaced slowly with changes in the patient’s position. In no case do complicated cysts contain a solid parietal mass (Fig. 1).

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**Table 1** BIRADS classification of cystic lesions.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>BIRADS</th>
<th>PPV</th>
</tr>
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<tbody>
<tr>
<td>Simple cyst</td>
<td>Imperceptible wall</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Anechoic content</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Posterior acoustic enhancement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complicated cyst</td>
<td>Thin wall</td>
<td>3</td>
<td>&lt;2%</td>
</tr>
<tr>
<td></td>
<td>Echogenic content</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluid/fluid level</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Posterior acoustic enhancement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex cystic mass</td>
<td>Thick wall &gt; 0.5 mm</td>
<td>4</td>
<td>2–95%</td>
</tr>
<tr>
<td></td>
<td>Thick septa &gt; 0.5 mm</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Intracystic mass</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Solid cystic mass &gt; 50%</td>
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</table>
Assessing the mobility of the echogenic component and detecting flow by power Doppler can be of help: if the echogenic component does not move or if no flow has been detected, it is impossible to distinguish between a solid parietal mass and hemorrhagic or inflammatory debris adhering to the wall of the lesion. On the other hand, detecting a Doppler signal indicates a real parietal mass.

According to Berg et al. (ACRIN 6666 study) [4], only 12% of complicated cysts reported actually seem to be solid lesions, with a malignancy rate of 0.42%. They placed these lesions in the ACR3 category and recommended follow-up at 6 months. If the size changed over 6 months by >20%, a diagnostic biopsy was indicated [8,13].

**Ultrasound signs of complex masses**

The majority of complex masses show posterior acoustic enhancement due to the cystic component. The margin may be macro- or microlobulated, indistinct or even irregular. Differentiating an intracystic mass from an intraductal mass is not always obvious, although intraductal masses are usually tubular in appearance (Fig. 2a and b). Sometimes intracystic hemorrhage can mask the solid component of a complex mass. Simply moving the patient into the lateral decubitus position may be enough to displace the internal echoes related to the hemorrhage, and thus reveal the solid component. If necessary, ultrasound-guided fine needle aspiration may confirm a true intracystic mass.

**Ultrasound classification of complex masses**

Berg et al. have defined 4 categories of complex masses depending on morphological criteria [4]:

- cysts with a thick wall (>0.5 mm);
- cysts with thick internal septa (>0.5 mm) (Fig. 3);
- predominantly cystic complex masses (cystic components at least 50%) (Fig. 4);
- predominantly solid complex masses (at least 50% solid components) including peripheral cystic components (Fig. 5).

**Cysts with a thick wall or internal septum > 0.5 mm**

**Benign conditions**

- inflammatory cysts, more or less ruptured;
- fibrocystic mastopathy associated with apocrine metaplasia. This often manifests as grouping of microcysts.

![Figure 1. Complicated cyst. Well-defined round shape showing a debris/fluid level.](image)

![Figure 2. a: diagram of the development of intraductal and intracystic lesions. Initially the lesion with a solid component gradually fills and dilates the lactiferous ducts involved. When there is considerable dilatation the lesion appears as a complex cystic mass; b: tubular intraductal lesion dilating and filling the duct (intraductal papilloma).](image)

![Figure 3. Type II complex cystic mass. This is a predominantly cystic mass, with many septa, which are >0.5 mm thick. Cyst with hemorrhagic changes.](image)
A simple fine needle aspiration biopsy will confirm the diagnosis;
- fat necrosis may be seen as an ultrasound mass with a thick wall. There is no hyperemia in the Doppler unless there is secondary inflammation. A connection to the scar on the skin may confirm this diagnosis;
- collections (hematoma, seroma, lymphocele): the clinical context will provide information as to whether traumatic or post-operative. (Fig. 6). Depending on the clinical presentation, a first reference ultrasound examination can be done at 4–6 months, since certain images persist for several months;
- a breast abscess is suggested from the clinical examination when faced with the trio of fever, pain, and local hyperemia with inflammatory skin signs, occurring classically in a post-partum, traumatic or surgical context. The associated risk factors are smoking, diabetes and belonging to a black race [14]. In ultrasound, it presents as a complex mass with posterior enhancement, and in color Doppler, as having thick hypervascularized walls. Fine needle aspiration biopsy establishes the diagnosis and allows material to be collected for bacteriological analysis (Fig. 7a–d);
- juvenile papillomatosis may be seen as a nodular image composed of multiple cysts. This is not a papillary lesion but a hyperplastic epithelial lesion which must be surgically ablated (a high risk lesion) [15];
- a cystic breast lymphangioma is a rare tumor belonging to the lymphatic malformation group. It is a multiloculated lesion occurring in children, female adolescents and young women. It grows slowly. Fine needle aspiration biopsy will reveal the presence of lymphocytes in the fluid aspirated. Biopsy will also find the presence of lymphoid cells thus confirming the diagnosis. There is no risk of these lesions becoming malignant, but nevertheless, because of their size, surgical ablation is indicated [16].

Malignant conditions
These diseases are classically highly proliferative necrotic cancers (poorly differentiated, grade III, necrotic invasive ductal carcinomas) (Fig. 8a and b). Nevertheless their walls are markedly thicker and more highly vascularized. They are also associated with suspicious mammography signs such as a mass with irregular, even spiculated margins, and the presence of microcalcifications and very often axillary lymphadenopathies (which are better explored by ultrasound).

Figure 4. a: type III complex mass (intracystic mass) corresponding to a modified cyst; b: similar appearance in another patient where power Doppler confirmed the solid character of the parietal bud by detecting the internal vascularization. In this case, it was an intracystic papillary carcinoma.

Figure 5. Type IV complex mass with a solid component of more than 50%, with small peripheral cystic recesses. Fibrocystic mastopathy.

Figure 6. Complex mass with cystic recesses and fibrin septa. Organized hematoma.
Complex cystic breast masses in ultrasound examination

Medullary cancer can also appear as a thick-walled cystic mass [17].

Predominantly cystic complex masses

Benign conditions

Differential diagnoses include:
- modified cysts with or without mobile debris (Fig. 9a–c);
- post-therapeutic fat necrosis revealed as a complex ultrasound mass. Obviously the medical history and correlation with the mammogram showing typical fat clarity can confirm the diagnosis without needing a biopsy for typical cases (Fig. 10a–c);
- a galactocele appears as a complex mass with several fluid/fluid levels. This image ought not to present a problem of diagnosis given the context of breast-feeding.
- papillary lesions (benign and atypical papillomas): papillomas occur at 40 to 50 years of age, while the age range for papillary cancers appearing is 63–67 years [18]. Clinically, these lesions may be associated with breast discharges, either serous (more particularly in cases of benign papillomas) or brownish/hemorrhagic (suggesting rather, a malignant lesion). Papillomas develop in milk ducts which are subsequently obstructed. They usually appear as cystic lesions with parietal nodules (Fig. 11a). In color Doppler, intralobal flow is observed in the vascular stalk (Fig. 11b). These lesions should be biopsied.
Figure 9. a: B mode ultrasonography detected an anechoic lesion with an image of focal parietal thickening; b: no signal was detected with color Doppler; c: shearwave elasticity image. Signal void appearance concordant with mainly fluid content. The echogenic parietal part is coded in blue; it is very soft with a value < 30 kPa An ultrasound-guided needle aspiration biopsy (14-gauge) targeted on the echogenic part revealed a modified cyst.

(Fig. 11c). Histological diagnosis is based on the presence of proliferation of “finger-in-glove” projections that are edged by an epithelium and have a fibrovascular core. It is difficult to tell from biopsy fragments whether a papillary lesion is benign, atypical or malignant, in situ or invasive, hence the need to analyze the entire lesion [19–21]. Papillomas said to be atypical show areas of apocrine metaplasia and/or atypical ductal hyperplasia (ADH) (Fig. 12a–c). The risk of breast cancer associated with an atypical papilloma is similar to the risk in patients who have ADH elsewhere in the breast (× 4–5). The risk of breast cancer is higher (× 7) in women with multiple atypical papillomas and peripheral papillomas. Moreover, the risk of underestimating a papillary carcinoma is 8–14%, hence surgical ablation is recommended in order to analyze the histology of the entire lesion [22].

Malignant conditions
Encapsulated intracystic papillary carcinoma
Encapsulated intracystic papillary carcinoma is a rare form of cancer, representing 0.6% to 1% of breast cancers [23–25]. The appearance is more heterogeneous compared with papillomas, and often associated with hemorrhagic changes (Fig. 13a). Fine needle aspiration biopsy is inadequate (Fig. 13b). A 10-G vacuum-assisted core biopsy with a post-biopsy marker is the procedure recommended.

Figure 10. a: thick-walled complex mass including solid parietal nodules; b; in another patient, the appearance of a similar complex mass where the connection to the cutaneous scar can be clearly seen; c: comparison with mammographic images found typically clear fat necrosis corresponding to the ultrasound image. Biopsy is not indicated in this case.

Figure 11. a: complex intracystic mass; b: color Doppler examination detected a vascular stalk within the solid component. Appearance suggestive of a papilloma – a biopsy is indicated; c: histology after the biopsy showing a papilloma with no signs of atypia or malignancy. Nevertheless surgical ablation to study the whole of the lesion is recommended (risk of underestimation).
Macroposcopically, the mass is friable or lumpy inside a cyst (Fig. 13c). Microscopically, it consists of one or more papillary carcinoma nodules surrounded by a thick fibrous capsule (Fig. 13d–e).

* A colloid, metaplastic or mucinous carcinoma

A colloid, metaplastic or mucinous carcinoma can also look like an intracystic mass but such an appearance is rare.

**Predominantly solid complex masses**

**Benign conditions**

- fibrocystic mastopathy;
- complex fibroadenomas: these are fibroadenomas which, as well as the dual fibrous and epithelial component, also present cysts larger than 3 mm, adenosis, epithelial calcifications and apocrine metaplasia (Fig. 14a–b);
- phyllodes tumors with, in particular peripherally, cystic slits. Seventeen percent of phyllodes tumors are observed with these features [26]. Surgical ablation to study the entire lesion is essential (Fig. 15a–c).

**Malignant conditions**

* Solid papillary carcinoma*

Solid papillary carcinoma can either be a completely solid mass (sometimes even containing microcalcifications), or a predominantly solid complex mass (Fig. 16a). Histologically, no clear papillae are observed. The underlying papillary structure is represented by a network of fibrovascular cores among the solid cell proliferation (Fig. 16b).

* Certain ductal carcinomas in situ*

Certain ductal carcinomas in situ exhibit papillary growth characterized by a fibrovascular core bordered by a neoplastic epithelium. These lesions are different from papilloma colonized by DCIS. They may be observed as complex masses containing microcalcifications.

* Invasive ductal carcinoma*

Invasive ductal carcinoma, sometimes of high nuclear grade (grade III). The importance of correlation with the clinical findings and the mammogram, as well as systematic exploration of the axilla using ultrasonography should not

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**Figure 12.** a: type III complex mass with discrete hemorrhagic changes; b: vacuum-assisted macrobiopsy with a 10-G system was performed; c: histological results showed a sclerosing papilloma with apocrine metaplasia. Surgical ablation recommended.

**Figure 13.** a: type III complex mass; b: the first ultrasound-guided needle aspiration biopsy collected cells with a papillary architecture, the exceptional richness of which was the reason for histological verification despite the absence of suspect cells. A macrobiopsy with insertion of marker confirmed the presence of malignant papillary cells; c: macroscopic examination of the ablated tissue showed an indented friable mass inside a cyst. The post-biopsy coil is visible; d and e: microscopic examination: essentially papillary tumor architecture, focally cribriform. The axes of the papillae are bordered by multistratified carcinomatous cells with moderate cytonuclear atypia.
Figure 14.  a: type IV round complex mass with essentially peripheral, cystic recesses; b: ultrasound-guided microbiopsy (14G) showing a fibroadenoma.

Figure 15.  a: type IV round complex mass with essentially peripheral, cystic recesses; b: ultrasound-guided microbiopsy (14G): phyllodes tumor; c: macroscopically, a solid mass was found in the ablated tissue with peripheral cystic components.

be forgotten, to avoid misinterpreting malignant lesions. (Fig. 17a and b).

Invasive lobular carcinoma
Invasive lobular carcinoma may also present this aspect (Fig. 18a–d).

Rare malignant lesions
Other tumors also show as complex masses, such as medullary mucinous carcinoma, metaplastic carcinomas, breast sarcomas and metastases, particularly melanoma.

Interventional diagnostic strategy

Sampling techniques

Complex cystic masses are a challenge for interventional breast radiologists because the technical difficulty is directly related to the presence of a fluid component. Indeed, aspiration of the cystic material and its collapse during biopsies makes the associated solid component imperceptible or hardly perceptible and therefore more difficult to sample with certainty. The indications for biopsy must be clear and precise, while avoiding unnecessary

Figure 16. Solid papillary carcinoma. a: complex mass with a predominately solid component and irregular margins. Intralesional fine microcalcifications can be distinguished; b: histological examination found a malignant papillary structure surrounded by a network of fibrovascular cores.
Complex cystic breast masses in ultrasound examination

Figure 17. a: young woman consulting for a mass that had recently appeared in the left breast. Ultrasound exploration showed a type IV complex mass. Given her young age fibrocystic mastopathy was wrongly suggested; b: axillary exploration on the other hand corrected the diagnostic error since it revealed clearly suspect axillary lymph nodes with a focally thickened cortex. It was a grade III IDC with lymph node invasion.

procedures. Correlation with the mammogram data and the patient’s history is essential to avoid sampling benign complex masses (hematoma, fat necrosis, galactocele), where the alternative of close monitoring would seem to be more appropriate.

Fine needle aspiration biopsy

For palpable complex masses, biopsy procedures should be under ultrasound guidance to ensure correct sampling of the solid component. Fine needle aspiration is indicated as the first interventional procedure when there is a problem of diagnosis between a complicated cyst and a predominantly cystic complex mass. If a purulent liquid is collected, bacteriological analysis should be requested. If the liquid is hemorrhagic, it should be sent for cytological analysis [27,28]. After any fine needle aspiration biopsy, the lesion must be reassessed. If there is partial or complete collapse of the lesion, a post-biopsy marker should be left at the site of the initial image [29].

Biopsies

If a solid component remains after fine needle aspiration biopsy, core biopsies should be performed in the same session; necrotic components of cancers may not contain malignant cells [30].

Where there is a proven solid component, core biopsies will be performed in the first place whenever there are unfavorable signs (microcalcifications or architectural distortion) in a mammogram. For predominantly solid lesions, a 14-gauge needle is perfectly suitable. On the other hand, for lesions which are predominantly cystic and have small parietal nodules, a vacuum-assisted macrobiopsy system

Figure 18. a: type IV complex mass; b: microbiopsy performed with a 14G system; c: because of partial collapse a post-biopsy clip was inserted; d: histology indicated invasive lobular adenocarcinoma. Proliferation of independent cells or cells connected in narrow lines within a scleroelastotic stroma. Marked cytonuclear atypia.
with 8 or 10-gauge needles is preferable. If the mass is associated with calcifications, an X-ray of the samples should be taken. A post-biopsy marker should always be inserted at the end of the procedure if the residual mass is difficult to see [29].

Radiologic/pathologic correlation

Radiologic/histopathologic concordance must be established and the lesion definitively classified (multidisciplinary staff). It must therefore be possible to explain the signs shown by each complex mass from the histopathological data. The pathologist must have a detailed description of the lesion to be able to compare the histopathological with the ultrasound appearance.

If there is concordance

If there is concordance between the imaging and the histopathology, follow-up after 6 months can be proposed before returning to classic monitoring, in order to minimize the risks of false negatives [30].

Any diagnosis of lesions with a risk

Any diagnosis of lesions with a risk of underestimation (papillary lesion, phyllodes tumor, atypical ductal hyperplasia, in situ nodular neoplasia) requires surgical ablation; the rate of malignancy found on ablated tissue varies between 30% and 38% [31–33]. The risk of underestimating the malignancy of papillary lesions is between 8% and 14% [22,34] and this is all the greater when the papillomas are peripheral (compared with centrally located papillomas, i.e. retroareolar).

If there is discordance

If there is discordance, the whole case should be reexamined: correct targeting, representativeness of the samples. If necessary new percutaneous biopsies or a surgical biopsy will be discussed.

Conclusion

Complex cystic masses are lesions of an indeterminate nature, classified at least as ACR4 and requiring percutaneous biopsy and/or surgical ablation. Ultrasonography under good conditions (correct adjustment, use of harmonic and/or compound mode, Doppler and elastography) can characterize these lesions and guide biopsies. There is a wide range of diagnoses, ranging from benign lesions (inflammatory and/or modified cyst, post-therapeutic changes, fibroadenoma) to high risk or atypical lesions (papilloma, phyllodes tumor), or even malignant lesions (intracystic papillary or solid carcinoma, necrotic ductal carcinoma, lobular carcinoma). With a rate of malignancy varying from 23% to 31%, any complex lesion must be characterized and carefully sampled. Papillomas and high risk lesions must be surgically ablated.

**TAKE-HOME MESSAGES**
- Complex masses are classified as ACR4.
- They require histological verification.
- Radiologic/pathologic correlation is essential (representativeness of the samples, suitable management).
- The rate of malignancy varies between 23 and 31%.

**Disclosure of interest**

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

**References**

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