CONTINUING EDUCATION PROGRAM: FOCUS...

Solid masses: What are the underlying histopathological lesions?

A. Jalaguier-Coudray\textsuperscript{a,}*, J. Thomassin-Piana\textsuperscript{b}

\textsuperscript{a} Department of Radiology, Institut Paoli-Calmettes, 232, boulevard Sainte-Marguerite, 13009 Marseilles, France
\textsuperscript{b} Biopathology Department, Institut Paoli-Calmettes, 13009 Marseilles, France

KEYWORDS
Breast;
Ultranosography;
Mass;
Benign;
Cancer

Abstract
The ultrasound signs of breast masses are explained by the histopathological data. Ultrasound masses are classified according to their shape and margin. Round or oval masses are benign when their margins are circumscribed (fibroadenoma, intramammary lymph node); on the other hand, with non-circumscribed margins (microlobulated or irregular), masses that are round or oval may be cancers. Seven histological types of round cancers have been identified: grade III invasive ductal carcinoma, colloid or mucinous carcinoma, medullary carcinoma, intramammary metastases, intracystic papillary carcinoma, lymphoma and high-grade phyllodes tumors. Irregularly shaped ultrasound masses with non-circumscribed margins are predominantly cancers but may in some cases be benign lesions such as sclerosing adenosis, a radial scar, fibroadenoma or phyllodes tumor.

The ultrasound signs of breast masses are explained by the histopathological data. The shape and the margin of a mass depend on its histological type and its tissue composition. In practice, in ultrasonography there are two major groups of breast masses: round or oval masses and irregularly shaped masses.

Round and oval masses

Fibroadenoma

Fibroadenoma (FA) is by far the most widespread benign breast tumor. A fibroadenoma can be encountered at any age, but most frequently occurs in young women (25–35 years old),

\textsuperscript{*} Corresponding author.
E-mail address: aureliejalaguier@yahoo.fr (A. Jalaguier-Coudray).

2211-5684/$ – see front matter © 2013 Éditions françaises de radiologie. Published by Elsevier Masson SAS. All rights reserved.
http://dx.doi.org/10.1016/j.diii.2013.12.014
with a second perimenopausal peak at about 50 years of age. FA is a hormone-dependent tumor, sensitive to estrogens: its radiohistological appearance thus varies over time.

Macroscopically, a FA appears oval or macrolobulated and typically may measure up to 3 cm. There is a peripheral pseudocapsule in contact with the packed and displaced adjacent mammary parenchyma, so that the surgeon is able to enucleate the lesion easily during surgery (Fig. 1). Microscopically, the FA develops at the expense of the terminal ductal lobular unit and contains a variable proportion of stroma and epithelial tissue (Fig. 2). The stromal component is more or less cellular and may include myxoid and hyaline changes and calcifications. When the FA shows cystic alterations, apocrine metaplasia or sclerosing adenosis, it is known as complex fibroadenoma (Fig. 3). The stromal component increases with the age of the patient and can become calcified; the epithelial component decreases (Fig. 4) [1].

The definition of juvenile FA is not the age at which it appears — only 5 to 10% of FAs in adolescents are juvenile FA — but the histological appearance. Juvenile FA is defined microscopically by the presence of a very richly cellular stroma. Differential diagnosis with a phyllodes tumor can be difficult, in particular from biopsy samples. The long axis of a juvenile FA can measure up to 6 to 10 cm (Fig. 5) [2,3].

FA is a benign tumor. In rare cases (1/1000), as in normal breast tissue, carcinomas in situ can develop within the FA. These are predominantly lobular carcinomas in situ but in 15% of cases they are ductal (Fig. 6) [4].

On clinical examination, a FA is a painless, mobile, firm mass. It may become painful when necrotic changes occur, particularly during pregnancy and lactation (partial or complete infarction). FAs may be multiple and bilateral in 20 to 25% of cases.

In ultrasound, the typical appearance of FA is of a slightly macrolobulated (two to three macrolobulations), oval mass, with its long axis parallel to the skin and a well-defined circumscribed margin, an isoechoic or discretely hypoechoic, homogeneous, internal echostructure, sometimes with posterior acoustic enhancement, and the presence of a fine continuous peripheral capsule (corresponding histologically to the adjacent compressed mammary parenchyma). The FA may have internal septa visible with ultrasound (Fig. 7a) [5–7].

FA may also have a less typical ultrasound appearance [8,9]:

Figure 1. Ultrasound and histological appearance of a typical fibroadenoma: a: ultrasound appearance of a well-defined oval mass, corresponding histologically to a fibroadenoma; b: histological section of a tumorectomy sample (×1.25 magnification) from a fibroadenoma. A peripheral pseudocapsule can be seen (arrows) due to compression of the adjacent breast parenchyma (asterisk).

Figure 2. Histological appearance of a fibroadenoma. Histological section (×20 magnification) of a fibroadenoma showing the uniformly distributed, biphasic, epithelial (arrows) and stromal (asterisk) proliferation.

Figure 3. Histological appearance of a complex fibroadenoma. Histological section (×10 magnification) showing a fibroadenoma with apocrine metaplasia and sclerosing adenosis (arrows).
Solid masses: What are the underlying histopathological lesions?

Figure 4. Ultrasound and histological appearance of an old fibroadenoma: a: ultrasound appearance showing a mass with poorly defined margins (arrows), classed as ACR4, in a 60-year-old patient. Ultrasound-guided biopsy was performed; b: histological section (×10 magnification) showing an old fibroadenoma with a largely stromal component (asterisk) responsible for the irregular margins seen with ultrasound.

Figure 5. Ultrasound and histological appearance of a juvenile fibroadenoma: a: ultrasound appearance of a macrolobulated oval mass, measuring 5 cm, in a 15-year-old girl. Ultrasound-guided biopsy was performed; b: histological section (×1.25 magnification) of a juvenile fibroadenoma; c: histological section (×10 magnification) of a juvenile fibroadenoma showing the presence of a richly cellular stroma.

Figure 6. Ultrasound and histological appearance of a fibroadenoma with carcinoma in situ lesions: a: ultrasound appearance of a round mass, containing fine central calcifications, classified as ACR4. Ultrasound-guided biopsy was performed; b: histological section (×10 magnification) showing a fibroepithelial component in a fibroadenoma colonized by carcinoma in situ lesions (arrows).

- it may be round (particularly for small FAs) (Fig. 7b);
- its echogenicity is variable and depends on its tissue composition: a cellular FA will be more hypoechoic and a fibrosed FA, with hyaline degeneration, will often be more hyperechoic (Fig. 8);
- its margin may be non-circumscribed, microlobulated, irregular or angular: as the patient ages or because of histological changes (infarction, hyalinization), the FA undergoes fibrous modifications with an increase in the stromal component: its margin becomes irregular or microlobulated in 5% of cases, its internal echogenicity becomes more heterogeneous, and posterior acoustic attenuation may appear, particularly when the FA becomes calcified. These changes may pose problems of differential diagnosis with a breast carcinoma (Fig. 4) [10].
Figure 7. Variable ultrasound appearance of a fibroadenoma: a: typical appearance of a fibroadenoma: ultrasound appearance of a fibroadenoma showing the presence of microlobulations and internal septa (arrows); b: round shape of a fibroadenoma in ultrasound.

Figure 8. Variable echogenicity of a fibroadenoma depending on its histological components: a: marked ultrasound hypoechogenicity of a fibroadenoma because of its histological fibroepithelial cellular component (asterisk); b: marked ultrasound hyperechogenicity of a fibroadenoma because of its histologically largely stromal component (arrows).

Phyllodes tumor

Phyllodes tumor (PT) is a rare tumor (1% of breast tumors, 2% of fibroepithelial tumors) and can be benign or malignant, with a high risk of local recurrence of about 30%. Frequency peaks between 40 and 49 years of age, but a PT can also occur in an adolescent.

Microscopically, a PT is a fibroepithelial tumor. The characteristic of a PT is the presence of a hypercellular fibromyxoid stroma containing fibroblasts, myofibroblasts (more rarely, giant cells) and large spaces covered by an epithelium with a fern leaf appearance (Fig. 9) [11].

PTs are classified into three categories depending on their degree of proliferation and stromal differentiation [12]:

- benign PTs (grade 1), frequent (60% of cases): the stroma has cells with a few mitoses (<5 mitoses in 10 fields) and little atypia; macroscopically the margins are regular (Fig. 9);
- borderline PTs (grade 2): the stroma show moderate atypia and a rate of mitosis of <5 in 10 fields;
- malignant PT or phyllodes tumor sarcoma (grade 3), (30% of cases): the stroma has atypical and pleomorphic cells, a high rate of mitosis (>5 in 10 fields) and macroscopically the margins are very irregular with infiltration of the peripheral mammary parenchyma. The presence of necrotic changes is highly suggestive of a malignant PT (Fig. 10).
Solid masses: What are the underlying histopathological lesions?

The diagnosis between a benign or malignant phyllodes tumor can be difficult on breast biopsies. In more than 80% of cases, PT is detected in the clinical examination, because of its rapid growth. Clinically, benign PT is similar to fibroadenoma. On the other hand, malignant PT presents characteristics in the clinical examination that are suspect, with tumors that are large, hard on palpation and not very mobile (because of the infiltration of peripheral breast tissue) (Fig. 10).

In ultrasound, grade 1 PTs can appear like FAs: oval, round or lobulated in shape, with a regular, circumscribed margin sometimes with posterior acoustic enhancement (Fig. 11). The following signs may point towards a diagnosis of PT but can also be present in remodeled FAs: an indistinct, non-circumscribed margin, internal heterogeneity, internal cystic changes (corresponding to gelatinous, cystic or necrotic areas or to epithelial fissures highly suggestive of phyllodes tumors) (Fig. 10c). Internal calcifications and posterior attenuation are rare [13–17].

Like other sarcomas, malignant PT rarely metastasizes to the lymph nodes. Hematological dissemination, on the other hand, is common, with extension to the liver and lungs.

Papilloma

Papillomas (PAP) are rare (1%), benign, fibroepithelial tumors. As a general rule, a PAP is indicated clinically, even when small, by a clear or bloody discharge (80%). It is rarely palpable. Histologically, a PAP is seen as a cellular proliferation organized on a fibrovascular core (Fig. 12) [18].

A PAP may be central or peripheral. We must differentiate (Table 1) between:

- a solitary or central papilloma, which occurs in perimenopausal women in the peri- or subareolar region. It is secretory, often resulting in lactiferous duct dilatation and a discharge from the nipple (70% of cases) (Fig. 12). Its size is variable (0.5 cm to 3.5 cm). A central PAP has a much lower risk of degeneration than a peripheral PAP; in rare cases, there are foci of atypical ductal hyperplasia or carcinoma in situ. The histological appearance of central PAP is variable (sclerosing adenosis, apocrine metaplasia). It can twist on its pedicle and become infarcted, leading to a bloody, single orifice discharge;
- peripheral PAP, which occurs in younger patients than central PAP. Nipple discharge is less common, so that it is usually discovered by ultrasound. Lesions are often multiple, small (< 2 –3 mm) and localized in the distal segments of the ducts. Peripheral PAPs are recurrent and in 12% of

Figure 9. Histological appearance of a grade 1 phyllodes tumor. Histological section (× 10 magnification) of a grade 1 phyllodes tumor showing the characteristic fern-leaf appearance (large spaces covered by an epithelium: arrows).

Figure 10. 45-year-old patient with a grade 3 phyllodes tumor: a: 45-year-old patient with a mass in the right breast, ulcerated to the skin; b: ultrasound appearance showing a well-defined mass, with central cystic alterations (arrows); c: histological appearance (× 40 magnification) showing fibroepithelial proliferation containing many atypical cells and numerous mitoses.

Figure 11. Ultrasound appearance of a grade 1 phyllodes tumor proven by microbiopsy.
cases are associated with precancerous lesions or cancers (atypical ductal hyperplasia, ductal carcinoma in situ);
- juvenile papillomatosis affects patients between 20 and 30 years old but can also be found in 50-year-old women. Histologically, juvenile papillomatosis consists of a great many small cysts presenting papillary hyperplasia, sometimes atypical (10% of cases) but without true papilloma. Its ultrasound appearance has given it the name ‘Swiss cheese disease’ because of the presence of many small cysts.

With ultrasound, the appearance of PAP depends on its size and extension to the ducts. When PAP is not associated with lactiferous duct dilatation, its appearance is difficult to differentiate from a benign breast nodule such as FA. A papilloma is easily identified with ultrasound when it is located in a dilated lactiferous duct: round in shape, with a circumscribed margin, hypoechoic, often heterogeneous with a central vascular pedicle in Doppler mode (Fig. 12). A PAP may seem to be encysted when the duct is obstructed and very dilated, looking like a nodular cyst. It may be remodeled and become infarcted, and consequently be more hypoechoic and attenuating, and calcifications may appear. PAPs show anterograde growth towards the nipple (Fig. 13). In ultrasound, the differential diagnosis is a dilated duct with sediment: making the patient change position causes movement of the sediment [19,20].

**Medullary carcinoma**

Medullary carcinoma (MC) is rare (5% of breast cancers). It is encountered in young women, representing 10% of breast carcinomas in patients less than 35 years old. It is more often bilateral (3–18%) and multicentric (10%). It grows rapidly and is often discovered by palpation. The prognosis for pure MC is intermediate between IDC and cancers with a good prognosis (mucinous, papillary, tubular carcinoma). The 5-year survival rate is 89%, but where there is lymph node invasion, it is no more than 42%. Several studies seem to have found a link between the presence of a BRCA1 mutation and the occurrence of medullary carcinoma (30 to 60% of medullary carcinomas are found in the context of a BRCA1 mutation) [21].

Macroscopically, MC is a well-delimited, lobulated cancer. The combination of a poorly differentiated carcinomatous component and a predominant lymphoid infiltration (WHO definition) (Fig. 14) characterizes its histological appearance. Its phenotypic profile is that of a triple-negative cancer [22].

![Figure 12. Ultrasound and histological appearance of a papilloma: a: single orifice clear discharge due to a papilloma in this 55-year-old patient; b: histological appearance (<4 magnification) of a papilloma showing cellular proliferation organized around fibrovascular cores; c: ultrasound appearance of a papilloma in a dilated lactiferous duct (arrow).](image1)

<table>
<thead>
<tr>
<th>Papilloma</th>
<th>Central or solitary</th>
<th>Peripheral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Perimenopausal</td>
<td>Younger</td>
</tr>
<tr>
<td>Location</td>
<td>Peri- or retroareolar</td>
<td>Distal ducts</td>
</tr>
<tr>
<td>Nipple discharge</td>
<td>Common 70%</td>
<td>Rare</td>
</tr>
<tr>
<td>Size</td>
<td>5–35 mm</td>
<td>Chance ultrasound discovery</td>
</tr>
<tr>
<td>Number</td>
<td>Single</td>
<td>&lt;2–3 mm</td>
</tr>
<tr>
<td>Associated precancerous or cancerous lesions</td>
<td>Rare</td>
<td>Multiple</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Common 12% (CIS, ADH)</td>
</tr>
</tbody>
</table>

Table 1

CIS: carcinoma in situ.

![Figure 13. Ultrasound view of a papilloma progressing towards the nipple (arrows).](image2)
Solid masses: What are the underlying histopathological lesions?

159

Figure 14. Ultrasound and histological appearance of a medullary carcinoma: a: macroscopic section showing a round mass, whitish/pink/beige on cutting; b: histological appearance (×1.25 magnification) showing a mass with smooth regular margins; c: histological section (×20 magnification) showing carcinomatous proliferation composed of syncytial cells with marked cytonuclear atypia; d: ultrasound appearance of the medullary carcinoma showing a well-defined, hypoechoic mass with macrolobulated margins, with posterior acoustic enhancement.

With ultrasound, pure MC is very hypoechoic with a pseudocystic appearance (Fig. 14). Doppler mode shows numerous intratumoral vessels allowing it to be differentiated from a cyst with thick contents. A MC always has posterior acoustic enhancement: this is explained by its high cellularity and the presence of necrotic/hemorrhagic changes. Because of their rapid growth, MCs show little or no peripheral stromal reaction [23–25], which explains why their margins are regular, most of the time microlobulated and non-circumscribed, but sometimes circumscribed.

Colloid carcinoma

Colloid carcinoma (CC), also called mucinous carcinoma, is rare (2% of breast cancers). In its pure form, its prognosis is favorable, even excellent, with a 10-year survival rate of 90%, whereas when combined with a ductal component, it has the same prognosis as IDC (only 60%). CC is more likely to affect older women (mean age 63 years). It develops slowly; the risk of nodal metastasis is low (<6%) but higher in its mixed form (36%).

Figure 15. Ultrasound and histological appearance of a colloid or mucinous carcinoma: a: histological section (×1.25 magnification) showing a colloid carcinoma with well-defined margins; b: histological section (×4 magnification) showing the presence of clumps of carcinomatous cells (arrows) within lakes of mucus (asterisk); c: ultrasound image showing the colloid carcinoma as a homogeneous, isoechoic, round mass with well-defined margins.
Microscopically, CC may be either pure or mixed. In its pure form, it is characterized by clumps of cells or isolated carcinomatous cells floating in large lakes of mucin, which are present in more than 75% of the tumor (Fig. 15). There is no associated peripheral stromal reaction. In its mixed form, it is combined with invasive ductal carcinoma. Microscopically, the morphological appearance of CC depends whether the form is pure or mixed. Pure CC has smooth or lobulated margins (Fig. 15). In its mixed form, CC presents a peripheral fibrous stromal reaction and is therefore more often palpable, with a hard tumor on clinical examination, and spiculated and irregular margins macroscopically.

The appearance in ultrasound varies depending whether the form is pure or mixed. In its pure form the mass is iso- or hypoechoic and microlobulated, most of the time with non-circumscribed margins (Fig. 15). In its mixed form, the ultrasound appearance depends on the percentage of invasive ductal carcinoma, giving it an angular, spiculated, non-circumscribed margin and posterior attenuation [26–28].

Intracystic papillary carcinoma

Papillary carcinoma (PAPC) is also rare (1–2% of breast carcinomas). It more often affects post-menopausal women (mean age 63–67 years old). PAPC is a cancer with a good prognosis.

Macroscopically, it is a well-defined lesion encapsulated by peripheral fibrosis (Fig. 16). It often appears blackish, because of frequent hemorrhagic changes (due to torsion around its pedicle). The presence of hemorrhagic changes, areas of infarction and fibrosis may result in irregular margins. Microscopically, PAPC is defined by a tumoral lesion with papillary architecture (Fig. 16) associated with the development of carcinoma in situ within a dilated lactiferous duct. Immunohistochemical markers targeting myoepithelial cells are negative, thus reflecting the invasive character.

With ultrasound, the papillary lesion shows as a solid nodule, with an often discreetly microlobulated margin, sometimes seen within a dilated duct. Its echostructure is more or less heterogeneous, corresponding to cystic or hemorrhagic changes (Fig. 16). Doppler mode reveals rich internal vascularization, with many vessels (Fig. 17). PAPC can also appear in an ultrasound examination as a cyst with a mural nodule or thick partitions. Most of the time, the wall thickening and thickened septa within a mammary cyst are the consequence of benign lesions (papillary apocrine metaplasia, clots). The presence of a dilated duct prolonging a cyst suggests a papillary lesion, but ultrasonography cannot differentiate between a papilloma and a papillary carcinoma [29,30].

Metastases

Breast metastases are rare (1% of breast carcinomas). Primary cancers, which tend to metastasize to the breasts are melanoma, bronchial cancer, lymphoma, ovarian carcinoma and digestive cancers. Other primary cancers, which can spread to the breast are medullary thyroid cancer and renal carcinoma. In men, prostate carcinoma can metastasize to the breast. These breast metastases most often appear in the context of polymetastatic disease. In 15% of cases, breast metastases are the way the cancer is revealed.

Macroscopically, breast metastases are often well delimited, because they displace the peripheral mammary tissue without invading it (absence of peripheral stromal reaction) (Fig. 18). Microscopically, intramammary metastases have the same appearance as the primary cancer. In some cases, when tumor proliferation is very undifferentiated, it is difficult for the pathologist to determine whether it is an undifferentiated primary mammary carcinoma or a secondary intramammary lesion: in this case, he may make use of immunohistochemical and hormone receptor techniques to make the diagnosis.

With ultrasound, breast metastases are single or multiple, round or oval masses, often with a microlobulated margin (because of the absence of any peripheral stromal reaction); they are hypoechoic, sometimes with posterior acoustic enhancement (because of their high cellularity) (Fig. 18). They may simulate benign mammary masses.

Figure 16. Ultrasound and histological appearance of an invasive intracystic papillary carcinoma: a: histological section (×1.25 magnification) showing a well-defined lesion with papillary architecture; b: histological section (×20 magnification) with a fibrovascular arborescence (arrows) with no myoepithelial cells at the periphery; c: ultrasound image showing a hypoechoic mass with a round, anechoic center (caused by central cystic changes) with discreetly irregular margins.
Solid masses: What are the underlying histopathological lesions?

Figure 17. Ultrasound and histological appearance of an intracystic papillary carcinoma: a: ultrasound image showing a discreetly heterogeneous, round mass with microlobulated margins, shown to be an infiltrating papillary carcinoma on microiopsy; b: power Doppler ultrasound image showing the presence of rich central vascularization.

Figure 18. Ultrasound and histological appearance of intramammary metastasis of a malignant melanoma: a: histological section (×1.25 magnification) showing a well-defined round lesion; b: histological section (×20 magnification) showing the presence of atypical tumor cells containing deposits of melanic pigment (arrows); c: ultrasound image showing a very hypoechoic, well-defined, oblong breast lesion which microbiopsy showed to be intramammary metastasis of a malignant melanoma.

Figure 19. Ultrasound and histological appearance of intramammary metastasis of an ovarian cystadenocarcinoma: a: ultrasound image showing a round intramammary mass with microlobulated margins; b: histological section from a microbiopsy sample (×40 magnification) of a proliferation of adenocarcinoma cells due to intramammary metastasis of a serous cystadenocarcinoma.
lesions rather than mammary carcinomas. No association with calcifications has been recorded in the literature, apart from for ovarian and medullary thyroid cancers, where amorphous calcifications can occur (Fig. 19) [31–34].

Lymphoma

Primary non-Hodgkin lymphoma of the breast (PNHLB) is rare. For it to be considered as primary, no other lymphomatous site must exist apart from possibly in the axillary lymph nodes. PNHLB may occur at any age (15–85 years, with a mean age of 55 years).

In the majority of cases (70%), there is a single breast mass, frequently associated with axillary lymphadenopathies (50% of cases). Multiple masses or an inflammatory breast are less common (9%). Clinically, PNHLB is seen as a rapidly developing palpable mass. It is frequently associated with edema and erythema affecting the area of skin covering it. PNHLB is richly cellular, which makes it appear very hypoechoic or even pseudocystic. There is no peripheral stromal reaction, which explains the circumscribed margin [35–37] (Fig. 20).

Intramammary Hodgkin lymphoma is rarer. Its ultrasound appearance is identical to PNHLB.

Grade III ductal carcinoma

Invasive ductal carcinoma (IDC) is the most common histological type. It originates in the terminal ductal lobular unit. The majority of IDCs do not have specific histological characteristics and are therefore classified as not otherwise specified (NOS). IDCs represent 80% of breast carcinomas. The mean age at diagnosis is 56.

Microscopically, Scarff Bloom Richardson (SBR) grade III IDC consists of a poorly differentiated carcinomatous proliferation composed of cells with moderate to marked cytologic atypia and a high mitotic rate (Fig. 21).

In ultrasound, the round shape of grade III IDCs results from the absence of peripheral stromal reaction, because of the rapid growth of the tumor. Grade III IDC appears as a rounded, hypoechoic lesion, the long axis of which is not parallel to the skin, and with a microlobulated margin. There is no posterior acoustic attenuation; on the other hand, real posterior acoustic enhancement can be seen due to the intratumoral hypercellularity [38–40] (Fig. 21).
Fibrocystic changes

Fibrocystic changes may occur in the terminal ductal lobular unit (TDLU) resulting in the formation of an ultrasound mass. The TDLU may be:

- distended by apocrine metaplasia or simple papillary hyperplasia (Fig. 22);
- distended by microcysts, not visible with ultrasound, containing apocrine metaplasia, debris and macrophages.

Fat necrosis

The ultrasound appearance of fat necrosis is very variable. Most of the time, it appears as a finely echogenic solid mass with a circumscribed margin. Sometimes, it can be associated with a mural intracytic nodule. If the mammographic appearance is typical, it is not necessary to biopsy (Fig. 23) [41–44]. On the other hand, fat necrosis can appear as an attenuating mass with an irregular margin, because of fibrous changes, making it impossible to differentiate it from a breast carcinoma without histological evidence.

Intramammary lymph node

Intramammary lymph nodes are common and can be visible with ultrasound. They are often smaller than axillary lymph nodes. They may be seen in any breast quadrant but tend to occur more in the superolateral quadrant (Fig. 24) [45].

Irregularly shaped masses

Grade I or II invasive ductal carcinoma

Grade I or II invasive ductal carcinoma (IDC) is accompanied by a peripheral stromal reaction. This reaction is not diffusion of the cancer into the peripheral breast tissue but the gradual attraction of peripheral breast tissue. The better differentiated the cancer, the greater the peripheral stromal reaction; this is seen in mammograms by the presence of spicules, and in an ultrasound examination by a hyperechoic peripheral rim (Fig. 25). Conversely, with a rapidly growing IDC (grade III) there is little or no peripheral stromal

---

**Figure 22.** Radiohistological appearance of apocrine metaplasia: a: ultrasound appearance showing a hypoechoic, oblong mass, classified ACR4 given the way it occurred and which underwent ultrasound-guided microbiopsy; b: histological section of a microbiopsy sample (×1.25 magnification) showing florid apocrine metaplasia; c: histological section of a microbiopsy sample (×10 magnification) showing proliferation with papillary architecture of large eosinophilic cells related to the apocrine metaplasia.

**Figure 23.** Radiohistological appearance of fat necrosis: a: ultrasound image of a cyst with a hyperechoic mural nodule, seen to be non-vascularized with power Doppler; b: corresponding mammographic image showing the typical appearance of fat necrosis; c: histological section (×10 magnification) showing the typical appearance of fat necrosis with central lipid vacuoles.
reaction, which explains ultrasound images and mammograms of well-delimited cancers [38].

Invasive lobular carcinoma

The particular histological appearance of invasive lobular carcinoma (ILC) explains the great difficulty of detecting it in imaging.

Its histology is characterized by a proliferation of small round, non-cohesive cells, typically arranged in single file and infiltrating the mammary tissue without disorganizing it (Fig. 26). Ultrasound can show invasive lobular carcinoma as a mass with an irregular margin or areas of attenuation or there may be nothing seen with ultrasound (Fig. 27) [46–50].

Tubular carcinoma

Tubular carcinoma (TC) is a rare cancer (2%). It tends to affect younger women (mean age: 40). The prognosis for tubular carcinoma is very good with a 15-year survival rate of 100% for lesions of less than 10 mm.

Histologically, tubular carcinoma is characteristically a very well differentiated carcinoma, forming tubes lined with a single layer of tumor cells. It is associated with a considerable fibrous stromal reaction around the tubes (Fig. 28). A carcinoma is said to be pure tubular when more than 50 to 90% of its content is TC. TC often develops within a radial scar [51–53].

With ultrasound, a tubular carcinoma has a spiculated, non-circumscribed margin, with a hypoechoic peripheral halo due to the considerable stromal reaction. It is either isoechoic or discretely hypoechoic, with posterior acoustic attenuation (Fig. 28).

Radial scar

A radial scar (RS) is a lesion commonly found by chance when it is small, in mastectomy tissue or in macrobiopsies performed for a focus of calcification.

Histologically, the RS is characterized by a fibrous, elastic center around which tubes and lobules are arranged radially (Fig. 29). The breast parenchyma, thus stretched,
Solid masses: What are the underlying histopathological lesions?

Figure 26. Histology of the invasive lobular carcinoma: a: Histological section (×20 magnification) showing the presence of small, round cells in single file due to an invasive lobular carcinoma; b: histological section (×10 magnification) showing tumor cells infiltrating the breast tissue without disorganizing it (arrows) caused by an invasive lobular carcinoma.

An RS is often detected on the mammogram from an image of distortion or a spiculated mass with a light center. Breast ultrasonography is performed to find a target for a biopsy. The ultrasound appearance of an RS is not specific. It appears as a lesion with a spiculated or angular non-circumscribed margin, with a peripheral hyperechoic rim and posterior acoustic attenuation (Fig. 30). It is impossible to differentiate an RS from a well differentiated IDC or TC using ultrasound [55,56].

Figure 27. Ultrasound images of the invasive lobular carcinoma: a: ultrasound image showing a mass with irregular margins. b: ultrasound image showing an attenuating hypoechoic area.

Figure 28. Ultrasound and histological appearance of a tubular carcinoma: a: histological section of the tumorectomy specimen (×1.25 magnification) showing the tubular carcinoma; b: Histological section of the tumorectomy specimen (×20 magnification) showing a very well differentiated carcinoma, forming tubes lined with a single layer of tumor cells, associated with a considerable fibrous stromal reaction around the tubes (asterisk); c: ultrasound image showing a mass with irregular margins and a peripheral hyperechoic halo indicating the considerable peripheral stromal reaction.

may show changes due to adenosis or apocrine metaplasia, or cystic changes. A radial scar can mimic TC; when viewed under the microscope, it is the presence of two cell layers, epithelial and myoepithelial, which distinguishes the two. In 10 to 30% of cases, the RS is associated with a carcinoma in situ or a tubular invasive carcinoma. The associated carcinoma is often small, partly touching the center of the radial scar (Fig. 30) [54]. For this reason, complete surgical ablation is recommended when the biopsy shows a spiculated mass related to a radial scar.
Figure 29. Histological appearance of a radial scar: a: histological section of a tumorectomy specimen (×1.25 magnification) showing a radial scar; b: histological section of a tumorectomy specimen (×10 magnification) showing a fibrous and elastotic center surrounded by tubes and lobules arranged radially.

Figure 30. Ultrasound and histological appearance of a radial scar associated histologically with a tubular carcinoma: a: ultrasound image showing a hypoechoic area with irregular, spiculated margins, with a peripheral hyperechoic rim and posterior acoustic attenuation (arrow); b: histological section of a microbiopsy sample (×1.25 magnification) showing a radial scar with a small tubular carcinoma in its center.

Sclerosing adenosis

Sclerosing adenosis is the benign hypertrophy of a lobule combined with fibrotic hypertrophy of its surrounding connective tissue. With ultrasound, it is seen as a nodule with a non-circumscribed microlobulated margin. If there is considerable fibrosis, the nodule may have a very angular and irregular margin simulating a carcinoma. There are frequently associated secretory dust-like calcifications, too small to be detected with ultrasound (Fig. 31) [57,58].

Figure 31. Ultrasound and histological appearance of a sclerosing adenosis: a: ultrasound appearance of sclerosing adenosis showing a mass with irregular margins; b: histological section of a microbiopsy sample (×10 magnification) showing hypertrophy of the surrounding tissue within a lobule.
Conclusion

To conclude, the ultrasound appearance of a mass depends on its histological composition. It is therefore essential for the radiologist to know the physiopathological and histological basics of mammary pathology. Indeed, a radiologist taking samples must analyze the histological results in the light of the radiological images and the ACR classification. He or she must therefore check the concordance or discordance of the results.

Disclosure of interest

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

References


