Inflammatory breast cancer- the real face of what you actually see

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Authors: E. V. Popa¹, M. Lesaru², M. Mihai²; ¹Braila/RO, ²BUCHAREST/RO
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Learning objectives

The aim of the study was:
- to review the imaging features of inflammatory breast cancer (IBC);
- to discuss the differential diagnosis;
- to point out the role of multimodality breast imaging in the management of the disease.
Background

Inflammatory breast cancer (IBC), also referred to as carcinomatous mastitis, is one of the rare subtypes of breast cancer, with an incidence of 2%-5% (1). The most important feature of this type of cancer is aggressive tumor growth that leads to a low 5-year survival rate of 25%-50% (2). The therapeutic management includes preoperative chemotherapy, mastectomy and radiation therapy, which has been shown to improve prognosis (3). Properly diagnosed disease is crucial to designing the best treatment modality and requires a multidisciplinary approach, where imaging plays a key role (1, 4).

Clinical features

At presentation, the breast is enlarged, indurated, warm, tender, erythematous and more or less painful, with the onset of symptoms within 3 month (4). Typically, the erythema involves more than one third of the skin, as compared to neglected locally advanced breast cancer with inflammatory developed changes (5). A common feature is that usually no palpable mass can be found (1). The skin is thickened, with a "peau d'orange" appearance, associated with flattening, blistering and even retraction of the nipple (1, 5). Palpable axillary lymph nodes, representing metastatic disease can be found in about 50% of cases (6).

Rapid progression of the disease is responsible in 20%-40% of patients with IBC for having distant metastases at presentation and common sites include the lungs, liver, bone and brain (7).

Imaging modalities

- Mammographic changes that should suggest the diagnosis are: enlarged breast, with diffuse increased density, stromal coarsening and skin thickening (1-3). Enlarged axillary lymph nodes are often present (1). Other rare yet important features include multiple tumor masses, architectural distortion and pleomorphic calcifications (1-3). Another role of mammography is in the surgical planning and to provide a baseline in assessing therapeutic response (1).

- Ultrasonography may also be an important tool in the initial diagnostic workup, when IBC is suspected. Whether a lump, focal edema and erythema or a mass discovered at mammography, US is helpful differencing a cystic lesion from a solid mass and further characterization of the mass lesion according to BI-RADS lexicon can be made: size, extent, margins (irregular, spiculated etc.) (1, 4). When mammographic changes are diffuse, US is performed in order to find a biopsy target and also guide the percutaneous core biopsy (1).
In cases of IBC, MR imaging is useful to assess the extent of the disease in the incident breast and the occult lesions in the contralateral breast (1, 9). Better evaluation of the lesion, considering size, contours, uptake, extent can be made at MRI, but one should bear in mind that tumor size can sometimes be very difficult to assess in extensive involvement, whatever the imaging modality (1). An initial MR examination provides a baseline for further follow-up assessment and treatment response (1). MR is the most accurate modality in detecting the primary breast lesion, especially when the conventional modalities indicate only diffuse abnormalities, in order to target biopsy (1, 4). Most common findings on contrast-enhanced MR are an irregular mass with spiculated margins, segmental or extensive nonmasslike enhancement with rapid uptake with wash-out or plateau curves and diffuse skin thickening (1, 10). Diffuse cutaneous and prepectoral high signal intensity on T2-WI indicating edema can increase the specificity of MRI for IBC and differentiate it from locally advanced breast cancer (1). In some cases, MR help indicate involvement of the pectoralis muscle by imaging abnormal pectoral enhancement, direct invasion or loss of the fat plane (1). Evaluation of the contralateral breast is of great value in women with inconclusive standard evaluation (1, 9, 10).

In order to confirm the diagnosis of carcinomatous mastitis both histologic proof of malignancy and clinical appearance of inflammation are required (1).

**Skin Punch Biopsy**

The pathologic characteristic of carcinomatous mastitis is the involvement of the dermal lymphatics which are blocked by tumor emboli and cause clinical signs of inflammation, although no true inflammatory criteria are found (12). However, this examination is not necessarily required because not all cases of IBC are positive with skin biopsy (1,12).

**Differential diagnosis** for carcinomatous mastitis include:

- breast infection (mastitis) caused by aerobic or anaerobic bacteria and granulomatous diseases, such as tuberculosis. A focal lump is usually indicative for abscess and prompt percutaneous drainage should be performed (1). If no or partial response to antibiotic therapy is obtained within 1-2 weeks, malignancy should be suspected (1).

- locally advanced non-inflammatory breast cancer. Large, superficially-located breast tumors may infiltrate the skin and produce erythema and induration that can mimic the appearance of IBS. Moreover, in such cases skin biopsy usually is not able to distinguish between the two types of neoplasm, because in both cases tumor emboli obstruct the dermal lymphatics (8). In order to differentiate this condition from IBC, one must consider the time period of symptomatic changes: a maximum three months period for carcinomatous mastitis and a more prolonged one (even years) for the locally-advanced non-inflammatory breast cancer (1).
Findings and procedure details

A retrospective review of a series of 128 patients who underwent US-guided core biopsy for the suspicion of breast neoplasm, between January 2014 and September 2015, in Fundeni Clinical Institute revealed histologically proved inflammatory carcinomas in 9 women (mean age 54 years, age range 37-82). In each patient, questionnaires, physical examination records, mammograms (at the time of diagnosis), records of the US examination and during biopsy, MR examinations (in selected cases) and histopathologic results were recorded and archived in our department and retrospectively analyzed. Where available, the start and duration of complaints were noted. The physical examination was performed by the radiologist in all the enrolled cases. At clinical examination, the presence of a mass- location, size, multiplicity, mobility related the deep structures, skin abnormalities- warmth, edema, erythema, nipple retraction, diffuse stiffness and axillary adenopathy were considered.

Mammographies in two standard planes of imaging (craniocaudal and mediolateral-oblique) were performed with Selenia Dimensions, Hologic. While analyzing the mammographies, the following features were regarded: skin thickening, trabecular coarsening and increased density, asymmetric focal density, presence of a mass, microcalcifications and the criteria were evaluated according to Breast Imaging Reporting System.

Both breast and axillary US was performed in all cases in order to detect a biopsy target or to assess axillary or intramammary lymphadenopathies.

All the enrolled patients had clinical evidence of inflammatory disease with the following skin abnormalities: warmth, erythema, edema, and/or "peau d-orange". Masses were detected in three cases at breast palpation.

Initial mammographies were abnormal in all the cases, with multiple findings underlined. The most common mammographic finding was skin thickening (in eight cases) (Fig. 1 on page 8, Fig. 2 on page 8, Fig. 4, Fig. 8 on page 14). Trabecular coarsening suggesting edema was found in four cases (Fig. 2 on page 8 Fig. 4). In one case the only mammographic changes were unilateral skin and trabecular thickening ( Fig. 2 on page 8 ).

Microcalcifications suspected of being malignant were identified in three cases (Fig. 1 on page 8 Fig. 4 Fig. 7 on page 13). The features were characterized as pleomorphic and all had an accompanying mass or asymmetric focal density. A diffuse increase in density was noted in three cases while one patient had a focal asymmetric density. Four women presented architectural distortion (Fig. 1 on page 8 Fig. 6 on page 12 ) and also four cases with spiculated masses were noticed (Fig. 7 on page 13 ). One
patient had diffusely decreased breast volume as compared to the contralateral (Fig. 1 on page 8).

At US both skin thickening and parenchymal echogenicity impairment, with dilated lymphatic channels associated, suggesting edema were seen in five patients (Fig. 2 on page 8, Fig. 3 on page 9, Fig. 8 on page 14). The US was also used to assess the masses discovered at mammography, or to find a biopsy target (Fig. 1 on page 8, Fig. 4, Fig. 5 on page 11, Fig. 6 on page 12, Fig. 7 on page 13, Fig. 8 on page 14). In one patient, only an intramammary lymphadenopathy was found, besides skin thickening and diffusely increased echogenicity of the parenchima (Fig. 3 on page 9) and another patient presented US signs of edema in the breast and axillary adenopathy (Fig. 2 on page 8).

In one patient MRI indicated an extensive nonmasslike enhancement in the right breast, highly suspicios for malignancy (Fig. 4).

One woman with previous surgery, more than 10 years before, for invasive ductal carcinoma, had in the same breast clinical signs of inflammation, mammographic abnormalities along with multiple small hypoechoic nodules found on US and was regarded as an inflammatory recurrence of a primary non-inflammatory breast cancer—also called secondary inflammatory breast cancer (1) (Fig. 8 on page 14).

All the 9 patients had pathologic confirmation of the malignancy. In 6 cases inflammatory infiltrates were present along with neoplastic features. Another one case with high clinical and imagistic suspicion of carcinomatous mastitis was reported as chronic granulomatous mastitis at the pathologic examination (Fig. 9 on page 15).
37-year-old woman presented with warmth, tenderness of the upper two thirds of the left breast, associated with peau d’orange aspect in the inferior half of the breast.

Fig. 1: Mammographic changes (a- craniocaudal projection) consist of global reduced volume of the left breast, skin thickening (arrows), trabecular coarsening (arrowheads) architectural distortion and multiple pleomorphic microcalcifications (a,b), highly suspicious for malignancy. US examination (c,d performed during-guided core biopsy) revealed three irregular hypoechoic nodules (c, d-white arrows), two of them containing hyperechoic spots, suggestive for microcalcifications (d- black arrows). Pathologic analysis: ductal invasive G2 carcinoma associated with DCIS high nuclear grade with cribriform and solid patterns.

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Fig. 2: Mediolateral oblique mammogram (a) shows only skin thickening (arrow) and trabecular coarsening (arrowhead) of the left breast and some benign bilateral calcifications. US findings consisted in diffuse edema in the adipose tissue and skin thickening (not shown). After incomplete clinical response to one-week of antibiotic and anti-inflammatory treatment the one month follow-up ultrasound appearance was the same with a slightly enlarged axillary lymph node with a nodular thickening of the cortex (b- arrow). US-guided core biopsy of the adenopathy (c) demonstrated poorly-differentiated carcinoma.

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Fig. 3: US shows skin thickening (star), diffuse edema in the adipose tissue with no suspect hypoechoic mass except for one small node suggestive for intramammary adenopathy in the upper-outer quarter (arrows). Axillary adenopathies were also found (b). US-guided biopsy from the intramammary node was performed and histopathological exam revealed lymph node metastasis from G2/G3 carcinoma ER+ PR+, equivocal HER2;
Fig. 4: Medio-oblique mammography (a): skin thickening and trabecular coarsening (arrow), stromal coarsening in the upper quarters and polymorphic microcalcifications (b) indicative of comedonecrosis. US (c): multiple hypoechoic masses (arrow), with irregular contours and some hyperechoic spots within the lesions, suggesting microcalcifications. MRI postcontrast maximum intensity projection (MIP) reconstruction (d): right breast diffusely enlarged with a nonmasslike enhancing lesion predominantly in the outer region (white arrows) and adenopathies (black arrow).

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Fig. 5: US shows a large hypoechoic mass (arrows), with irregular, angular margins, corresponding to the clinical abnormality, along with skin thickening (brace). US-core guided biopsy revealed G3 ductal invasive carcinoma.

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Fig. 6: Craniocaudal mammography (a) reveals skin thickening (star) and architectural distortion. US-guided core biopsy of a 4 cm hypoechoic, irregular mass (b- arrows), corresponding to the palpable abnormality revealed G2 ductal invasive carcinoma.

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Fig. 7: Medio-oblique (a) and craniocaudal (b) mammography show in the retro-areolar region an irregular mass with spiculated margins (small arrow) that includes microcalcifications and associates architectural distortion and nipple retraction (arrowhead). Global skin thickening and trabecular coarsening (star) as well as enlarged axillary lymph nodes (large arrow) are evident. The US equivalent of the mammographic abnormality was an irregular hypoechoic mass (arrow) with posterior shadow (arrowheads). Pathological report: Invasive G2 carcinoma with mixt pattern-lobular and ductal.

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48-year-old woman with prior surgery for IDC (invasive ductal carcinoma), 10 years earlier, in the right breast, had at presentation erythematous, tender, indurated right breast with no palpable mass.

Fig. 8: Mammography (a- craniocaudal incidence) shows skin thickening (arrows), trabecular coarsening (arrowheads), diffuse stromal coarsening and architectural distortion. US shows multiple hypoechoic nodules (b,c) with irregular margins (arrows) and posterior shadowing (arrowheads). Note also skin thickening (brace). Pathologic report: Ductal invasive carcinoma associated with DCIS high nuclear grade. It was regarded as secondary inflammatory breast cancer.

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58-year-old woman with enlarged, swelling, erythematous right breast that started 3 months prior entering our unit, with partial response to antibiotics and anti-inflammatory treatment. At physical examination, a 4-cm palpable mass in the upper-outer quadrant and slight skin infiltration were noted.

**Fig. 9:** At US there was a heterogeneous mass, with predominant hypoechoic aspect and nodular hyperechoic lesions included. Pathologic report: Chronic granulomatous mastitis.

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Conclusion

Imaging plays an important role in lesion diagnosis and treatment planning for patients with IBC as well as in assessing therapeutic response and detecting recurrence. Mainly ultrasound is a valuable tool in detecting the target lesion for biopsy.
Personal information

Elisabeta Popa, MD

Resident Doctor in the fourth year of training in Fundeni Clinical Institute, Bucharest, Romania.

e-mail: elisa_braila@yahoo.com
References


