BIRADS score and histopathological prognostic factors: histopathological grade and intrinsic subtypes of breast cancer

Poster No.: C-1367
Congress: ECR 2015
Type: Educational Exhibit
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Keywords: Breast, Mammography, Ultrasound, Surgery, Biopsy, Cancer
DOI: 10.1594/ecr2015/C-1367

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Learning objectives

The aim of this study was to evaluate the BIRADS score, the histological grade and intrinsic subtype of invasive ductal carcinoma of the breast and to highlight the fact that invasive breast carcinoma is a heterogeneous disease with varied imaging and morphological appearances, molecular features, behavior, and response to therapy.

Multidisciplinary preoperative and postoperative tumor board meetings are important in confirming radiological findings and guiding us to adopt the correct strategy.

The histological grade of the invasive breast carcinomas and the the intrinsic subtype are indispensible for diagnostic and prognostic in the treatment of breast cancer.

Background

Breast cancer is a heterogeneous disease with increased incidence among women.

In order to decide and to adopt the correct strategy for patients with invasive carcinoma of the breast is important that we make a correlation between imaging findings, BIRADS classification and histopathological results.

Breast Imaging Reporting and Data System (BI-RADS) was developed by the American College of Radiology, in order to standardize the terminology:

• Category 0: Mammography: Incomplete-Need additional imaging evaluation and prior Mammograms for comparison; Ultrasound & MRI: Incomplete- need additional Evaluation
  • Category 1: Negative
  • Category 2: Benign
  • Category 3: Probably Benign
  • Category 4: Suspicious- Mammography & Ultrasound: (4A: low suspicion for malignancy; 4B: moderate suspicion for malignancy; 4C: high suspicion for malignancy)
  • Category 5: Highly suggestive of malignancy
  • Category 6: Known biopsy - proven malignancy
One of the most important prognostic factors in breast cancer is histological grade, which represents the morphological assessment of tumor biological characteristics and has been shown to be able to generate important information related to the clinical behavior of breast cancers. Histological grade may also influence the imaging of the lesions.\[1,2\]

Histological grade of breast cancer are assessed by the Nottingham Grading System:

- well-differentiated tumor (grade I)
- moderately differentiated tumor (grade II)
- poorly differentiated (grade III)

Molecular methods provide prognostic and predictive information and may help identify new therapeutic targets, and the interest in molecular classifiers and their potential application is very important.\[2\]

The presence of hormone receptors is a good prognosis; their absence is a less favorable prognosis. The overexpression of HER2 is a factor of poor prognosis.\[1\]

According to the European Society for Medical Oncology the intrinsic subtype classification of invasive breast cancer we can distinguish:

- Luminal A: ER-positive, HER2-negative, Ki67-low, PgR-high;
- Luminal B: a) HER2-negative: ER-positive, HER2-negative and either Ki67-high or PgR-low; b) HER2-positive, ER-positive and any Ki67/any PgR;
- HER2 overexpression: HER2-positive, absent ER and PgR;
- Basal-like: Triple negative: HER2-negative and ER, PgR-absent

Studies described the radio-histological aspects of invasive carcinomas of the breast and the radiologist should be familiar with this aspects because the influence that this prognostic factors may have on to the imaging aspects.\[1,2,3\]

Findings and procedure details

We considered 216 patients diagnosed with invasive breast carcinoma, thus we gathered data from the medical records from 2011-2013, and retrospectively analyzed the imaging (ultrasound and mammography data) and histopathological findings.

Mammographic and ultrasound findings as well as BIRADS assessment were acquired from the database.
All the patients underwent surgical intervention (conservatory breast surgery/ mastectomy); after the histological examination the final diagnostic in all patients was invasive breast carcinoma.

67.6% of the cases were classified as BIRADS 5 on imaging, 27.8% were classified as BIRADS 4 and 4.6 were classified as BIRADS 3.

Histopathologic results: 35.2% were high grade, 44.4% intermediate grade and 20.4% were low grade.

More often BIRADS 4 score was associated with intermediate histological grade: 73.3% that were classified as BIRADS 4 on imaging had intermediate histological score at the histopathologic examination.

60.95% of the cases that were classified as BIRADS 5 on imaging were high histological grade at the histopathologic examination.

Intrinsic subtype classification of breast cancer was possible for 179 of the cases:

• 35.19% (63 cases) of the cases were "luminal A-like": from these 23 cases were low histological grade, 26 cases were intermediate histological grade and 14 cases were high histological grade; from these 4 cases had BIRADS 3, 28 cases had BIRADS 4 and 31 cases had BIRADS 5.

• 49.72% (90 cases) were "luminal B-like": from these 12 were low histological grade, 38 were intermediate histological grade and 40 cases were high histological grade; from these 1 case had BIRADS 3, 50 cases had BIRADS 4 and 39 had BIRADS 5.

• 11.73% (20 cases) were "basal-like": from these 2 were low intermediate grade, 7 cases were intermediate histological grade and 11 cases were high histological grade; from these 9 cases had BIRADS 4 and 11 cases had BIRADS 5.

• and only 3.35% (6 cases) had Her-2 overexpression from these 2 cases were intermediate histological grade and 4 cases were high histological grade; from these 3 cases had BIRADS 4 and also 3 cases had BIRADS 5.

With BIRADS 4 score were associated 44.4% (n=28) of the luminal A subtype, and 55.5% (n=50) of the luminal B subtype. With BIRADS 5 score were associated 49.2% (n=31) of the luminal A subtype, 55% (n=11) of the basal-like subtype and 43.3% (n=39) of the luminal B subtype. (Fig.1)

Case no. 1:

73 years old woman

Mammography: In the upper outer quadrant: irregular, microlobulated mass with the maximum diameter of 25/23 mm, with microcalcifications. (Fig.2, Fig.3)
Ultrasound: Left Breast- In the upper outer quadrant irregular, not circumscribed Hypoechoic mass, with posterior enhancement, with periferic vascularity(Fig.4, Fig.5)

BIRADS 5

Diagnostic: Invasive breast carcinoma NST (No Special Type), Histologic grade III (according to Elston and Ellis System)(Fig.6)

Intrinsic subtype: Luminal A: ER=60%(positive), PgR=80%(high), Ki67=10%(low), HER2=negative

Case no. 2:

59 years old woman

Mammography: Left breast- Irregular, spiculated mass of 32/24 mm with diffuse calcifications in the upper outer quadrant(Fig.7, Fig.8)

Ultrasound: hypoechoic mass, not circumscribed, irregular with present vascularity, of 40/24 mm, posterior enhancement.(Fig.9, Fig.10)

BIRADS 5

Diagnostic: Invasive breast carcinoma NST (No Special Type), Histologic grade II (according to Elston and Ellis System)(Fig.11)

Intrinsic subtype: "non-luminal" HER2 overexpression

Case no. 3:

68 years old woman

Mammography: Breasts with scattered areas of fibroglandular density. Left breast- In the upper outer quadrant: irregular speculated, high density mass of 33/31 mm, with few microcalcification and architectural distortion. Periareolar a mass with the same features of 17/15 mm (Fig.12, Fig.13)

Ultrasound: irregular, not circumscribed, hypoechoic mass with posterior enhancement of 29/22 mm(Fig.14). Suspicious left axilary lymph nodes(Fig.15).

BIRADS 5

Diagnostic: Invasive breast carcinoma NST (No Special Type), Histologic grade II (according to Elston and Ellis System)(Fig.16)

Intrinsic subtype: Luminal B: ER=90% (positive), PgR=70% (high), Ki67=60%(high),HER2=negative
Case no. 4:

54 years old woman

**Mammography:** The breasts are almost entirely fatty; focal asymmetry and associated calcifications. (Fig.17, Fig.18)

**Ultrasound:** left breast in the upper outer quadrant irregular, hypoechoic, not circumscribed mass with no posterior features

BIRADS 4C

**Diagnostic:** Invasive breast carcinoma NST (No Special Type), Histologic grade I (according to Elston and Ellis System) (Fig.19)

Intrinsic subtype: Luminal B: ER=90% (positive); HER2=negative; Ki67=50% (high)

Case no. 5:

74 years old woman

**Mammography:** the breasts are almost entirely fat. Left breast in the upper outer quadrant a high density, round, spiculated mass (20/20 mm). No calcifications. Architectural distorsion (Fig.20, Fig.21)

**Ultrasound:** Left breast-In the upper outer quadrant hypoechoic mass, not circumscribed of 12/15 mm. Internal vascularity. (Fig.22)

BIRADS 5

**Diagnostic:** Invasive breast carcinoma NST (No Special Type), Histologic grade I (according to Elston and Ellis System)

Intrinsic subtype: Luminal B: ER=90% (positive), PgR=10, Ki67=50, HER2=negative

Case no. 6:

59 years old woman

**Mammography:** scattered areas of fibrogladular density; high density lobulate mass with circumscribed margins, in the lower inner quadrant, no associated features.

**Ultrasound:** heterogeneous mass, lobulate margins, posterior enhancement, no calcification no associated features, in the lower inner quadrant. (Fig.23)

BIRADS 4C
**Diagnostic:** Invasive breast carcinoma NST (No Special Type), Histologic grade III (according to Elston and Ellis System) with a metaplastic component (Fig. 24)

Intrinsic subtype: Basal-like (triple negative): ER=negative, PgR=negative, HER2=negative

**Images for this section:**

![Image of BIRADS score and Molecular Intrinsic subtype classification of breast cancer](image)

**Fig. 1:** BIRADS score and Molecular Intrinsic subtype classification of breast cancer
Fig. 2: Case no.1: (73 years old woman) mammogram mediolateral oblique view
Fig. 3: Case no.1:(73 years old woman)mammogram craniocaudal view
Fig. 4: Case no.1:(73 years old woman) ultrasound image-Left Breast- In the upper outer quadrant irregular, not circumscribed Hypoechoic mass, with posterior enhancement, with peripheral vascularity
Fig. 5: Case no.1:(73 years old woman) Left Breast- In the upper outer quadrant irregular, not circumscribed hypoechoic mass, with posterior enhancement
Fig. 6: Case no.1 (73 years old woman) Invasive breast carcinoma NST, grade III
Fig. 7: Case no.2: 59 years old woman Mammogram mediolateral oblique view
Fig. 8: Case no.2: (59 years old woman) Mammogram craniocaudal view
Fig. 9: Case no.2: (59 years old woman) Left breast-upper outer quadrant
Fig. 10: Case no.2: (59 years old woman) hypoechoic mass, not circumscribed, irregular with present vascularity, of 40/24 mm, posterior enhancement.
Fig. 11: Case no.2 (59 years old woman) Left breast-Invasive breast carcinoma NST, grade II
Fig. 12: Case no.3 (68 years old woman): Left breast mammogram mediolateral oblique view
Fig. 13: Case no.3 (68 years old): Left breast mammogram craniocaudal view
Fig. 14: Case no.3 (68 years old woman): Left breast ultrasound
Fig. 15: Case no.3 (68 years old woman): Ultrasound image of left axilla-suspicious lymph nodes
Fig. 16: Case no.3 (68 years old woman): Invasive breast carcinoma NST, grade II
Fig. 17: Case no.4 (54 years old woman): mammogram mediolateral oblique view
Fig. 18: Case no.4 (54 years old woman): mammogram craniocaudal view
Fig. 19: Case no.4 (54 years old woman): left breast ultrasound image in the upper outer quadrant
**Fig. 20:** Case no.5 (74 years old woman): mammogram mediolateral oblique view
Fig. 21: Case no.5 (74 years old woman): mammogram craniocaudal view
Fig. 22: Case no.5 (74 years old woman): Ultrasound image of the left breast-upper outer quadrant
Fig. 23: Case no.6 (59 years old woman): Ultrasound image: heterogeneous mass, lobulate margins, with posterior enhancement, in the lower inner quadrant of the left breast.
Fig. 24: Case no.6 (59 years old woman): Invasive breast carcinoma NST, grade III with a metaplastic component
Conclusion

In clinical practice luminal A type correspond to invasive ductal carcinomas grade I and II and these were also the findings in our study (36.5% respectively 41.26%) but we also found 14 cases (22.2%) that were grade III; and only 49.20% of the luminal A type were considered highly suspicious on imaging.

Although in the literature the most common subtype is luminal A, in our casuistry the most common subtype was luminal B.

Luminal B type corresponds to invasive carcinoma grade II (42.20%) and III (44.4%), and from these 55.55% were considered suspicious on imaging and 43.3%, highly suspicious.

HER2 overexpression (6 cases) correspond to II and III histological grade and all of them were considered suspicious on imaging.

From the "Basal like" subtype (triple negative) (n=20) 43.3% were grade III and considered suspicious on imaging.

The radiologist should be familiar with the aggressiveness of each histological grade and with the molecular classification of breast cancers in order to adapt the care of an aggressive sub-type.

Given the complex nature of breast invasive carcinoma multidisciplinary tumor board meetings are essential to clinical decision-making and patient management.

Personal information

References


