Invasive pleomorphic lobular carcinoma and classic invasive lobular carcinoma: What's the difference?

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Purpose

This study aims to characterize a series of pleomorphic lobular carcinoma (PLC) from the clinical, radiological histological and imunohistochemical characteristics. In addition, these aspects are compared with invasive lobular carcinoma (ILC) of classic variant.

Methods and Materials

Material and methods

This study analyze a series of 43 ILC diagnosed in our department from January 2004 to July 2009.

Patients

The analytic data concerned: patient characteristics (age, hormonal status), clinical presentation, radiological characteristics and presence of initial metastatic diseases. We also describe cases with recidivated disease. Finally we report disease free survival and overall survival.

Histological analysis

The classic variant (CV) of invasive lobular carcinoma (ILC) corresponded to a proliferation of non-cohesive cells disperse in a fibrosis tissue and arranged in single file linear cords that invade the stroma. The pleomorphic variant (PV) exhibited a greater degree of cellular atypia and pleomorphism than CV.

Tumor lesions are characterized according with location (laterality, multicentricity and multifocality), mix lesions - ILC and invasive ductal carcinoma (IDC), this last as minor component (<50%), in situ lesions and cytonuclear (Bloom Richardson) grade. Sentinel lymph node (SLN) was analyzed after serial section (100 µm thickness) using classical staining - Hematoxylin and Eosin (H&E) and IHQ (MNF116) when classic stain negative or inconclusive. Lymph nodes obtained from axillary dissection were studied in order to identify invasion.

Immunohistochemical analysis

Histological sections were routinely incubated with monoclonal antibodies to assess estrogens receptors (ER), progesterone receptors (PR) and ErbB2 expression.

Statistics

Descriptive statistics are reported as frequencies, percentages, means and standard deviation. Distributions of categorical variables were compared using $\#^2$ test. Parametric variables were tested using *t student* test. Statistical analysis was performed using SPSS 17.0 version.

Results

Results

The series of 43 invasive lobular carcinoma (ILC) was composed of 11 cases of the pleomorphic variant (PV) and 32 cases of the classic variant (CV).

Focusing on PV, mean age at diagnosis was 57,9±13,6[40-81] and women were mainly post-menopausal (58%-n=7). The disease presented as palpable lesion in 82% (n=9). Radiologically, tumors were diagnosed as a mass (usually spiculated) in 82% (n=9), architectural distortion in 9% (n=1) and focal assimetry associated with microcalcifications in 9% (n=1). Initial metastatic diseases was diagnosed in 7 cases (58%), representing 3 cases with axillary lymph node (ALN) invasion, one case with bone and another with pulmonary metastasis and 2 cases with disseminated diseases. Table 1 represents the comparison of these clinical and radiological parameters between PV and CV patients.

Table 1: Comparison of clinical and radiological parameters between PV and CV patients.

	PV N=11 26%	CV N=32 74%	p value
Mean age	57,9±13,6 [40-81]	61,4±10,4 [43-79]	n.s.
Hormonal status:			
Pre-menopausal	4 (42%)	6 (18%)	n.s.
Post-menopausal	7 (58%)	26 (82%)	
Clinical presentation:			
Palpable lump	9 (82%)	21 (66%)	n.s.
Imaging alteration	2 (18%)	11 (34%)	
Radiological alteration:			
Mass	9 (82%)	26 (82%)	n.s.
Architectural distortion	1 (9%)	4 (12%)	
Microcalcifications (*)	1 (9%)	2 (6%)	
Focal assimetry (*)	1 (9%)	0	
Initial metastatic diseases:	9 (81%)	15 (47%)	0.037
Ganglionar invasion	5 (45%)	15 (47%)	
Distant metastasis	4 (31%)	0	

Fig.: PV - Pleomorphic variant ; CV - Classic variant. (*) One patient had focal assimetry associated with microcalcifications.
References: M. Seco; Clinica Universitária de Imagiologia, Hospitais Universidade Coimbra, Coimbra, PORTUGAL

Bilateral and multicentric tumors were exclusively found on PV cancers (p=n.s. and p=0.017 respectively). Multifocal lesions were histologically detected in 45% (n=5) of the PV and 28% (n=9) of the CV (p=n.s.). Mix lesions were more frequent in CV than PV tumors (p=0.037). On one hand PV tumors were classified as G2 or G3 but on the other hand CV tumors were G1 or G2 (p<0.001). Table 2 summarizes histological characteristics of PV and CV tumors.

Table 2: Comparison of histological parameters between PV and CV patients.

	PV N=11 26%	CV N=32 74%	p value
Bilateral lesion	1 (9%)	0	n.s.
Multicentric lesions	2 (8%)	0	0.017
Multifocal lesions	5 (45%)	9 (28%)	n.s.
Mix lesions	1 (9%)	13 (41%)	0.037
In situ lesions	2 (8%)	10 (31%)	n.s.
Cytonuclear grade			
G1	0	18 (56%)	<0.001
G2	5 (45%)	14 (44%)	
G3	6 (55%)	0	

Fig.: PV - Pleomorphic variant ; CV - Classic variant
References: M. Seco; Clinica Universitária de Imagiologia, Hospitais Universidade Coimbra, Coimbra, PORTUGAL

In patients submitted to surgery as primary treatment (7 cases in PV and 32 cases in CV), histology revealed ganglionar invasion in 71% of PV patients and 47% in CV patients (p=n.s.).

Immunohistochemical studies revealed ER positivity in 97% of CV. ER negative wre reported in 46% of PV tumors (p=0.001). PR were more frequently positive in CV than PV (p=0.003). Triple negative tumors were exclusively diagnosed on PV breast cancers (p<0.001).

Table 3: Immunohistochemical studies.

	PV N=11 26%	CV N=32 74%	p value
ER positive	6 (54%)	31 (97%)	0.001
PR positive	4 (36%)	27 (84%)	0.003
HerbB2 positive	2 (18%)	3 (9%)	n.s.
Triple negative	4 (36%)	0	<0.001

Fig.: PV - Pleomorphic variant ; CV - Classic variant
References: M. Seco; Clinica Universitária de Imagiologia, Hospitais Universidade Coimbra, Coimbra, PORTUGAL

Follow up varied from 4 to 95 months (mean 27.1 months). Three patients of PV died of disease between 7 and 20 months. One patient of CV died 30 months after breast removal. Overall survival (OS) of PV patients corresponded to 70% at 20th months compared to 93% at 30th months for CV patients. Disease free survival (DFS) was 62% at 12 th months for PV patients and 90% at 18 th months for CV patients.

Images for this section:

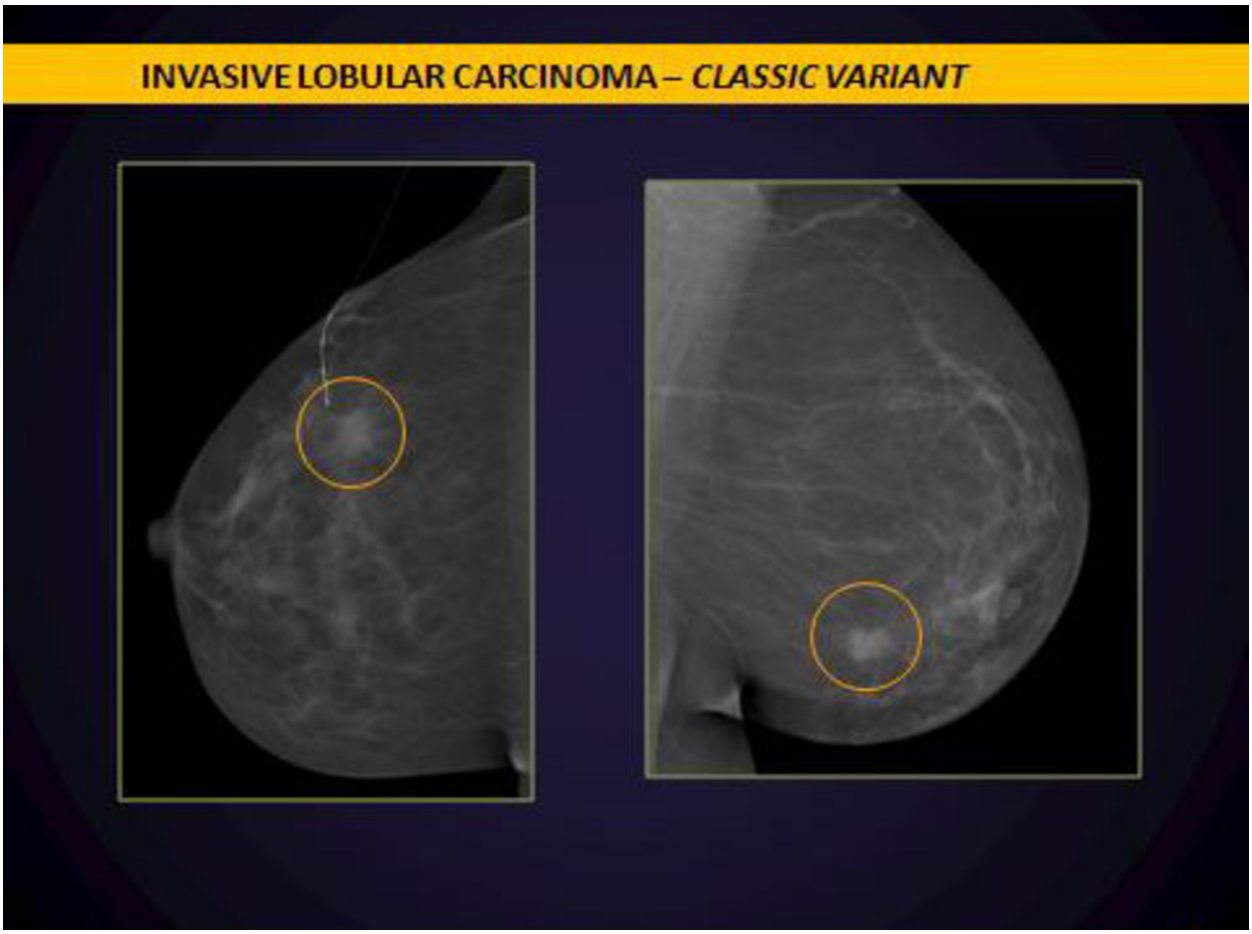

Fig. 1: Spiculated masses (circles) in two different patients with the classic variant.

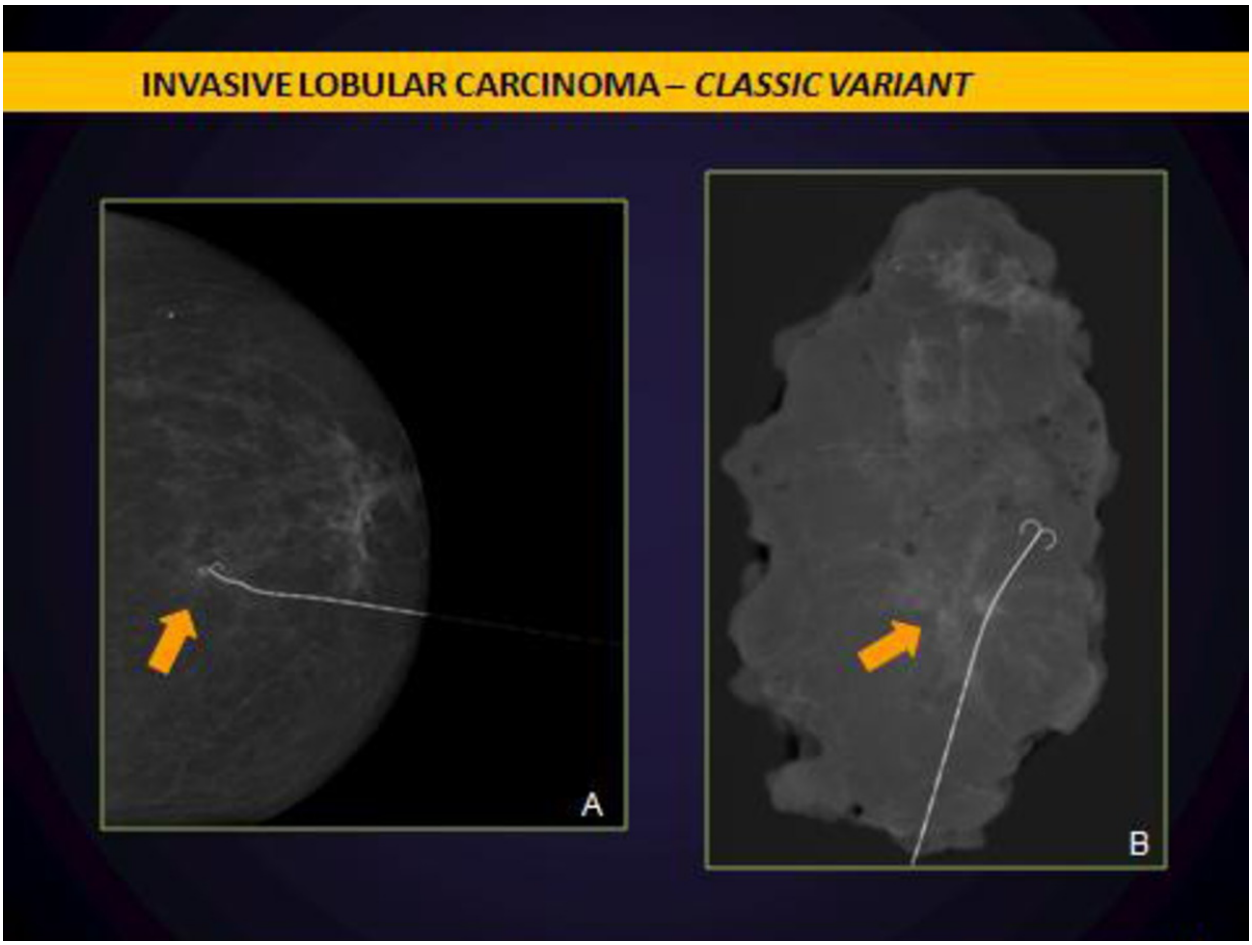

Fig. 2: Architectural distortion (arrows) in a patient with the classic variant. A. Mamography - Craniocaudal view. B. The lesion was removed as shown by the mamography of the specimen.

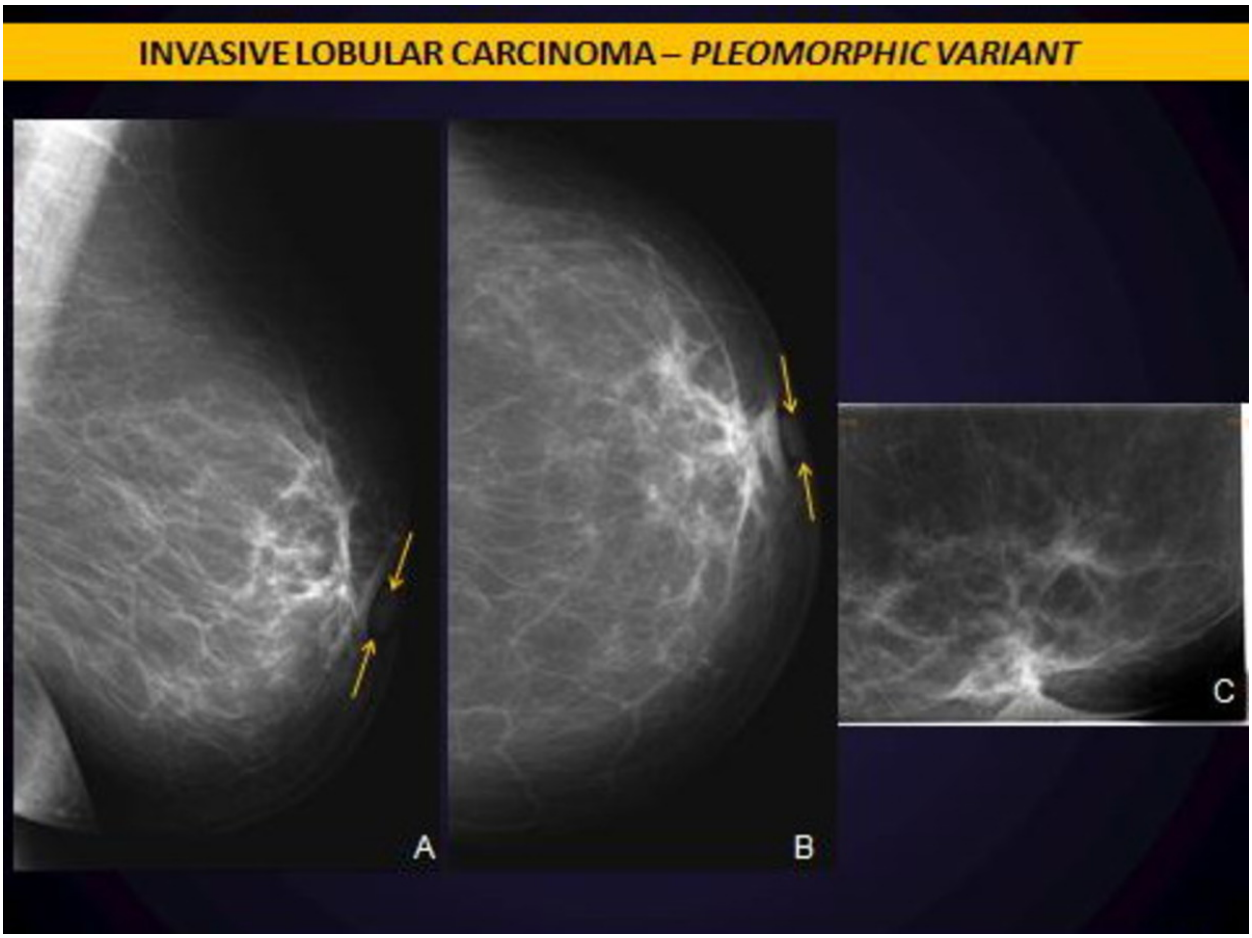

Fig. 3: A. MLO view. B. CC view. C. Magnification view. Retro-mamilar architectural distortion associated with nipple (arrow) retraction.

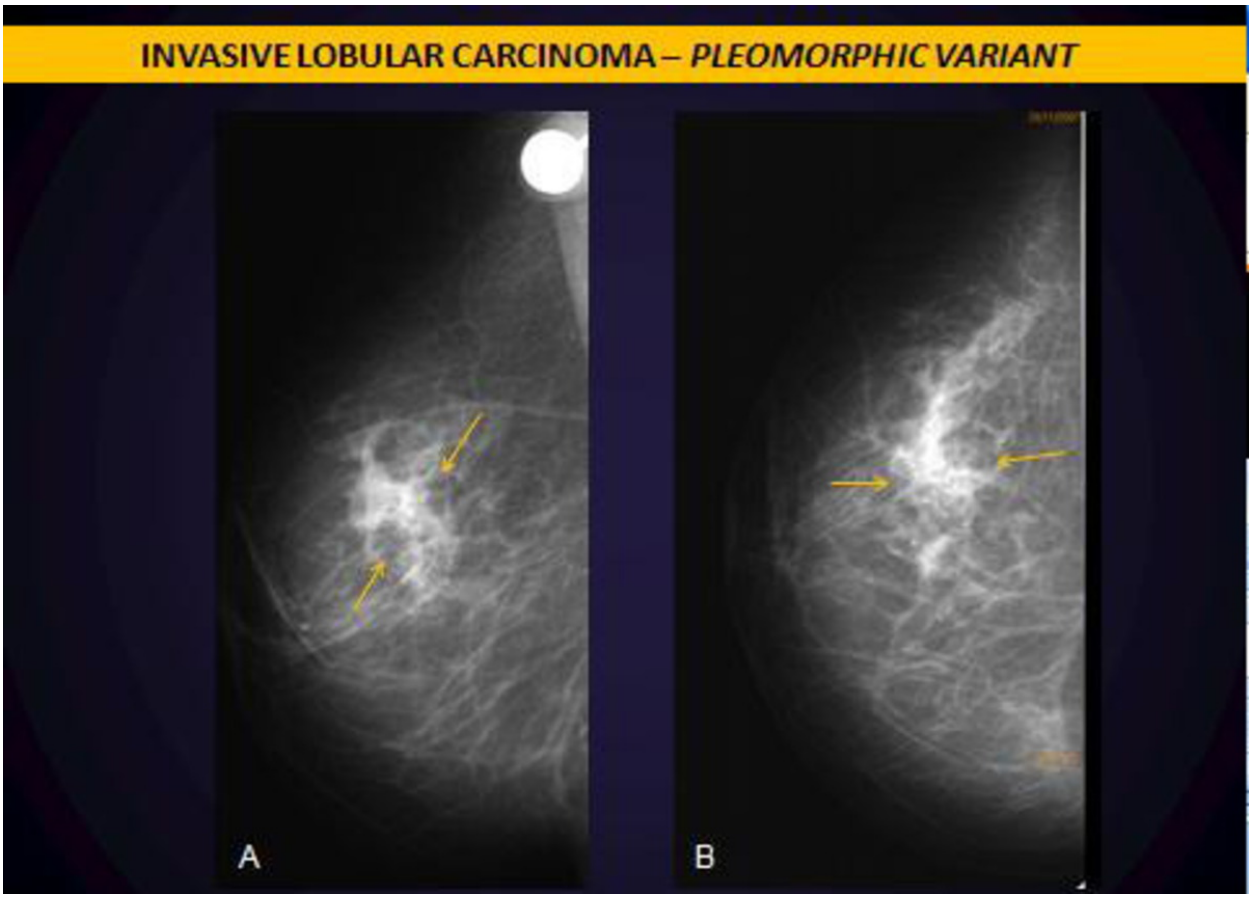

Fig. 4: A. MLO view. B. CC view. Focal assimetry (arrows) associated with microcalcifications.

Conclusion

Lobular carcinoma is still a confusing clinicopathologic entity, particularly focusing on classification, biological behavior and therapeutic strategies. PLC is a distinct subtype of these types of carcinomas and represents 1% of all epithelial malignancies of the breast. Despite being rare, the incidence of ILC is increasing in proportion to breast cancers. The use of hormonal replacement therapy is hypothesized as one of the causes for this increase.

The characterization of a distinct subtype of ILC is useful for clinical practice? This is still a question of debate. But the profound knowledge on this subtype can delineate therapeutic and follow up strategies in a near future. Previous pathological studies emphasized E-cadherin expression to differentiate lobular from ductal lesions, but a spectrum of molecular alterations in E-cadherin/catenin complex are still obscure in the characterization of lobular neoplasia.

The current study emphasizes some clinicopathological features of PLC, particularly when comparing with CV. When we compare PV with CV, PV patients were more frequently post-menopausal than CV patients and presented clinically mainly with a palpable lump, despite not reaching statistical significance. Initial metastatic disease was statistically more associated with PV patients. Axillary lymph node invasion was particularly identified in these patients. It can evidence a propensity for lymphatic vessels dissemination, a phenomenon correlated with aggressive clinical behavior.

Pleomorphic variant seems to have a worse prognosis than classic variant.

References

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Personal Information

Fig.: Personal information.
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