

LOBULAR CARCINOMA OF THE BREAST, EXPERIENCE OF THE MOHAMMED VI CENTER FOR THE TREATMENT OF GYNECO-MAMMARY CANCERS

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INTRODUCTION

Considered as first cancer in women, the incidence of breast cancer is increasing in Morocco.

Its management has benefited from remarkable progress, from the advent of a conservative treatment to the expansion of the range of adjuvant treatment offered.

Lobular carcinoma is an anatomopathological entity that represents 10% of all invasive carcinomas, which presents originality due to the clinical and mammographic diagnostic difficulty and to its mode of proliferation and dissemination different from infiltrating ductal carcinoma.

We aim through this work a study of the epidemiological characteristics of this type of cancer and the evaluation of its prognosis.

Patients and methods

This is a two-year retrospective study of twenty cases of infiltrating lobular carcinoma collected from January 2017 to December 2018.

Data were carefully collected on data sheets (Figure 1)

RESULTS

On the epidemiological level

The overall incidence was 2.45% of all breast cancers diagnosed during this period at our facility.

The mean age was 55 years, with extremes ranging from 25 to 89 years.

90% of our patients were multiparous, of which 70% were breastfed for 2 years.

Combined oral contraception was used by 41% of patients.

65% of patients were menopausal at the time of diagnosis.

No benign mastopathy was found, and 25% of the cases studied had a history of breast cancer.

Regarding the clinical study

The average consultation time was four months.

The telltale signs were varied

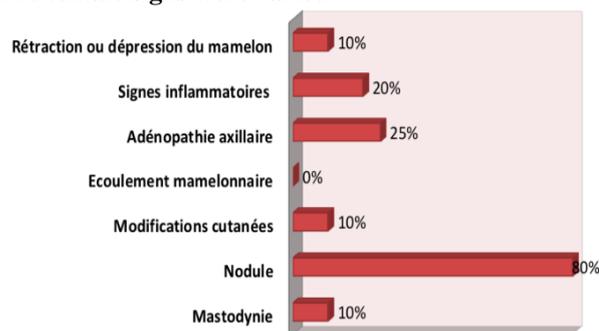


Figure 2: Telltale signs of CLI in our series.

The CLIs were located in the left breast in 55% of cases and bilaterally in 10%, and the QSE in 60% of cases.

20% of the patients had homolateral axillary adenopathy at the time of diagnosis and only one patient had supraclavicular adenopathy.

On mammography, all patients had a suspicious opacity, 40% were associated with microcalcifications and only 25% were multifocal

On breast ultrasound, the signs were varied:

Table 1: Sonographic aspects of CLI.

	Nombre	Pourcentage
Formation hypoéchogène et / ou hétérogène avec des contours flous	20	100%
Signes d'atténuation	15	75%
Micro calcifications	4	20%
Epaississement du tissu sous cutané	2	10%
Adénopathies axillaires suspectes	12	60%
Images tissulaires	4	20%

On breast MRI**Table 2: MRI aspects of CLI.**

	Nombre	Pourcentage
Masse nodulaire unique	6	30%
Lésions multifocales	6	30%
Adénopathies axillaires homolatérales	6	30%
Epaississement des enveloppes cutanées	1	5%
Nodosités diffuses avec infiltration de la graisse	1	5%

Histological verification was done by trust biopsy, which revealed CLI in 100% of the cases, confirmed after study of the operative parts. The in situ component was found in 20% of cases.

The SBR guard was rated at two in 90% of cases.

Hormone receptors were positive in 100% of cases, HER2 was positive in 3 cases or 15%. The ki67 was higher than 20 in 45% of cases.

E-cadherin was tested in nine patients, for which the classical histological examination could not be conclusive, it was negative on all nine specimens.

Only one patient had suspicious pulmonary nodules at the time of diagnosis, 2 others had secondary bone localization. In addition, the extension work-up was negative in the rest of the patients.

For the TNM classification

60% were classified T2, 20% were classified N+, 15% were classified M+.

Surgical treatment was radical in 70% of cases.

17 patients received adjuvant therapy.

Complete remission was observed in 9 patients, 3 were metastatic at diagnosis, 3 are still on adjuvant therapy and 3 have been lost to follow-up.

DISCUSSION

CLI is a rare pathology since it represents only 0.34 to 2.9% of the results of a breast biopsy for all indications^[1], which is the same as the percentage found in our series.

For some studies, the average age is 54.4 years (40-69 years).^[3]

Because of the rarity of lobules in men, only 2 cases of CLI in this sex have been found in the literature, diagnosed because of the histological features and the negativity of E-cadherin.^[3] Our series did not find any male cases.

A 2002 case-control study from Sweden identified 5 years of increased breast cancer incidence after the birth of the first child^[4], due to the complexity of remodeling that follows the post-lactational involution period.

As with other protective effects, the age of the mother is important. Women who had their first child at age 30 have been shown to achieve a lower risk than nulliparous women.

Furthermore, the results are inconsistent with the literature, with nulliparity representing only 10%, whereas the multiparity rate is 90%.

In our study, 18 patients had their first child before the age of 30, i.e., a rate of 90% of cases, while only one patient had her first child after the age of 30.

Regarding the use of contraception, a recent study in Italy by Del Pup L. et al found that the relative risk of hormonal contraception is still high and well established.^[5] It is 1.2%, and 70% of our patients have used hormonal contraception for a mean duration of 12.5 years

Regarding the age of menopause, the late age of menopause is associated with an increased risk of breast cancer, due to a longer secretion of estrogens, especially during peri-menopause.^[6-7]

In our series, 13 cases, i.e. 65% of the patients were postmenopausal, 12 of them before the age of 55, and the only one after 55.

****(rf)The time between the appearance of the first clinical symptoms and the first consultation can be more or less long and differs from case to case.

This delay was 7.8 months on average for Khlifi^[14], and 7 months for El Alouani.^[15]

As for our patients, they consulted within an average period of 4 months with extremes of 20 days to 24 months, 59% of these patients consulted before 3 months. Comparing our results with those of the literature, we note that our patients consulted within a shorter period of time than those of the other series.

Lobular carcinomas have generally less rich symptomatology than intracanal carcinomas. They are discovered incidentally in 20% of cases.^[13,44] This could explain its later diagnosis. Autopalpation of a nodule seems to be the most frequent revealing sign.^[15] This is consistent with our result.

For the majority of authors, lobular carcinoma is often located in the left breast. For Wasif *et al*^[11] and Molland *et al*^[46] the tumor is located in the left breast in 50.9% and 51.09% of cases respectively.

CLI is known to be often bilateral compared with other breast cancers.^[44,46] This bilaterality may be simultaneous or secondary.

Several authors have found a high incidence of contralateral tumors in patients with CLI.^[48-52]

If we consider the tumor location of CLI in the breast according to the different quadrants that can be affected, we note according to several authors that the superior-external quadrant is the most often affected.

For Dedes^[52], the CLI is located in the superior-external quadrant in 37% of cases, this rate is 36.7% for Wasif.^[11]

The second location is the retromammary area, followed by the superior-internal quadrant.^[52] In addition, infiltrating lobular carcinoma has a slight tendency to sit in the central region, compared with ductal carcinoma.

Table 3: Mammographic aspects of CLI.

Etudes	Opacité suspecte(%)	micro calcifications	Asymétrie focale de densité	Distorsion isolée	Négatifs	Autres signes
Evans(78)	60	11	9	20	-	-
Uchiyama(79)	38	20	16	16	2	8
Weinstein(77)	30	-	5	10	48	7
Albayarak, ZK(80)	42	13	29	-	29	-
Hilleren(64)	53	-	4	16	16	7
Le Gal(67)	50	-	19	18	-	12
Notre étude	100	40	-	-	-	25%

It should be noted that when coupled with tomosynthesis, digital mammography significantly increases the detection of CLI (+107%) compared with the detection of CCI (+30%).^[84]

The use of ultrasound as an adjunct to mammography has been shown to significantly improve the detection of CLI. Butler^[88] and colleagues examined 81 lesions that were invisible on mammography, and then found that

Consistent with the literature, our tumors were bilateral in 10% of cases, located at the QSE in 60% of cases.

Regarding tumor size, clinically, a recent study in Shanghai by Yu *et al*^[57] analyzed 2809 cases of CLI and 48% of the cases had a tumor size greater than 2 cm, thus agreeing with Arpino's results.

In our series, tumor sizes between 2 and 5 cm predominate with a rate of 60%, and a mean tumor size of 4.7 cm.

For lymph node involvement, which is an important element in the evaluation of breast cancer prognosis and influences the choice of treatment, it has been found that lymph node involvement is slightly lower than for invasive ductal carcinomas^[44,57,58], although they are diagnosed at more advanced stages.

As for the stage at diagnosis, in our study, no early-stage (T1) was found, whereas 46 to 52% in the series of Arpino *et al*^[45] and Molland *et al*.^[47] A T4 stage was found in 20% of the patients in our series; this rate varies in the literature between 6.5% and 14%.^[13,45,47]

On the subject of mammography, it has been reported that the sensitivity of mammography for lobular carcinoma of the breast ranges from 57% to 81%^[64,66,67] and the false-negative rate generally ranges from 19% to 43% in the literature.^[63,64,68] The single tumor cell base and the frequent absence of reactive stroma account for most "occult" lesions on mammography. Also, because the cells are often distant from the ductal and lobular epithelia, intra luminal necrosis is less common, which explains the lower frequency of micro calcifications.

Table 3 summarizes the different aspects found on mammography compared to our study.

87.7% of the lesions were readily detectable on ultrasound.

MRI is widely recognized as the most sensitive detection modality in invasive lobular carcinoma: 83-100%, with two prospective studies finding 95 and 97% sensitivity.^[69,98]

This sensitivity is superior to other paraclinical examinations: 65 to 98% for clinical examination, 81 to 98% for mammography, 68 to 98% for ultrasound.^[62,64,67,68]

The most common morphology on MRI is a mass-like enhancement, with an incidence of 21-95%.^[99,100,101]

Well-circumscribed and round forms have also been described.^[103,104] On mammography, this lesion is most often seen as a spiculated mass.^{[101][20]} According to Schelfout *et al.*^[100], who compared mammographic and MRI images, six masses on MRI were visible as architectural distortion on mammography and two as density asymmetry. In pathology, a single mass with irregular contours is most often found^[101]

The majority of other presentations are therefore grouped here. The second most frequently described MRI image typically associated with infiltrating lobular carcinoma is multiple enhancements:

- The lesions observed are either multiple foci connected by linear enhancement (Fig. 38) or clustered enhancement.^[100] Histologically, the first type corresponds to a discontinuous tumor with cells in a single file. The second type correlates with small clusters of cells separated by normal breast tissue;
- Regional, ductal, segmental, and diffuse enhancement are also found.^[102]

In cases where a mass is not visible on mammography, the MRI lesion is most often a non-mass enhancement. In addition to conventional mammography and ultrasound, the sensitivity of MRI reaches 100%. Breast MRI is strongly recommended by several learned societies in the pre-therapeutic workup of invasive lobular carcinoma for its diagnostic accuracy in estimating lesion size, screening for multifocality, and exploration of the contralateral breast.^[102,105,106]

The extension of CLI is peculiar, and this peculiarity has been well demonstrated by the study of Harris *et al.*^[120] who published the ability of CLI to extend to unusual sites: peritoneum, retroperitoneum, and hollow viscera.

Overall, CLI is characterized by diffuse infiltration of these organs, similar to lymphomas. These particular localizations tend to occur late in the metastatic process and may go unnoticed clinically.^[120]

The surgical management, the choice of adjuvant or neoadjuvant treatment is similar to the other histological types of breast cancer.

But a poor response to chiropractic therapy from CLIs compared to CCIs is still noteworthy.

Regarding prognostic factors, the particularities of CLI are the advanced age of onset, low percentage of lymphatic metastases despite advanced stage, the less frequent presence of vascular emboli, more frequent expression of hormone receptors, a rare expression of HER2, generally low proliferation index.

The evaluation of the 5-year survival for CLI, according to several studies, is shown in Table 4:

Table 4: Overall survival of invasive lobular carcinoma.

ETUDES	Survie à 1an	Survie à 5ans	Survie à 8 ans	Survie à 10 ans	Survie à 17 ans
Sariego J <i>et al.</i> (231)	94,6%	75%	–	64,3%	–
Elston CW <i>et al.</i> (232)	89%	80,5%	67%	–	–
Sastre-Garau J <i>et al.</i> (13)	93%	87%	–	67%	–
Yeatman TJ <i>et al.</i> (76)	95%	77%	–	–	–
Moreno-Elola <i>et al.</i> (196)	89,4%	80,8	65,5%	65%	54,5%

CLI should be monitored similarly to other histological types.

CONCLUSION

The incidence of CLI has increased significantly in recent years, which justifies the knowledge of the particularities of this type of breast cancer. This study has allowed us to highlight the different epidemiological, clinical, anatomical-pathological, therapeutic, and evolutionary particularities.

Emerging technologies such as cDNA genome mapping can further elucidate the molecular differences, allowing for a new strategy in the management of this histological type.

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