**Case Series**

# Overdiagnosis of lobular carcinoma of breast- A review of histomorphological features and immunohistochemistry: A case series

Priyadarshini Rajkumari[1],*, Aravind Pallipady[1]

[1]AJ Institute of Medical Sciences and Research Center, Mangaluru, Karnataka, India

## ARTICLE INFO

## ABSTRACT

**Introduction**: Invasive lobular carcinoma (ILC) accounts for 5%–15% of all invasive breast cancers (BCs) and is the second most common type of BC behind invasive ductal carcinoma (IDC) of no special type. ILC of the breast is characterized morphologically by small, noncohesive cells that infiltrate the stroma in a single-file pattern(Indian file pattern). ILC tumours display features associated with a good prognosis, being low grade, oestrogen receptor positive and is mainly associated with the complete loss of E-cadherin (E-cad) expression.

**Objectives:** To review the cases of invasive lobular carcinoma and to immunohistochemically categorize IDC and ILC.

**Materials and Methods:** This is a retrospective study including all the modified radical mastectomy cases of invasive lobular carcinoma of breast reported in the department of Pathology of a tertiary care centre from January 2021 to January 2022. Histopathological and immunohistochemical analysis of those cases were reviewed.

**Results:** We encountered 10 cases of invasive lobular carcinoma of breast from January 2021 to January 2022. The average age of the patients was 55.9 years old (35–72). The classic presentation was a breast lump found in 100% of the cases. On physical examination, breast carcinoma was suspected in all the patients. The average size of the tumours was 4.5 cm (1.4– 9cm). Out of those 10 cases, 4 cases were right sided lesion and modified radical mastectomy was performed in all the 10 cases. All the 10 cases were diagnosed as invasive lobular carcinoma on histopathology and review of those cases showed 7 out of 10 cases to be IDC. Those cases showed pitfalls in histomorphological analysis which were later confirmed by immunohistochemistry. The findings are presented in the study.

**Conclusion:** Our study found that there was a histomorphological pitfall in the diagnosis of IDC. In ambiguous cases with histologically equivocal features, a strong, complete, membranous E-cadherin expression may help in resolving the problem and in aiding in the subclassification of invasive breast carcinoma.

## 1. Introduction

Invasive lobular carcinoma (ILC) accounts for 5%–15% of all invasive breast cancers (BCs) and is the second most common type of BC behind invasive ductal carcinoma (IDC) of no special type.[1,2] ILC of the breast is characterized morphologically by small, non-cohesive cells that infiltrate the stroma in a single-file pattern(Indian file pattern).[3] ILC tumours display features associated with a good prognosis, being low grade, oestrogen receptor positive and is mainly associated with the complete loss of E-cadherin (E-cad) expression.[4,5]

Our aim through this case series is to report our experience and discuss the diagnostic pitfall in

* Corresponding author.
E-mail address: drpriyarajkumari2020@gmail.com (P. Rajkumari).

histopathological evaluation alone.

## 2. Case Presentation

We report a case series of 10 modified radical mastectomy specimens which were diagnosed as invasive lobular breast carcinoma for a period of 1 year: January 2021 to January 2022. The mean age of our patients was 55.9 years old (35–72). All the patients included were female. The classic presentation was a breast lump found in all the cases (100%). The lesions were in the right breast in four cases (40%) and the left one in six cases (60%). The average size of the tumours was 4.5 cm (1.4-9 cm). Clinically, lesions suspicious of breast carcinoma were present in all the 10 patients (100%). All the 10 patients had undergone modified radical mastectomy and the specimens were sent to our laboratory for histopathological diagnosis. (Table 1)

The 10 cases of breast cancer were first diagnosed as invasive lobular carcinoma of the breast on histopathological evaluation alone (Table 2) with 10 cases (100%) showing Indian file pattern or linear file pattern (Figures 1 and 2) followed by targetoid pattern in 2 cases (20%). 6 cases (60%) were given a histological staging of $T_3$ followed by $T_4$ staging in 2 cases (20%). 3 cases (30%) had $N_1$ nodal status with $N_2$ and $N_3$ nodal status seen in 2 cases (20%) each.(Table 3).

Final immunohistochemical analysis showed 6(60%) cases with estrogen and progesterone receptor positivity. 9(90%) out of those 10 cases were Her2/Neu negative. E-cadherin analysis was done in all the 10 cases which showed positivity in 7(70%) out of 10(100%) cases. (Figure 3)(Table 5). Review after final immunohistochemical analysis yielded 7/10 cases to be IDC.
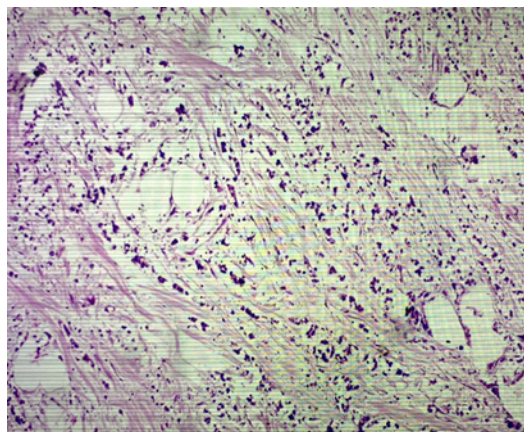


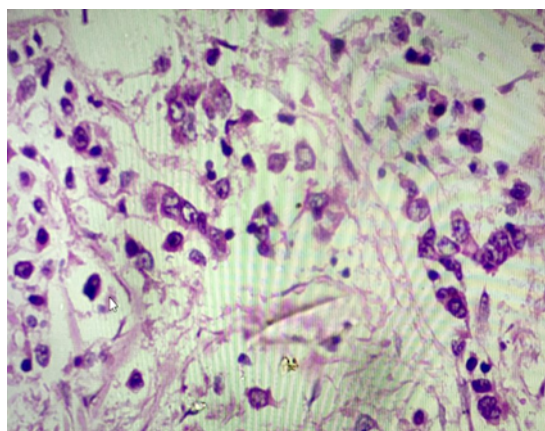**Fig. 1:** H and E section (10x-low power)



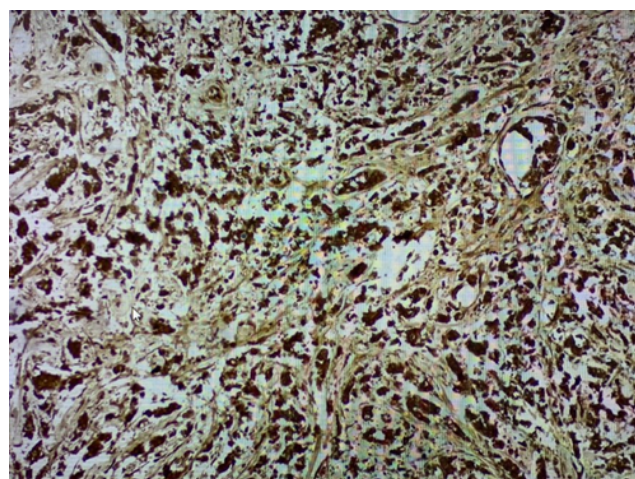**Fig. 2:** H and E section (40x-high power)



**Fig. 3:** E-cadherin IHC: Positive in tumor cells

## 3. Discussion

In the first study of lobular carcinoma of breast done by Foote and Stewart in 1941, they described lobular carcinoma where the tumor shows linear infiltration in surrounding stroma in rows or Indian file pattern or targetoid appearance around the ducts as seen in our study (Figure 1). But the assignment of a growth pattern to either ductal or lobular or mixed type(NST/ILC) remains to some extent subjective as found in a study done by Matthias Christgen et al. ILC and its variants i.e Solid, alveolar, tubulo-lobular and the pleomorphic variants add difficulty in distinguishing the IDC of no special type, with the cord like or the trabecular patterns. Hence, High grade invasive breast carcinoma-NST should be kept in mind as differential diagnosis of invasive lobular carcinoma and its variants.[6] As in a study done by R Singhai et al., diagnostic difficulties had occurred in some cases, because IDC showed a dispersed growth pattern, which included infiltration around the benign ducts in a targetoid manner, which is similar to that in ILC.The loss of

**Table 1:** The patient characteristics and the findings

| Patients | Age (in years) | Chief complaints | Laterality | Tumor size(in cms) | TNM classification | Histological diagnosis | Surgery |
|---|---|---|---|---|---|---|---|
| 1 | 35 | Breast lump | Right | 5*4.2*1 | $pT_3N_0M_X$ | ILC | MRM |
| 2 | 57 | Breast lump | Right | 5*4*3.5 | $pT_3N_0M_X$ | ILC | MRM |
| 3 | 61 | Breast lump | Right | 1.4*1*0.9 | $pT_{1C}N_{1a}M_X$ | ILC | MRM |
| 4 | 67 | Breast lump | Left | 1.4*1*0.7 | $pT_{4b}N_{2a}M_X$ | ILC | MRM |
| 5 | 40 | Breast lump | Left | 5*5*4 | $pT_3N_{2a}M_X$ | ILC | MRM |
| 6 | 44 | Breast lump | Left | 6*5.5*3.5 | $pT_4N_{3a}MX$ | ILC | MRM |
| 7 | 72 | Breast lump | Left | 4*3.6*2.4 | $pT_3N_{1a}M_X$ | ILC | MRM |
| 8 | 48 | Breast lump | Right | 9*4.5*1.6 | $pT_3N_{3a}M_X$ | ILC | MRM |
| 9 | 67 | Breast lump | Left | 3*2.9*2.7 | $pT_2N_0M_X$ | ILC | MRM |
| 10 | 68 | Breast lump | Left | 6*6*4.2 | $pT_3N_{1a}M_X$ | ILC | MRM |

**Table 2:** Histological pattern of invasive lobular carcinoma as reported

| Histological Pattern | No. of cases |
|---|---|
| Indian file pattern | 10 |
| Targetoid pattern | 2 |
| Solid pattern | 0 |
| Tubulo-alveolar pattern | 1 |
| Pleomorphic pattern | 1 |

**Table 3:** Histological stage at the time of diagnosis

| Characteristics | No. of patients (%) |
|---|---|
| **Median age at diagnosis:** | 55.9 Years |
| **Laterality** | |
| Right | 4(40%) |
| Left | 6(60%) |
| Bilateral | 0 |
| **Histology** | |
| **T stage** | |
| $T_1$ | 1(10%) |
| $T_2$ | 1(10%) |
| $T_3$ | 6(60%) |
| $T_4$ | 2(20%) |
| **NODAL stage** | |
| $N_0$ | 3(30%) |
| $N_1$ | 3(30%) |
| $N_2$ | 2(20%) |
| $N_3$ | 2(20%) |
| **Metastasis** | |
| $M_X$ | 10 |

**Table 4:** Immunohistochemical diagnosis

| Case | ER Status | PR Status | Her2/Neu | E-Cadherin | Final Diagnosis |
|---|---|---|---|---|---|
| 1 | + | + | - | + | IDC |
| 2 | + | + | - | - | ILC |
| 3 | + | + | - | - | ILC |
| 4 | + | + | - | - | ILC |
| 5 | + | + | - | + | IDC |
| 6 | - | - | - | + | IDC |
| 7 | + | + | - | + | IDC |
| 8 | - | - | - | + | IDC |
| 9 | - | - | + | + | IDC |
| 10 | - | - | + | + | IDC |

**Table 5:** Distribution of IHC findings

| IHC Markers | No. of patients (%) |
| --- | --- |
| **Estrogen receptor** | |
| Positive | 6(60%) |
| Negative | 4(40%) |
| **Progesterone receptor** | |
| Positive | 6(60%) |
| Negative | 4(40%) |
| **Her2/neu** | |
| Positive | 1(10%) |
| Negative | 9(90%) |
| **E-Cadherin** | |
| Positive | 7(70%) |
| Negative | 3(30%) |

E-Cadherin can be reliably checked, for distinguishing the ILC variants from IDC.[7] A negative E-cadherin stain acts as a sensitive and specific biomarker to confirm the diagnosis of invasive lobular carcinoma.[8]

## 4. Authors' Contribution

Data collection, review of the literature and drafted the manuscript. All authors have read and approved the final manuscript.

## 5. Source of Funding

No funding was received.

## 6. Conflict of Interests

The authors declare no conflict of interests.

## References

1. Gogia A, Raina V, Deo SV, Shukla NK, Mathur S, Mohanti BK, et al. Clinico-pathological characteristics and treatment outcome in invasive lobular carcinoma of the breast: An Indian experience. *Indian J Cancer*. 2018;55(4):344–47.
2. Cristofanilli M, Gonzalez-Angulo A, Sneige N, Kau SW, Broglio K, Theriault RL, et al. Invasive lobular carcinoma classic type: response to primary chemotherapy and survival outcomes. *J Clin Oncol*. 2005;23(1):41–8.
3. Pandiar D, Smitha T. Single file" pattern in histopathology. *J Oral Maxillofac Pathol*. 2020;24(2):204–5.
4. Rakha E, Ellis I. Lobular breast carcinoma and its variants. *Semin Diagn Pathol*. 2010;27:49–61.
5. Front, Oncol. 2021. Available from: https://doi.org/10.3389/fonc.2020.591399.
6. Jagtap SV, Beniwal A, Chougule PG, Shah HP, Jagtap SS. Invasive Lobular Carcinoma of Breast Histopathological Subtypes: Clinicopathological Study. *J Int Med Res*. 2016;49(6). doi:3000605211017039.
7. Pai K, Baliga P, Shrestha BL. E-cadherin expression: a diagnostic utility for differentiating breast carcinomas with ductal and lobular morphologies. *J Clin Diagn Res*. 2013;7(5):840–4.
8. Christgen M, Steinemann D, Kühnle E, Länger F, Gluz O, Harbeck N, et al. Lobular breast cancer: Clinical, molecular and morphological characteristics. *Pathol Res Pract*. 2016;212(7):583–97.

## Author biography

**Priyadarshini Rajkumari,** Final Year Postgraduate

**Aravind Pallipady,** Professor