MOH

Journal of Medical Case Reports

# Non-mucinous, Invasive Mixed Ductal Lobular Carcinoma with Metastatic Mucinous Features in Lymph Nodes and Overexpression of HER-2 and Estrogen: Case Report and Review of the Literature

*Fadi Jamaleddin[1], Chantal Markarian[1], Fardowsa Robow[2], Stephanie McCarthy[1], Melissa Candela[1], Andressa Balbi[1], Racquel Kaizer[1], Neda Sohrabi[1], Jessica Jahoda[1,3*], and Mohamed Aziz[3]*

## Abstract

Invasive ductal carcinoma (IDC) and invasive lobular carcinoma (ILC) are the most common types of invasive breast carcinoma. However, there are several cases where both ductal and lobular characteristic features are present in the same tumor. These types of mixed tumors are referred to as invasive mixed ductal lobular carcinoma (mDLC). Mixed ductal lobular carcinoma represents a unique clinical entity that integrates certain attributes from both lobular and ductal breast carcinoma. Mucinous breast carcinoma is an uncommon type defined as pure mucinous carcinoma (PMC) when it shows at least 90% mucinous component and mixed mucinous carcinoma (MMC) when it shows less than 50% mucinous component. The categorization of invasive breast cancer into discrete subtypes based on tumor histology holds specific importance for diagnostic and prognostic considerations. This report details a case of invasive mixed ductal lobular carcinoma in a 42-year-old woman, notable for the absence of a mucinous component in the primary tumors. At the same time, two out of nine positive axillary lymph nodes exhibit characteristics consistent with mucinous carcinoma. We review the relevant literature and attempt to understand the mechanisms behind the phenomenon of the changing features of a metastatic tumor from the primary tumor.

## Introduction:

Breast cancer (BC) is the most common cancer among women in the United States and is the second leading cause of cancer death in women after lung cancer. Breast cancer is estimated to affect 13% of women in the general population at some point in their lives.[1] On the other hand, by the time they are 70–80 years old, 55%–72% of women who inherit a BRCA1 gene mutation and 45%–69% of women who inherit a BRCA2 variant will have breast cancer.[1] Several factors influence a woman's risk, some of which are still being investigated. In the realm of histopathology, invasive breast cancer manifests as a histologically diverse entity. Predominantly, invasive ductal carcinoma (IDC) emerges as the prevailing archetype, constituting 70–75% of reported cases.[2] Subsequently, invasive lobular carcinoma (ILC) follows suit, contributing to 5–15% of cases.[2] A subset of cases, approximately 5%, manifest as invasive mixed ductal and lobular carcinoma (mDLC), displaying features of both IDC and ILC.[3] Breast mucinous carcinoma (MC), colloquially known as colloid cancer, represents a relatively rare category, encompassing about 4% of all breast cancer cases.[4] Recently, there has been an observable escalation in the prevalence of lobular breast tumors, notably among postmenopausal women. This surge has been correlated with compelling indications proposing that the heightened utilization of hormone replacement therapy in contemporary years has augmented the risk of developing invasive lobular carcinoma (ILC) and mixed invasive ductal and lobular carcinoma to a greater extent than that of invasive ductal carcinoma.[5]

We present the case of a 42-year-old woman who developed multifocal invasive mDLC. Although there was no evidence of a mucinous component in the primary tumor masses, two of the nine positive axillary lymph nodes showed features of metastatic mucinous carcinoma after neoadjuvant chemotherapy. Metastatic malignancy usually follows the same features as primary malignancy, with few exceptions. In this report, we review the relevant literature to explain the reasons behind the changes occurring in metastatic tumors and why the non-mucinous breast carcinoma showed lymph node metastasis with features of mucinous carcinoma.

Affiliations

[1]*American University of the Caribbean Medical School, USA*

[2]*St. George's University School of Medicine, Grenada, West Indies*

[3]*Research Writing & Publication (RWP), LLC, NY, USA*

## Case Presentation:

A 42-year-old woman presented with multiple left breast masses involving the outer half of her left breast, discovered during a breast examination. Two years ago, the patient's mammogram showed multiple left breast dense nodularities, and she was advised to follow up with her primary physician right away. She did not follow the recommendation. A physical examination showed two palpable masses in the upper outer quadrant (UOQ) and lower outer quadrant (LOQ). The mammogram showed two main masses (#1= at least 4.5 cm and #2= at least 3.2 cm) and multiple smaller ones (4 nodules), each smaller than 0.5 cm. In addition, the left axilla showed multiple nodularities suspicious of metastatic carcinoma in the lymph nodes. At the age of 63, the patient's mother developed invasive ductal breast carcinoma that tested positive for ER but negative for Her-2 and required lumpectomy, radiation, and hormonal therapy. BReast CAncer (BRCA) gene testing was not performed at that time.

A core biopsy of the two large masses showed the same features of invasive mixed ductal lobular carcinoma and ductal carcinoma in situ (DCIS). Both tumors were positive for Her-2 and ER. The second mass at the LOQ showed more lobular features than the first mass. Immunohistochemistry (IHC) studies, including negative E-Cadherin, outlined the lobular component in the mixed tumors. No mucinous component was identified in either biopsy. An axillary lymph node biopsy showed metastatic carcinoma with the same ductal and lobular features and no evidence of a mucinous component. Due to the strong family history, the patient was tested for BRCA genes and was positive for both BRCA-1 and BRCA-2. The patient's two sisters decided to perform BRCA testing. The older sister showed positivity for BRCA-1, while the younger sister was negative for BRCA-1 or BRCA-2. The body survey showed no evidence of metastatic disease. A multidisciplinary tumor board recommended mastectomy and axillary dissection following neoadjuvant chemotherapy. Neoadjuvant chemotherapy with doxorubicin, taxanes, and pertuzumab was started to shrink the tumors and evaluate the therapy effect.

The patient decided to undergo a bilateral mastectomy and reconstruction. The right breast mastectomy examination showed no evidence of malignancy. The pathological findings in the left mastectomy were described as follows: Invasive mixed ductal and lobular carcinoma and DCIS. Two residual viable post-therapy masses were identified: #1 at the 2:00 o'clock location, measuring 1.4 cm (Figure 1A,B), and #2 at the 5-6:00 site, measuring 1.3 cm (Figure 1C,D). Both masses showed prominent therapy effects, with moderate sclerosis estimated at 80% of the original tumors and no mucinous features. In addition, multiple scattered viable tumor foci, each measuring less than 0.3 cm, were present. The mastectomy surgical margins were free of tumors, with at least a 4 mm safe margin.

A left axillary dissection revealed nine out of 14 lymph nodes positive for mixed ductal and lobular carcinoma. Also, several small fibrotic nodules were found. Following therapy, these were probably metastasized lymph nodes with complete necrosis and fibrosis (Figure 2A). Pure mucinous carcinoma involved more than 75% of two of the nine positive lymph nodes (Figure 2B). Extracapsular extension of the metastatic tumor was noted in most of the positive lymph nodes. It was pointed out that small and medium-sized blood vessels and lymphatics had spread around the tumor masses and the left axillary area. None of the vascular invasion fragments showed any mucinous component (Figure 2C). There was no non-cancerous breast tissue found in the axillary tissue, which ruled out the possibility of other primary mucinous carcinomas in ectopic breast tissue. There were diagnostic areas of mucinous carcinoma in both lymph nodes, which ruled out the possibility of a mucocele-like lesion in the left axilla. Neural invasion was also identified in the dissected axillary tissue (Figure 2D).

Therapeutic analysis was performed on both major masses, and the results were as follows: Tumor #1 at 2:00 o'clock was positive for ER (ID5) with 95% strong nuclear staining, PR negative with <1% nuclear

staining, Ki67 (MIB-1) with high proliferation 40% nuclear staining and Her-2 3+/positive. Tumor #2 at 5-6:00 o'clock was positive for ER with 95% strong nuclear staining, positive for PR with 90% strong nuclear staining, intermediate proliferation with Ki-67 10% nuclear staining, 2+/equivocal Her-2, but 2.3/positive with Her-2 and Cep 17 FISH studies. Immunohistochemistry (IHC) studies and therapeutic analysis were the same for pre-and post-operative tumor analysis. Negative E-Cadherin outlined the lobular component in both tumor masses, which was more prominent in tumor #2. Both tumors were negative for MUC1 and MUC2 in the initial biopsies. Nevertheless, the sampling phenomenon most likely explains why the tumors in the mastectomy specimen were positive for MUC1 and negative for MUC2. The patient received adjuvant chemotherapy, including doxorubicin, taxanes, and trastuzumab with pertuzumab, in addition to hormonal therapy.

After four years with no evidence of recurrence or metastasis, the patient began to develop moderate coughing and episodes of severe dyspnea, in addition to gradual changes in mental status. Imaging studies confirmed the presence of multiple metastatic masses involving both the lungs and the brain. The condition was considered terminal, and the patient was provided with hospice care, which lasted for three weeks, after which the patient expired.

## Discussion:

Breast cancer (BC) is the most diagnosed cancer in women in the United States. It is the second most common cause of cancer death in women after lung cancer. Ductal carcinoma of the breast is the most common breast malignancy, followed by lobular carcinoma. Mucinous carcinoma (MC) is a special type of breast carcinoma that is defined as pure mucinous carcinoma (PMC) when it shows at least 90% mucinous component and as mixed mucinous carcinoma (MMC) when it shows less than 50% mucinous component.[6] With some exceptions, metastatic tumors usually have the same histomorphological features as the primary tumor. These exceptions typically include changes in tumor grade, metaplastic changes, or tumor dedifferentiation. Mucinous carcinoma has a better prognosis than invasive ductal or lobular carcinoma, and lymphatic metastasis is uncommon.[4,6]

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.[7] Characteristic attributes of invasive lobular carcinoma (ILC) encompass the absence of the cell-cell adhesion molecule E-Cadherin, leading to the propagation of small dyscohesive cells in linear arrangements.[7] Additionally, ILC is characterized by positive expression for both estrogen receptor (ER) and progesterone receptor (PR) while concurrently exhibiting negativity for human epidermal growth factor receptor 2 (HER-2).[8] Indeed, ductal carcinoma in situ and low-grade invasive ductal carcinoma typically manifest heightened E-cadherin (ECAD) membrane staining compared to the staining observed in normal breast epithelial cells. This phenomenon indicates an upregulation in expression rather than a reduction.[9] Invasive lobular carcinoma (ILC) exhibits a higher propensity for multifocality and bilaterality in contrast to invasive ductal carcinoma (IDC).[7] A loss of cellular adhesion typifies ILC and its subtypes, frequently the result of biallelic inactivation where there is gene mutation combined with gene deletion of the CDH1 gene encoding E-cadherin, although other mechanisms of expression loss also feature.[10] The loss of the E-cadherin gene is a hallmark feature of ILC that can aid in molecular diagnosis. The E-cadherin gene encodes a 120 kDa single transmembrane glycoprotein, or CDH1, found on human chromosome 16q22.1.[11] There is a correlation between having the mutation on CDH1 and ILC, and it was discovered that 89% of cases with heterozygous deletion of chromosome 16 had this mutation.[11]

The key pathological features of dyscohesive morphology and proliferation into single-file strands, alongside the diffuse growth pattern of ILC, make establishing a diagnosis particularly challenging. ILC is difficult to detect upon physical examination and with standard imaging techniques.[12] However, magnetic

resonance imaging (MRI) reported greater sensitivity in detecting and characterizing ILC than "gold standard" mammography. Systemic therapy is an integral part of the multidisciplinary approach to treating BC, and this often involves the use of chemotherapy. However, due to the unique molecular biology of ILC, treatment response to chemotherapy is often predictably poor, resulting in lower rates of complete pathological response, thus leading to an increase in mastectomy rates in these patients.[12,13] Despite challenges, key features such as ER and PR positivity are associated with an excellent response to hormonal treatment (HT) among ILC patients. Evidence suggests that using an aromatase inhibitor such as letrozole should be the treatment of choice in ILC due to the inevitable endocrine resistance associated with tamoxifen. In the case of advanced BC, targeted therapies such as CDK4/6 inhibitors combined with traditional HT are warranted. This is currently being investigated in the neoadjuvant setting in the PELOPS clinical trial.[14] Mutations within the CDH1 gene are common factors in the pathogenesis of ILC alongside mutations within the PI3K pathway. Therefore, therapies targeting these pathways represent an attractive option for ILC patients. Furthering our understanding of the unique biology of ILC is essential to facilitate the development of novel therapeutic strategies, moving toward precision medicine for patients diagnosed with all subtypes of ILC.[12]

Invasive mixed ductal lobular carcinoma (mDLC) remains a poorly understood subtype of breast cancer composed of coexisting ductal and lobular components. These cases might show clinical and pathological characteristics other than pure ILC or IDC.[5] A meta-analysis evaluating mDLC showed shared features with both ILC and IDC, with significantly more ER-positive and fewer high grades in mDLC compared to IDC, although mDLCs were significantly smaller and included fewer late-stage tumors compared to ILC.[15] One study investigated clinicopathologic features to determine whether mDLC is clinically more similar to IDC or ILC. They observed a higher concordance in clinicopathologic characteristics between mDLC and ILC compared to IDC.[16] Additionally, they noted the trend for higher rates of successful breast-conserving surgery after neoadjuvant chemotherapy in patients with mDLC compared to patients with ILC, which is known to be lower than in those with IDC.[16] The favorable prognosis of mDLC compared with ILC was noted in a recent study by Metzger-Filho et al., which compared the management course for 474 patients with invasive mDLC and 337 patients with ILC. Their results showed that mastectomy was more common in ILC patients than in invasive mDLC patients. However, there were no appreciable variations in the frequency of radiation. Nevertheless, the study showed that individuals with ILC received chemotherapy less frequently, even though their tumor burden was more considerable upon diagnosis. In the same study, 91 patients (44 patients with ILC and 47 patients with invasive mDLC) were found to have recurrences of the disease. The consistent pattern of relapse after year 5 was probably the reason for the poor outcomes linked to ILC.[17] More studies are necessary to fully understand the biology and clinical importance of tumors containing mDLC, which are less frequent. Compared to ILC and IDC, invasive mDLC metastasizes to far-off locations, with a greater preference for the liver and peritoneum. In our case, metastasis occurred in the lung and the brain. The metastatic lesions caused by invasive mDLC tumors show IDC, ILC, and invasive mDLC traits. Ongoing genetics investigations will likely illuminate details on the pattern of invasive mDLC tumor metastases.[5] Nasrazadani et al. compared the response to systemic therapy between invasive mDLC and ILCs and the overall prognosis and predictive significance of histologic grade. They demonstrated that patients with invasive mDLC tumors, particularly postmenopausal women, had a better prognosis than those with ILC. Their findings could affect practices for follow-up. Furthermore, they reported that histologic grade showed a substantial predictive value in invasive mDLC, highlighting its clinical relevance in guiding decisions on invasive mDLC treatment, even though it could not stratify ILC risk.[16] In addition, their study concluded that adjuvant aromatase inhibitors were

superior to tamoxifen for disease-free survival in ILC, and this was also true for invasive mDLC.[5,16]

Breast mucinous carcinoma (MC) is classified as a special subtype of breast cancer in the most recent World Health Organization (WHO) classification of breast cancers (2019). The main characteristic of breast MC is mucin synthesis, with extracellular mucin production predominating.[4] Breast MC is classified into two categories based on the extent of mucin production by the breast epithelial cells: 1) Pure mucinous carcinoma of the breast (PMC), in which tumor cells expressing both extracellular and intracellular mucin make up over 90% of the tumor mass. This variant is more common: 2) Mixed mucinous carcinoma (MMC), where mucin makes up less than 90% of the tumor mass, which includes infiltrating elements with features of ductal or lobular breast cancer.[6] Compared to invasive ductal carcinoma (IDC), mucinous carcinoma has a higher MUC2 expression predominance and higher expression levels of the progesterone receptor (PR) and estrogen receptor (ER). The significant synthesis of mucin has been linked to the overexpression of MCU2, making it a unique property.[18] It is also important to remember that MC can rarely show HER2 positivity. These Her-2-positive cases, particularly those with ER+ and PR+ HER2+ patterns, should be treated with anti-HER2 therapy, chemotherapy, and hormone therapy containing aromatase inhibitors.[20,21]

The characteristic of cancer that causes the most cancer-related deaths is metastasis. It still needs to be better understood, though. To explain the phenomenon observed in our case, where the metastatic tumor of a primary non-mucinous carcinoma showed lymph node metastasis with features of mucinous carcinoma, we should comprehend the principles that control the metastatic process from the beginning to the end. A few of the molecular foundations of this dispersion process have been identified by the ongoing development of investigations in cancer biology and the introduction of novel paradigms in the study of metastasis.[21] Can genomic and epigenomic changes of cancer cells and their interaction with the surrounding tissue explain the changes in the metastatic features of the primary tumor reported in our case? The answer to this question will require continued reporting of cases with findings like ours to enrich our understanding of this phenomenon. J. Fares and his group examined the most recent developments in the study of metastasis and highlighted the most recent discoveries that have shaped this characteristic of cancer. While traveling to the target location, the invasive tumor cell interacts with other cells and proteins. In this study, they found that identifying these relationships enhanced some of the basic concepts governing the mobility and adaptability of the metastatic cell. They demonstrated that through communication with the tumor microenvironment, invasive cancer cells can settle and colonize despite stromal obstacles. In addition, changes in the genome and epigenome of the tumor cell and the surrounding tissue cause these features of cancer cells. They concluded that determining the molecular principles behind the metastatic process is essential to identifying windows of opportunity for effective therapeutic interventions.[22] A review of the literature revealed that most studies looked at tumor-grade alterations. The frequency with which metastases change in grade from their primary tumors and whether a higher grade of metastases influences prognosis remain unknown.[23] Most cancers, if not all of them, develop and spread in response to intense evolutionary pressure from trophic, metabolic, immunological, and therapeutic variables. These elements have varying relative effects on tumor evolution throughout time and space, ultimately supporting the development of a neoplastic microenvironment with significant genetic, phenotypic, and behavioral heterogeneity among its constituents.[24]

We report an unusual case of a breast primary tumor with features of mixed ductal and lobular carcinoma, with a lobular component predominating and no mucinous characteristics. Interestingly, two of the nine positive axillary lymph nodes showed features typical of mucinous carcinoma metastases after receiving neoadjuvant treatment. While the possibility of a new axillary mucinous-type tumor mass is contemplated,

the lack of residual non-cancerous breast tissue eliminates the possibility of a new MC originating from axillary ectopic breast tissue. The mucinous component that was identified could be a possible result of the neoadjuvant treatment. Remarkably, most carcinomas do not experience significant morphological changes after chemotherapy, and the changes are usually a decrease in cellularity and an increase in nuclear atypia, as reported by Moll UM et al.[25] Nevertheless, some instances of altered tumor histology following neoadjuvant chemotherapy have been documented in recent studies. The most reported modifications were to HER-2 and estrogen receptor expression. According to IHC investigations, changes in tumor type and grade were also reported.[26,27] Except for the emergence of mucinous carcinoma in two metastatic lymph nodes, our reported tumor pathology did not alter following chemotherapy. A further scenario is that the metastatic tumor is combined with an axillary mucocele lesion. The absence of histologic evidence of a mucocele and the presence of diagnostic mucinous cancer in the two lymph nodes ruled out this scenario.

A core biopsy is usually used to diagnose breast cancer. This limited core tissue sample represents a tiny portion of the tumor mass and is not necessarily representative of the entire tumor, considering the usual tumor heterogenicity. It should be noted that the initial size of the larger primary tumor mass in our case was large, measuring more than 4 cm, raising the possibility of limited sampling. The initial diagnostic core biopsy may not have sampled a mucinous component. In addition, none of the malignant fragments inside vasculatures noted with vascular invasion showed a mucinous component. It is difficult to determine if the changes that have been noticed represent heterogeneity in the initial tumor or result from the chemotherapy. Prospective studies using multiple sampling areas of large tumors may be necessary to examine and explore this possibility. An extensive literature review failed to explain the changes in the metastatic tumor noted in our case. This report aims to alert breast cancer professionals to this phenomenon, promoting increased awareness, encouraging further investigations, and reporting on this unusual presentation.

## Figures:

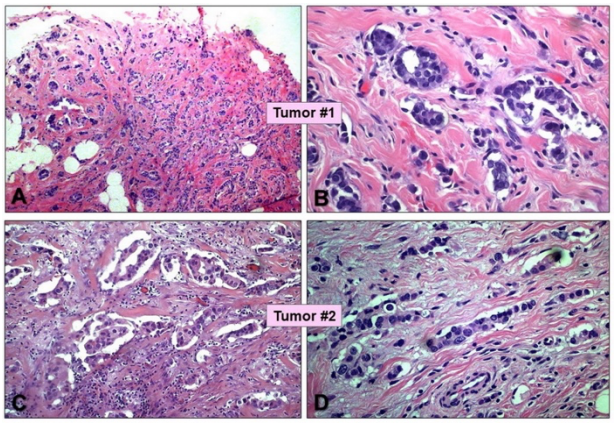


Figure 1: Microscopic examination of post-chemotherapy tumor masses #1 and#2
1A: Low-power view of tumor mass #1 showing infiltrating carcinoma with mixed ductal and lobular features (H&E stain X20)
1B: High-power view of tumor #2 showing infiltrating ductal glands and infiltrating single lobular cells (H&E stain X40)
1C: Low-power view of tumor mass #2 showing infiltrating mixed ductal lobular carcinoma with a predominance of lobular features (H&E stain X40)
1D: High-power view of tumor #2 showing infiltrating prominent lobular features with single lines of malignant lobular cells (H&E stain X40)

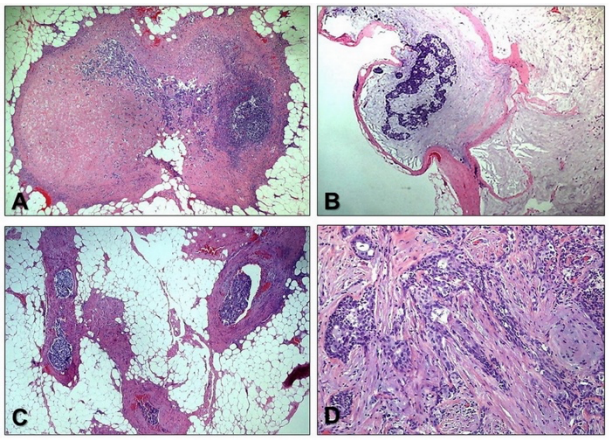


Figure 2: Axillary lymph nodes with metastasis and vascular/neural invasion
2A: A low-power view shows a lymph node subtotal replaced by dense post-therapy fibrosis, residual lymphoid tissue, and scattered residual viable tumors in the center of the nodule. (H&E stain X20)

2B: A low-power view shows a lymph node replaced by metastatic mucinous carcinoma and mucinous spread in the axillary tissue. (H&E stain x20)
2C: A low-power view shows axillary blood vessels invaded by clusters of tumor cells (H&E stain x20)
2D: A high-power view shows axillary tissue with neural invasion by tumor clusters

## Acknowledgements:

Special thanks to Alisa Lu, Tallen Cavenah, and Marium Choudhry, MD candidates, for their assistance in preparing manuscript images and reviewing the final manuscript

**Submitted:** November 26nd, 2023 | **Accepted:** December 3rd, 2023 | **Published:** January 2nd, 2024

***Corresponding author:** Jessica Jahoda*, Research Writing & Publication (RWP) LLC, 2475 Lefferts Place, Bellmore, NY 11710, USA, Tel: 954-479-0890, Email: jessicajahoda94@gmail.com



**Citation:** Jamaleddin F, Markarian C, Robow F, McCarthy S, Candela M, Balbi A, Kaizer R, Sohrabi N, Jahoda J, and Aziz M, Non-mucinous, Invasive Mixed Ductal Lobular Carcinoma with Metastatic Mucinous Features in Lymph Nodes and Overexpression of HER-2 and Estrogen: Case Report and Review of the Literature, 2024 December 1(3), 7-14.

## References:

1. Howlader NN, Noone AM, Krapcho ME, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS. SEER Cancer Statistics Review, 1975–2016. National Cancer Institute. 2019 Apr 8;1.
2. Pestalozzi BC, Zahrieh D, Mallon E, Gusterson BA, Price KN, Gelber RD, Holmberg SB, Lindtner J, Snyder R, Thürlimann B, Murray E. Distinct clinical and prognostic features of infiltrating lobular carcinoma of the breast: combined results of 15 International Breast Cancer Study Group clinical trials. Journal of clinical oncology. 2008 Jun 20;26(18):3006-14.
3. Corben AD. Pathology of invasive breast disease. Surgical Clinics. 2013 Apr 1;93(2):363-92.
4. Tan PH, Ellis I, Allison K, Brogi E, Fox SB, Lakhani S, Lazar AJ, Morris EA, Sahin A, Salgado R, Sapino A. The 2019 WHO classification of tumours of the breast. Histopathology. 2020 Feb 13.
5. Altundag K. Is mixed invasive ductal lobular carcinoma distinct from invasive lobular carcinoma?. Breast Cancer Research and Treatment. 2023 Nov;202(2):409.
6. Hanagiri T, Ono K, Baba T, So T, Yamasaki M, Nagata Y, Uramoto H, Takenoyama M, Yasumoto K. Clinicopathologic characteristics of mucinous carcinoma of the breast. International surgery. 2010 Apr 1;95(2):126-9.
7. Li CI, Anderson BO, Daling JR, Moe RE. Trends in incidence rates of invasive lobular and ductal breast carcinoma. Jama. 2003 Mar 19;289(11):1421-4.
8. Luveta J, Parks RM, Heery DM, Cheung KL, Johnston SJ. Invasive lobular breast cancer as a distinct disease: implications for therapeutic strategy. Oncology and therapy. 2020 Jun;8:1-1.
9. Jeschke U, Mylonas I, Kuhn C, Shabani N, Kunert-Keil C, Schindlbeck C, Gerber B, Friese K. Expression of E-cadherin in human ductal breast cancer carcinoma in situ, invasive carcinomas, their lymph node metastases, their distant metastases, carcinomas with recurrence and in recurrence. Anticancer research. 2007 Jul 1;27(4A):1969-74.
10. McCart Reed AE, Kalinowski L, Simpson PT, Lakhani SR. Invasive lobular carcinoma of the breast: the increasing importance of this special subtype. Breast Cancer Research. 2021 Dec;23(1):1-6.
11. Pramod N, Nigam A, Basree M, Mawalkar R, Mehra S, Shinde N, Tozbikian G, Williams N, Majumder S, Ramaswamy B. Comprehensive review of molecular mechanisms and clinical features of invasive lobular cancer. The Oncologist. 2021 Jun 1;26(6):e943-53.
12. Wilson N, Ironside A, Diana A, Oikonomidou O. Lobular breast cancer: a review. Frontiers in Oncology. 2021 Jan 15;10:591399.
13. Boughey JC, Wagner J, Garrett BJ, Harker L, Middleton LP, Babiera GV, Meric-Bernstam F, Lucci A, Hunt KK, Bedrosian I. Neoadjuvant chemotherapy in invasive lobular carcinoma may not improve rates of breast conservation. Annals of surgical oncology. 2009 Jun;16:1606-11.
14. Dziadzko M, Bouteleux A, Minjard R, Harich J, Joubert F, Pradat P, Pantel S, Aubrun F. Preoperative Education for Less Outpatient Pain after Surgery (PELOPS trial) in orthopedic patients—study protocol for a randomized controlled trial. Trials. 2022 May 21;23(1):422.
15. Zhao H. The prognosis of invasive ductal carcinoma, lobular carcinoma and mixed ductal and lobular carcinoma according to molecular subtypes of the breast. Breast Cancer. 2021 Jan;28:187-95.

16. Nasrazadani A, Li Y, Fang Y, Shah O, Atkinson JM, Lee JS, McAuliffe PF, Bhargava R, Tseng G, Lee AV, Lucas PC. Mixed invasive ductal lobular carcinoma is clinically and pathologically more similar to invasive lobular than ductal carcinoma. British journal of cancer. 2023 Apr 6;128(6):1030-9.
17. Metzger-Filho O, Ferreira AR, Jeselsohn R, Barry WT, Dillon DA, Brock JE, Vaz-Luis I, Hughes ME, Winer EP, Lin NU. Mixed invasive ductal and lobular carcinoma of the breast: prognosis and the importance of histologic grade. The oncologist. 2019 Jul 1;24(7):e441-9.
18. Hugen N, Simons M, Halilović A, van der Post RS, Bogers AJ, Marijnissen-van Zanten MA, de Wilt JH, Nagtegaal ID. The molecular background of mucinous carcinoma beyond MUC2. The Journal of Pathology: Clinical Research. 2015 Jan;1(1):3-17.
19. Zhao X, Yang X, Gao R, Zhai L, Yang L, Yu K. HER2-positive pure mucinous breast carcinoma: A case report and literature review. Medicine. 2020 Aug 8;99(33).
20. Lubert J, Shirah J, Ramirez R, Hassan R, Williams R, Murry K, Aziz M. Primary Mucinous Cystadenocarcinoma of the Breast: Case Report and Review of the Literature. Journal of Medical Case Reports. 2022 Sep 28;1(1):36-9.
21. Lambert AW, Pattabiraman DR, Weinberg RA. Emerging biological principles of metastasis. Cell. 2017 Feb 9;168(4):670-91.
22. Fares J, Fares MY, Khachfe HH, Salhab HA, Fares Y. Molecular principles of metastasis: a hallmark of cancer revisited. Signal transduction and targeted therapy. 2020 Mar 12;5(1):28.
23. Keck KJ, Choi A, Maxwell JE, Li G, O'Dorisio TM, Breheny P, Bellizzi AM, Howe JR. Increased grade in neuroendocrine tumor metastases negatively impacts survival. Annals of surgical oncology. 2017 Aug;24:2206-12.
24. Romero I, Garrido C, Algarra I, Chamorro V, Collado A, Garrido F, Garcia-Lora AM. MHC intratumoral heterogeneity may predict cancer progression and response to immunotherapy. Frontiers in Immunology. 2018 Jan 29;9:102.
25. Moll UM, Chumas J. Morphologic effects of neoadjuvant chemotherapy in locally advanced breast cancer. Pathology, research and practice. 1997 Jan 1;193(3):187-96.
26. Sethi D, Sen R, Parshad S, Khetarpal S, Garg M, Sen J. Histopathologic changes following neoadjuvant chemotherapy in locally advanced breast cancer. Indian journal of cancer. 2013 Jan 1;50(1):58-64.
27. De La Cruz LM, Harhay MO, Zhang P, Ugras S. Impact of neoadjuvant chemotherapy on breast cancer Subtype: Does subtype change and, if so, how? IHC profile and neoadjuvant chemotherapy. Annals of surgical oncology. 2018 Nov;25:3535-40.