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## Case Report

# Coexisting lactating adenoma and invasive breast carcinoma: A case report and review of literature

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### ABSTRACT

Lactating adenomas are the most common masses occurring during pregnancy. Although they are not thought to carry an increased risk of malignancy, there are rare cases of co-existence of Lactating adenoma and Invasive breast carcinoma. We present a 28-year-old lactating woman with an enlarging breast lump for 1 year. Histopathological examination of the resected mass showed lactating adenoma and invasive ductal carcinoma, no special type. This may have been a collision between a separate lactating adenoma and an invasive ductal carcinoma or a malignant transformation of a lactating adenoma. Analysing this case and more such cases can enable us to better understand the etiological factors, clinical and histological characteristics, and the prognosis of invasive ductal carcinoma associated with lactating adenoma.

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## 1. Introduction

Lactating adenoma (LA) is a benign condition of the breast, secondary to the hormonal changes associated with pregnancy and lactation. Although a rare entity, they are the most commonly encountered mass in pregnant and lactating women.<sup>1</sup> Aggressive LA may present with a large ulcerating mass, mimicking malignancy and creating diagnostic confusion.<sup>2</sup> Pregnancy-associated breast cancer (PABC) is reported in 1/3000 pregnancies.<sup>3</sup> On doing a literature search through Google scholar and PUBMED, only 7 cases of concurrent lactating adenoma and invasive breast carcinoma have been reported in current English literature, with our case being the eighth.<sup>4–9</sup> The underlying pathogenesis behind its coexistence remains unclear, and the evaluation of such cases is needed to help determine whether it's a mere coincidence, a malignant transformation, or an increased association between the two.

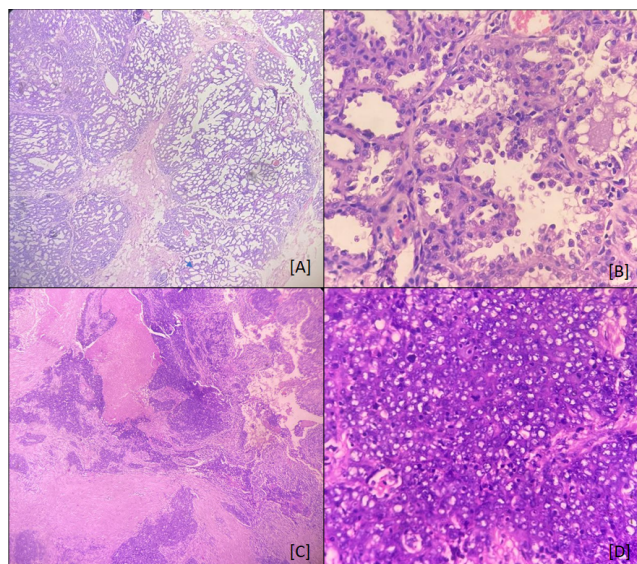
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## 2. Case Report

A 28-year-old woman, breastfeeding for the past 7 months, presented with a progressively enlarging, painless breast lump for 1 year. On examination, a firm to hard, non-mobile, non-tender lump was felt in the left breast. No associated nipple discharge or skin changes were observed. Ultrasonography findings showed an ill-defined, heterogeneous, predominantly hypo-echoic collection in the upper outer quadrant of the left breast with a few sub-centimetric lymph nodes in left axilla. 6 ml straw-colored fluid was aspirated on fine needle aspiration and was reported as an abscess. On histopathological examination of the breast lump, a focally necrotic grey-white single mass measuring 9x8.5x7 cm was seen. Serial sectioning showed a circumscribed, grey-tan lobulated area with adjacent focus showing grey-white areas with focal necrosis. Microscopy of the grey-tan lobulated region showed well-circumscribed proliferation of lobules lined by secreting cuboidal cells, with small nuclei showing focal hobnailing and granular to

vacuolated cytoplasm (Figure 1 A and B). Adjacent grey-white area showed sheets of tumor cells having pleomorphic vesicular nuclei with multiple prominent nucleoli and moderate eosinophilic cytoplasm, frequent mitoses with few atypical forms surrounded by desmoplastic and necrotic stroma (Figure 1C and D) with a clearly defined boundary between the two lesions. The invasive component was of no special type, modified Nottingham histologic grade 3. Immunohistochemistry demonstrated estrogen receptor (ER) positivity, progesterone receptor PR and HER2 negativity and a high Ki67 proliferation index of ~ 90%. A final diagnosis of Invasive Breast Carcinoma, NST along with coexisting LA was made. Post-surgical PET-CT scan revealed metastatic ipsilateral lymph nodes and a metastatic nodule in the upper lobe of the left lung. The patient has received 4 cycles of injection Epirubicin and Cyclophosphamide and 4 cycles of paclitaxel, followed by mastectomy. She is now scheduled for radiotherapy at 8 months of regular follow up.



**Figure 1:** H&E Photomicrograph, [A and B] 10X, 40X: Lactating adenoma showing luminal secretion, cytoplasmic vacuolations and nuclear hobnailing) [C and D] 10X, 40X: Invasive Breast Carcinoma, not otherwise specified, showing sheets of pleomorphic cells with frequent mitoses and abundant necrosis.

### 3. Discussion

Lactating adenomas, though being the most common mass occurring during pregnancy, are a rare entity.<sup>1</sup> Breast carcinomas, on the other hand, usually occur in older females but may occur in pregnant or lactating women with a low incidence rate of 1 in 3000 pregnancies.<sup>3</sup>

To the best of our knowledge, only 7 cases of concurrent lactating adenoma and invasive breast carcinoma have been reported in current English literature, with our case

being the eighth.<sup>4-9</sup> The underlying pathogenesis for its coexistence remains unclear. The popular opinion is lactating adenomas are benign entities and their coexistence with invasive carcinoma is a mere collision tumor, however, few consider it to have malignant potential.

The role of hormones is well established in the development of both, lactating adenoma as well as infiltrating ductal carcinoma. Saglam et al<sup>4</sup> proposed that high levels of prolactin and progesterone in lactating adenoma may help initiate carcinogenesis leading to its malignant transformation.

PABCs are usually large and high-grade tumors with lymph node metastases and poor prognosis.<sup>3</sup> The aggressive nature of PABC may be attributed to its late detection as these may be misinterpreted as physiological changes in the breast or due to the marked changes in the breast microenvironment in the form of vascular and ductolobular units' proliferation which may lead to the rapid tumor growth and metastasis.<sup>10</sup> On reviewing the literature of cases with concurrent lactating adenoma and breast carcinoma (Table 1), all the cases had a single mass on clinical and gross examination supporting the theory of malignant transformation, but it may also be due to the difficulty in detecting the tumor at an earlier stage as a separate entity, owing to pregnancy-associated changes. On microscopic examination, half the cases had distinct areas of malignant and benign lesions supporting the theory of collision, and one case showing intermingling of the two cell populations suggesting infiltration. However, Kumar et al<sup>6</sup> and Dakhure et al<sup>7</sup> reported carcinoma in situ admixed with LA, and Sharma et al<sup>9</sup> reported carcinoma in the center of LA suggesting a malignant potential of LA. The present case had IBC adjacent to LA, with a distinctly demarcated boundary separated by an area of fibrosis.

IHC study by Genin et al. concluded that PABC has two times more frequent HER2 positive and hormone-negative status.<sup>10</sup> The IBC cases with coexisting LA in this literature review also demonstrated a similar ratio of hormone receptor negativity (5/7 cases) and a high HER2 positivity (4/7 cases), indicating them to be similar to PABC at the molecular level, albeit more such case studies are needed to make a more accurate estimation. Our case was the only ER-positive case in the current literature review. More than half the cases (5/8 cases) reviewed showed lymph node metastases and some cases (2/8 cases), including our's, also had additional distant metastases (Table 1), another finding similar to PABC.

In our literature review, we found the cases of IBC with concurrent LA to be similar to other PABC cases, having higher grades, hormone receptor negativity, increased metastatic potential, and an overall poor prognosis. In addition, the literature review findings are more in favour of these lesions being a collision and benign lactating adenomas are unlikely to have a malignant potential.

**Table 1:** Review of literature of concurrent lactating adenoma and invasive breast carcinoma cases

Author	Age (years)	Laterality	Treatment	Gross features	Total Mass size/LA/ tumor (maximum dimension)	Microscopic Relation between the two lesions	Tumor histologic grade	Metastasis	Molecular profiling
Sagliam et al, 2005 <sup>4</sup>	36	Left	MRM, followed by chemotherapy	Lobulated with focal grey-white area	-/7/9 cm	Two lesions with intermingling benign and malignant components at the border	3	LN +ve	ER-ve, PR+ve, HER2 +ve
Khanna et al, 2015 <sup>5</sup>	28	Left	Lumpectomy followed by chemotherapy and radiotherapy	Firm, well-circumscribed	4.5/-/- cm	Two lesions at separate adjacent foci	-	Absent	ER-ve, PR-ve, HER2 +ve
Kumar et al, 2015 <sup>6</sup>	25	Right	Lumpectomy, lost to follow up	Diffuse grey-white with necrosis	5/-/-cm	Intermingled areas of LA, carcinoma in situ and infiltrative carcinoma	1	Absent	-
Dakhure et al, 2016 <sup>7</sup>	25	Right	lumpectomy	Well circumscribed, firm, grey-white	4.5/-/-cm	Focal Intermingled areas of LA, carcinoma in situ and infiltrative carcinoma	-	LN +ve	ER-ve, PR-ve, HER2 +ve
Umar et al, 2020 <sup>8</sup>	19	Right	Biopsy, no mention of treatment	-	5/-/-cm	Two lesions at separate foci	-	LN +ve	Triple-negative
Sharma et al, 2023; 9 case1	29	Right	MRM, lost to follow up at 7 months	Grey-white gritty area and grey-brown cystic area	-/4/6cm	Two lesions at separate adjacent foci	2	LN +ve, distant metastasis +ve	Triple-negative
Sharma et al, 2023; 9 case2	34	Right	MRM	Brown spongy mass with central grey-white area	6/6/2cm	LA with central carcinoma components	3	Absent	ER-ve, PR-ve, HER2 +ve
Present case	28	Left	Lumpectomy, followed by chemotherapy, MRM and intended radiotherapy	Lobulated with focal grey-white necrotic area	11.5/5/6cm	Two lesions at separate adjacent foci	3	LN +ve, distant metastasis +ve	ER+ve, PR-ve, HER2-ve

MRM: Modified radical mastectomy; LA: Lactating adenoma; LN: Lymph node; ER: Estrogen receptor; PR: Progesterone receptor; HER2: Human epithelial growth factor receptor 2.

However, analysis of more such cases may enable us to better determine its etiopathogenesis thereby improving its management and prognosis. Till then, all cases of LA should be dealt with a pinch of caution by the clinicians and advised regular follow-up.

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#### 5. Conflict of Interest

None.

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