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Research Article

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Lactating Adenoma Co-Existing with High Grade Invasive Ductal Carcinoma; Collision Tumour or Mere Co-Incidence

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Abstract

Background: Lactating adenoma are benign lesions that can presents as a solitary or multiple freely movable breast mass during pregnancy or puerperium. The lesion is actually a localized focus of hyperplasia in the lactating breast, which may also develop in ectopic locations such as the axilla, chest wall, or vulva. Breast cancer developing during pregnancy or puerperium is known as pregnancy associated breast cancer. We report a case of lactating adenoma co-existing with high grade invasive ductal carcinoma in young patient in puerperium with a positive family history of breast cancer. We present a 19-year-old female with a palpable mass on her right upper outer quadrant of her right breast measuring 5x4x2cm with ipsilateral supraclavicular lymph node enlargement. Cytomorphology of the lesion showed tumour cells arranged in nests and solid sheets with abundant fibromyxoid stroma. Also seen are abnormal mitosis and areas of lymphovascular invasion. Proliferating glands are seen lined by cuboidal cells with cytoplasmic vacuolations. Immunohistochemical stain show tumour cells were triple negative (negative for progesterone receptor (PR), estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) and strongly positive for EMA in both tumours.

Conclusion: This study indicated that lactating adenoma can co-exist with high grade invasive ductal carcinoma in a young patient in puerperium. The fact that this patient has a positive family history of breast cancer in first degree relative may explain the presentation at a very young age. It may be very difficult to ascertain whether this is a collision tumour or a mere co-incidence of lactating adenoma with breast cancer in this patient.

Keywords: Lactating Adenoma, Invasive Ductal Carcinoma, Collision Tumour, Co-Incidence.

Introduction

Lactating adenoma is the most common benign breast lesion seen during pregnancy and puerperium and is often seen during the third decade of life [1]. Lactating adenoma is not associated with the increased risk of breast cancer but there are some reports of co-incidence with breast carcinoma in the literature [2-4]. Lactating adenoma is a benign breast mass related to physiological changes during pregnancy and increased levels of estrogen, prolactin and progesterone levels [5]. These increased levels of estrogen, progesterone and prolactin results in growth of milk ducts and lobules, dilation of milk ducts and increasing stromal fat, resulting in increased volume and consistency of the breast. These changes can be confused with breast cancer on FNAC. On the other hand, invasive breast cancer is the most common carcinoma in women. It accounts for 22% of all female cancers, 26% in affluent countries, which is more than twice the occurrence of cancer in women at any other site [6]. Invasive ductal carcinoma coexisting with lactational adenoma is rarely reported in the literature.

Materials and Methods

The surgically resected breast specimen was fixed with 10% buffered formalin and embedded in paraffin. H&E and immunohistochemical sections were cut. Immunohistochemical analysis was performed using four antibodies ER, PR, HER2, and EMA. DB BIOTECH protocol was adapted in this study. Antigen retrieval was performed with Tris- EDTA buffer, pH 8 and incubated at 90-97oC in water bath for 25 minutes. Endogenous peroxidase blocking was done using 3% hydrogen peroxide. The primary antibodies used are anti-EMA (S35-V; 1:100 dilutions; DB BIOTECH, Slovak Republic), human epidermal growth factor receptor 2 (HER2) (dilution 1:100; DB BIOTECH Slovak Republic), progesterone receptor (PR) (X22-C, dilution 1:100; DB BIOTECH Slovak Republic), estrogen receptor (ER) (S21-V, dilution 1:100; DB BIOTECH Slovak Republic). Breast ductal carcinoma was

used as positive control.

Results

Case Presentation

The patient was a 19-year-old female who presented to the clinic 4 weeks after delivery with a palpable mass on her right upper outer quadrant of her right breast measuring 5x4x2cm with ipsilateral supraclavicular lymph node enlargement. She had a positive family history of breast cancer involving her mother and elder sister with her mother dying of the disease some years back. Her elder sister was diagnosed with invasive ductal carcinoma nos in October 2016. She was sent to the pathologist for FNAC of the affected breast and lymph node which was reported as malignant (C5) in the breast and metastatic deposits on the ipsilateral supraclavicular lymph node. Biopsy showed an infiltrating tumour growing in nests and solid sheets, the cells were markedly pleomorphic with hyperchromatic nuclei and moderate cytoplasm (Figures 2 and 3). The stroma is abundant and fibromyxoid. Areas of lymphovascular invasion and abnormal mitosis were observed. Areas of lactating adenoma seen separated from the infiltrating tumour (Figures 1 and 2). Immunohistochemical stains show ER-, PR-, HER2- and diffuse cytoplasmic and membranous staining with EMA on both the areas of lactating adenoma and invasive ductal carcinoma (Figures 4-8).

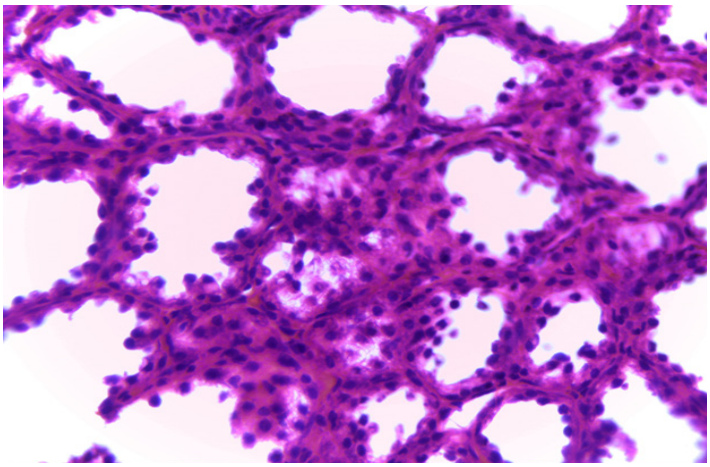

Figure 1: Photomicrograph showing proliferating glands line by cuboidal cells. H&Ex100

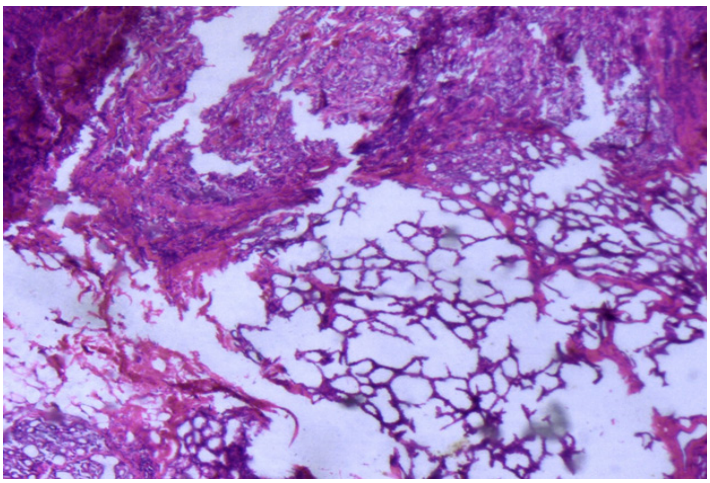

Figure 2: Photomicrograph showing lactating adenoma at the bottom and high grade invasive carcinoma at the top. H&Ex40

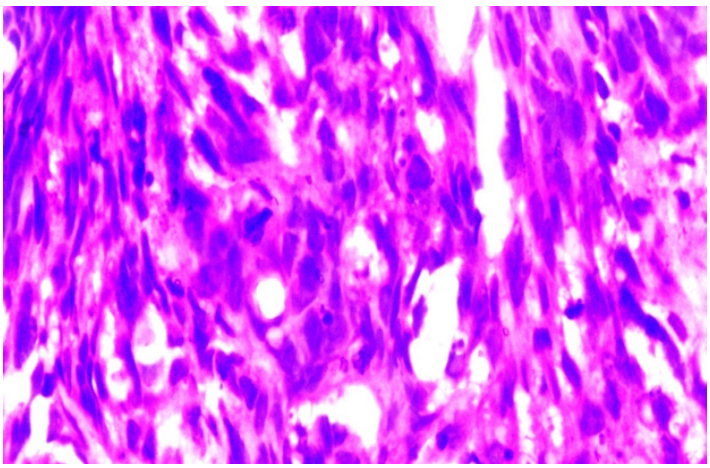

Figure 3: Photomicrograph showing markedly pleomorphic cells and mitosis. H&Ex100

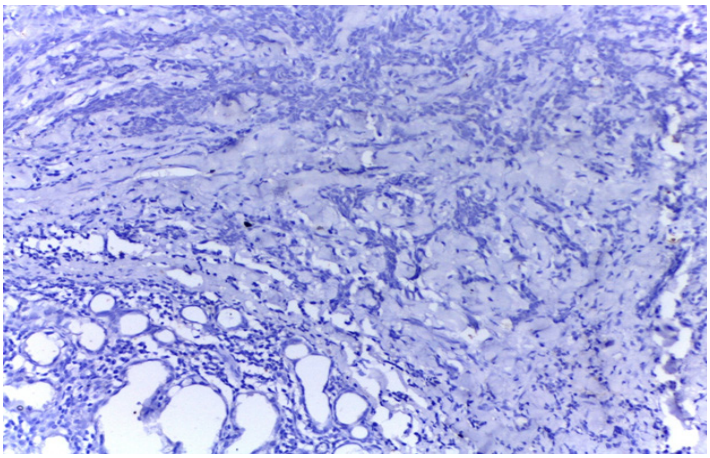

Figure 4: ER showing negative staining in both tumours.x40

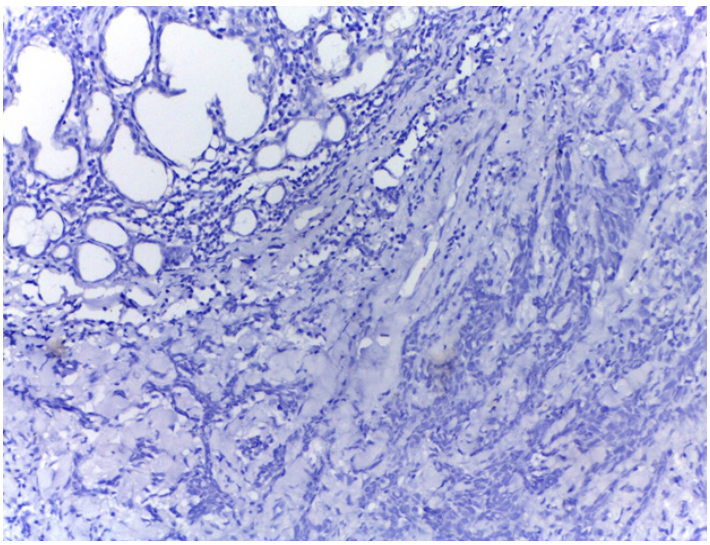

Figure 5: PR showing negative staining.x40

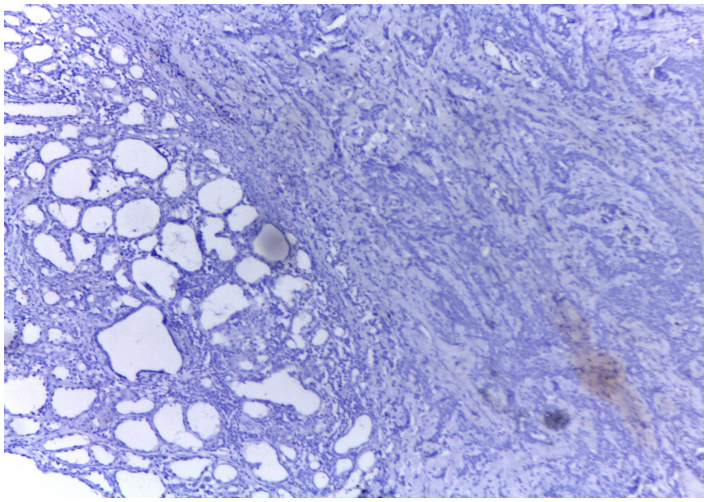

Figure 6: HER2 showing negative staining.x40

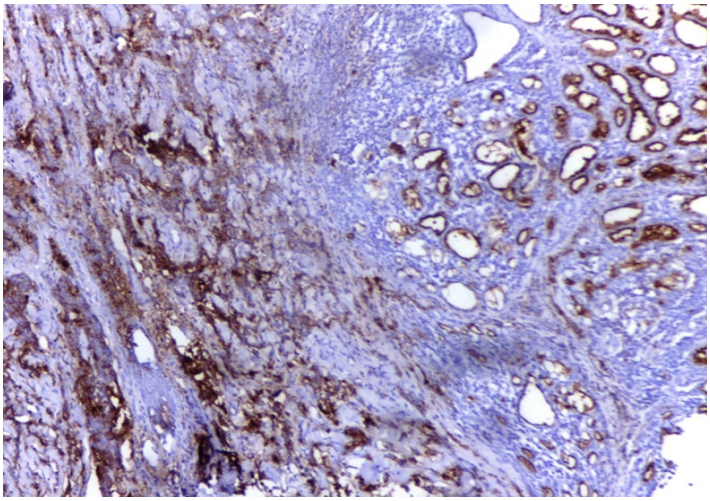

Figure 7: EMA showing positive staining on both tumours.x40

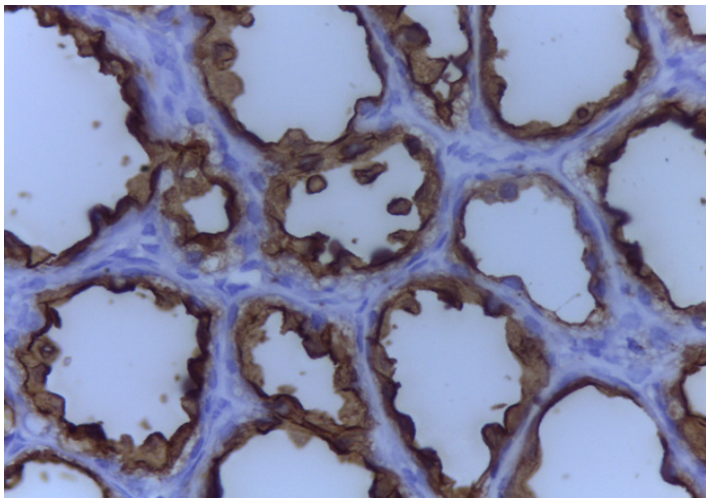

Figure 8: EMA positive stain in lactating adenoma.x100

Discussion

Lactating adenomas are the most prevalent breast masses seen in pregnant women [7]. Although they are not thought to carry an increased risk of cancer, Hertel et al reported the case of a patient who developed invasive ductal adenocarcinoma in the previous excision site of a lactating adenoma, and Geschicker and Lewis reported a lactating adenoma containing an associated infiltrating carcinoma [8, 9]. Pregnancy associated breast cancer is very rare and various studies have shown that they are of high grade tumours with nodal metastasis, low expression of hormonal receptors and overall poor prognosis [10]. This may also be true for our patient with possible metastasis to the ipsilateral supraclavicular node via the hematogenous route. The presentation of this patient with invasive carcinoma at an early age (19 years) and the history of first degree relative with breast cancer in addition to the immunohistochemical profile of triple negative suggest the possibility of inheriting the BRCA1/2 gene although genetic testing was not done. Early-onset breast cancers as seen in this case are typical among BRCA1/2 mutation carriers and a high proportion of cancers occur before the age of 40. Hormonal levels rise dramatically during pregnancy and two groups found pregnancy to be a risk factor for early breast cancer in BRCA1/2 mutation carriers. Johannsson et al. reported teen pregnancy-related breast cancers in 37 BRCA1/2 mutation carriers, versus the expected (3.7), while Jernstrom et al. reported that the risk of breast cancer increased with each pregnancy in BRCA1/2 carriers before the age of 40 [11, 12]. In the general population, pregnancy offers protection against breast cancer after the age of 40, but appears to increase the risk for very early-onset breast cancer. This is consistent with the hypothesis that the ovarian hormones produced during pregnancy are mitogenic, and accelerate the growth of existing tumours [13]. A case-control study of breast-feeding and breast cancer in BRCA1/2 mutation carriers reported a protective effect in women with BRCA1 mutations, but not with BRCA2 mutations [14]. BRCA1 mutation carriers who breast-fed for more than one year were 40% less likely to have breast cancer than those who breast-fed for a shorter period ($p = 0.01$). The observed protective effect among BRCA1 carriers was greater than that observed for members of the general population [15]. In these index case areas of clear demarcation from lactation adenoma to frank carcinoma can clearly be identified signifying a collision tumour and that malignant transformation of a lactating adenoma to frank carcinoma is unlikely. On the other hand, inheritance of BRCA1/2 genes markedly increase her susceptibility to early onset breast cancer which may have develop during pregnancy and that lactational adenoma was a mere co-incidence that develop after the index patient delivered and started breast feeding because lactating adenomas have been shown to express high amounts of the prolactin receptor [5, 15]. Whatever the case may be, this case illustrate the need for further investigation to resolve this dilemma. In a resource poor setting like ours, this case has also illustrated the need for more funding of research in our society for early detection of molecular pathways of cancers and possible novel therapies to improve survival and quality of life in our patients.

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