

Breast lesions during lactation diagnosed by fine needle aspiration cytology

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Summary:

Background: The breast function as a secretory gland during pregnancy and lactation due to the interaction of estrogen, progesterone and other pituitary hormones. The ductules of the terminal duct lobular unit become hyperplastic and manifest cytoplasmic vacuolization and luminal secretion. Occasionally this change results in a discrete nodule, called a lactating adenoma(LA), which is difficult to distinguish clinically from a malignancy.

Patients and method: A review of the clinical and cytological features of 60 lactating women present with breast lesions, over the period from August 2005- May 2010 in the Main Referral Center for Early Detection of Breast Tumors, Medical City, Baghdad Teaching Hospital. Those who present with a breast mass underwent fine-needle aspiration using 10ml disposable syringe (20-22gauge), the aspirated material spread on slides and fixed with 95% alcohol and stained with Pap-stain and examined under light microscope.

Results: Clinicocytological study of 60 lactating women presented with breast lesions including the age, chief complaint, the site of the lesion; the main morphological types of the lesions, and the main cytological findings and the difficulty in diagnosing malignancy during lactation. The mean age of the whole cases is 30.05 years; while the mean age for the six cases that were diagnosed as carcinoma during lactation is 37.5 years.

The main cytologic features that differentiate breast carcinoma from benign conditions during lactation are: crowding and overlapping of nuclei, dyscohesion and enlarged, pleomorphic nuclei, irregular nuclear membrane, coarse nuclear chromatin and mitosis.

Conclusions: The majority of breast lesions during lactation are benign. The physiologic changes associated with lactation make it difficult to recognize, diagnose new breast pathology and delay in diagnosis of breast carcinoma is common due to the difficulty in feeling masses. A diagnosis of carcinoma during lactation can be made by Fine-needle aspiration cytology, however, caution should be exercised in interpreting cytology specimens in this setting, because cellular features can mimic malignancy. The main cytologic features that differentiate breast carcinoma from benign conditions during lactation are crowding and overlapping of nuclei, dyscohesion of the cells and enlarged pleomorphic nuclei with irregular nuclear membrane, coarse nuclear chromatin and mitosis.

Keywords: breast lesions, lactation, fine-needle aspiration.

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Introduction:

The breast functions as a secretory gland during pregnancy and lactation due to the interaction of estrogen, progesterone and other pituitary hormones. The secretory unit is the lobule. (1) During pregnancy and lactation the ductules of the terminal duct lobular unit become hyperplastic and manifest cytoplasmic vacuolization and luminal secretion. Occasionally this change results in a discrete nodule, called a lactating adenoma(LA), which is difficult to distinguish clinically from a malignancy. (2) When the epithelial cells of the lobule are stimulated by hormones growth takes place principally during first and second trimesters of pregnancy, thereafter, growth proceeds slowly but continuously because acinar expansion by secretion as well as hypertrophy of myoepithelial cells. (1) Because carcinoma is occasionally diagnosed in the setting of pregnancy and lactation, where the majority of the lesions are benign, this diagnosis must be excluded in a pregnant or lactating women. (2)

Fine needle aspiration cytology in this setting may be especially useful because a diagnosis of pregnancy or lactational changes

could at least postpone and even spare the women an excisional biopsy. (2)

Surgical biopsy may occasionally be necessary to exclude malignancy in the rare cases with marked cytological atypia. (3)

Following delivery, full secretory development is reached. Dilated acini are distorted by crowding and partial fusion. (1) Extrusion of the content of the cells into the lumen as well as accumulation of extracellular fluid produce the milk that is carried by the ducts to the expansile lactiferous sinuses for storage. Cessation of lactation leads to regressive changes. (1) Puerperal mastitis occurs within 2-3 weeks of the start of lactation and is usually the result of infection via the mammary duct system. (4)

With infection the patient becomes febrile and the whole breast becomes hard, reddened, and painful. (5) Changes develop like a cascade; first little erosions caused by suckling of the infant lead to severe nipple and areolar pain. (6&7) Pain anticipates an undisturbed breastfeeding relationship and leads to an insufficient emptying of the breast by the newborn. An

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insufficient emptying of the breast subsequently lead to a stasis in the mammary alveoli, which augments pain and opens intercellular junctions between the milk and duct epithelial cells caused by a rise of intraductal pressure. Breast milk then moving into the connective tissue, leads to a primary sterile inflammation, followed by a secondary bacterial infection. (6&7) In the worst cases this results in a puerperal mammary abscess which is a firm, tender mass, which has to be surgically drained. (4,5,6&7)

The cytological appearance of these lesions depends on the chronicity of the process, varying from acute inflammation that may be accompanied by focal necrosis to organized chronic abscess. (7)

Galactocele is the breast lesion most commonly found during pregnancy and lactation easily diagnosed by mammography and ultrasound examination. (8) It is a simple milk-filled cyst probably form because of ductal obstruction, about 2cm in diameter, the patient complains of a tender mass, usually peripheral in the breast and needle aspiration both diagnostic and curative. (4,6&8)

Fibroadenoma may manifest with growth, infarction, large cyst, prominent ducts and secretory hyperplasia during lactation. (1,6,8&10) both rapid growth and infarction may be associated with pain and a mass difficult to distinguish from cancer. (6&10)

Infarction is reportedly more common in lactating women with already existing fibroadenoma. Necrotic cells and nuclear debris possibly accompanied by inflammatory cells are seen in a fine-needle aspiration specimen. Cells with hyperchromatic, atypical appearing nuclei may suggest carcinoma but in this inflammatory background such changes should not be considered to be definite, where excisional biopsy must be done. (4&5)

Lactating adenoma occurs only in association with gestation and is seen from the 3rd trimester through the period of lactation, clinically it is firm, mobile and non-tender single or multiple masses that regress spontaneously after cessation of breast feeding. (6,9&10)

The incidence of breast cancer during pregnancy and lactation is low. About 3% of breast cancers are diagnosed during this period. (6,8,9,11&12)

The average age of women who have breast cancer during lactation is the mid to late 30s. (11) The usual presenting symptoms is painless mass. (11)

Evaluation of mass lesions becomes much more difficult and may be obscured by surrounding physiological hyperplasia. Indistinct lesions can be less prominent as the breast enlarges and becomes more nodular. (6&11) for this reason breast carcinomas tend to be more advanced neoplasms at diagnosis and a poorer prognosis due to delayed diagnosis and a more aggressive biologic pattern. (6,8&12)

A diagnosis of carcinoma during lactation can be made by fine-needle aspiration biopsy, however caution should be exercised in interpreting cytology specimens in this setting, because hyperplastic and lactating parenchyma can appear atypical in cytologic preparations and the material often consists of

abundant, discohesive cells. Incisional or excisional biopsy is preferable. (11,13&15)

Observational data by many studies indicate that the risk of breast cancer increases with nulliparity and late age at first conception and there is a good evidence that the risk for premenopausal breast cancer is decreased with lactation. (14) There is a consistent evidence that lactation has either a protective effect against breast cancer or a neutral one. Where it reduces the number of ovulations proportionally to its duration and intensity and maintains a lower estrogen level than the level observed during the menstrual cycle. (14).

Patients and methods:

Retrospective study of 60 lactating women who attended the main Referral Training Center for Early Detection of Breast Cancer, Baghdad Teaching Hospital, Medical City, were retrieved over the period from August 2005- May 2010.

A review of the clinical and cytological features of these cases; those who present with a breast mass underwent fine-needle aspiration using 10ml disposable syringe (20-22gauge), the aspirated material spread on slides and fixed with 95% alcohol and stained with Pap-stain and examined under light microscope.

Results:

Clinicopathological study of 60 lactating women presented with breast lesions including the age, chief complaint, the site of the lesion; whether in the left or right breast for the malignant masses the main morphological types of the lesions, and the main cytological findings and the difficulty in diagnosing malignancy during lactation.

The mean age for the 60 lactating women is 30.05 years; while the mean age for the six cases that were diagnosed as carcinoma during lactation is 37.5 years.

As seen in table 1: Between 31-40 years, 27(45%) lactating women present with breast lesions.

Between 21-30 years, 26(43.4%) lactating women present with breast lesions. Four (6.6%) lactating women present with breast lesions below the age of 20 years, where the youngest was 16 years.

And 3 cases (5%) of lactating women present with breast lesions between 41-50 years, where the oldest woman was 45 years.

Table 1: age of 60 lactating women with breast lesions

| age | Number of cases | % |
|---------------|-----------------|-------|
| <20 years | 4 | 6.6% |
| 21 - 30 years | 26 | 43.4% |
| 31 - 40 years | 27 | 45% |
| 41 - 50 years | 3 | 5% |
| total | 60 | 100% |

In table 2; 19 cases(31.6%) of lactating women present with breast mass only, while those present with breast pain are 31 cases (51.6%).

Eight(13.6%) lactating women present with breast mass and pain.

One woman presents with breast pain and nipple discharge(1.6%), and one other lactating woman presents with breast pain and nipple retraction(1.6%). There were no favored sites or lateralization of nodules for the benign lesions ; while the six malignant cases , five of them were found on the left breast and only one on the right breast.

Table 2: chief complaint of 60 lactating women with breast lesions

| Chief complaint | Number of cases | % |
|---------------------------------|-----------------|-------|
| Breast mass | 19 | 31.6% |
| Breast pain | 31 | 51.6% |
| Breast pain & mass | 8 | 13.6% |
| Breast pain & nipple discharge | 1 | 1.6% |
| Breast pain & nipple retraction | 1 | 1.6% |
| total | 60 | 100% |

According to table 3:

Main morphological types of 60 lactating breast lesions diagnosed by fine-needle aspiration cytology are hormonal changes related to lactation;31 cases(51.6%) ;where 5cases(8.4%) of the 31 show hormonal changes with varying degree of atypia from mild-sever were referred to excisional biopsy.

Six cases (10%) diagnosed as carcinoma during lactation, 5 cases (8.4%) diagnosed as galactocele, and mastitis for each.

About 6.6% diagnosed as abscess (4 cases).

lactating adenoma , fibroadenoma, and fibrocystic changes, 3cases for each (5%).

Table 3: The main morphological types of 60 lactating women present with breast lesions diagnosed by fine-needle aspiration cytology

| The morphological types | Number of cases | % |
|-------------------------|-----------------|-------|
| Hormonal changes | 31 | 51.6% |
| Lactating adenoma | 3 | 5% |
| Fibroadenoma | 3 | 5% |
| Galactocele | 5 | 8.4% |
| Mastitis | 5 | 8.4% |
| Abscess | 4 | 6.6% |
| Fibrocystic changes | 3 | 5% |
| Carcinoma | 6 | 10% |
| Total | 60 | 100% |

The main cytological findings of the 60 lactating women present with breast lesions are those of hormonal effect which are 31cases (51.6%) and include the following features: (figure-1 and 2)

Moderately cellular specimen, numerous isolated epithelial cells or stripped nuclei,nuclear enlargement without variation in size or shape, prominent nucleolus,abundant delicate and wispy granular or finely vacuolated cytoplasm,cytoplasm easily strips away because of: 1.foamy proteinaceous background.2. many naked nuclei. Occasional small ductal cell clusters and portions of lobules.(2).

Six cases (10%) of lactating women who present with breast masses show cytomorphological features of carcinoma including: (figure-3 and 4) Increased cellularity, multilayering, enlarged and pleomorphic nuclei, single or multiple nucleoli, mitosis and numerous isolated tumor cells, secretory changes were scanty, the background was foamy and necrotic.

Increased cellularity with nuclear atypia, single cells and a dirty background was seen in benign and malignant conditions.

The main cytologic features that differentiate breast carcinoma from benign conditions during lactation are: Crowding and overlapping of nuclei, dyscohesion and enlarged, pleomorphic nuclei, irregular nuclear membrane, coarse nuclear chromatin and mitosis.

Lactation related hyperplastic changes with atypia can potentially result in a false positive diagnosis of carcinoma, therefore ultrasound is the preferred initial study for evaluating a palpable mass in this group of patients but it cannot be relied upon to distinguish benign from malignant lesion, so ultrasound guided core biopsy is often necessary for a definitive diagnosis.

Discussion:

In our study the commonest breast lesion found during lactation is hyperplastic changes due to hormonal effects which presents as breast pain or single or multiple discrete masses and most breast masses encountered during lactation are benign.

These physiologic changes associated with lactation make it difficult to recognize, diagnose and treat breast pathology.(6) Josep M et al 2007(8) found that galactocele is the breast lesion most commonly seen during lactation and manifest as either pseudolipoma, cystic mass with fat-fluid level, or pseudohamartoma.

Sumkin JH et al 1998(9) found that lactating adenoma is the most commonly encountered solid mass in a pregnant or lactating patients.

In the current study breast carcinoma during lactation represents 10%, with mean age 37.5years.

A study by Scott-Conner CEH et al 1995(6) shows that approximately 12%- of breast cancers are diagnosed during lactation this number increases as the tendency to defer childbirth in older women.

Ishida T et al 1992(11) reported that the frequency of breast carcinoma during pregnancy and lactation is 13%-, and the average age of women is the mid to late 30s. With the trend for women in some ethnic and social groups to delay pregnancy to their late 30s and 40s, it is likely that more cases will be encountered.Sumkin JH et al 1998(9) mentioned about 3% of breast cancers are diagnosed during pregnancy and lactation. Micheal Helewa et al 2002⁽¹⁴⁾ found that there is a good evidence that the risk for premenopausal breast cancer is reduced with lactation. This protective effect seems to be best for women who had extended periods of breastfeeding during their lifetime. A longer duration of lactation, especially if extended to 24 months and younger age at first lactation seem to confer a more beneficial effects. Since breast milk is the ideal nutrient for the newborn, and since breastfeeding is a modifiable risk factor,

all women should encouraged to breastfeed their children. Women with familial risks could potentially benefit from breastfeeding. All women should encouraged to practice breast self-examination during lactation, however, the evaluation of mass lesions becomes much more difficult as the breast enlarges and become more nodular.(11&14). The effectiveness of mammography is reduced during pregnancy and lactation by increased parenchymal density. Ultrasound is the preferred initial study for evaluating a palpable mass during lactation. This determine the solid or cystic nature of the mass. However, once a solid mass is diagnosed, ultrasound cannot relied upon to distinguish benign from malignant lesion.(6&8&9&11)

A diagnosis of carcinoma during lactation can be made by fine-needle aspiration cytology but it is important that the cytologist is made aware that the cellular features can mimic malignancy and that there are main cytologic features that differentiate breast carcinoma from benign conditions.(9&13&15)

Fine-needle aspiration cytology has been associated with some false positive and false negative results, therefore ultrasound guided core biopsy is necessary for a definitive diagnosis.(9)

Conclusions:

The majority of breast lesions during lactation are benign. The physiologic changes associated with lactation make it difficult to recognize and diagnose new breast pathology and delay in diagnosis of breast carcinoma is common due to the difficulty in feeling masses. A diagnosis of carcinoma during lactation can be made by Fine-needle aspiration cytology, however, caution should be exercised in interpreting cytology specimens in this setting, because cellular features can mimic malignancy. The main cytologic features that differentiate breast carcinoma from benign conditions during lactation are crowding and overlapping of nuclei, dyscohesion and enlarged, pleomorphic nuclei with irregular nuclear membrane, coarse nuclear chromatin and mitosis

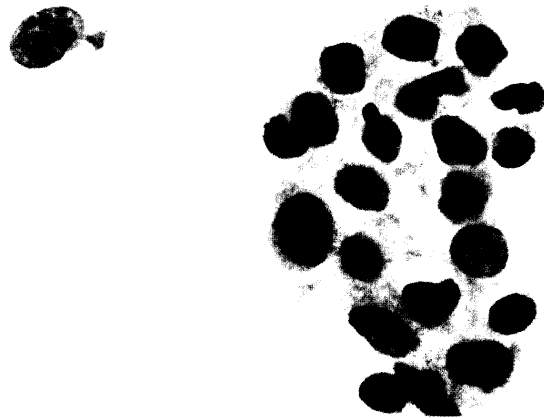


Figure-2: Cells arranged in loose clusters are seen. Nuclei are round to oval and regular with prominent nucleoli due to hormonal effect. (Papanicolaou stain),(X400).



Figure-3: Ductal carcinoma. The specimen is cellular and the cells are present both singly and in loosely cohesive clusters (Papanicolaou stain),(X250)

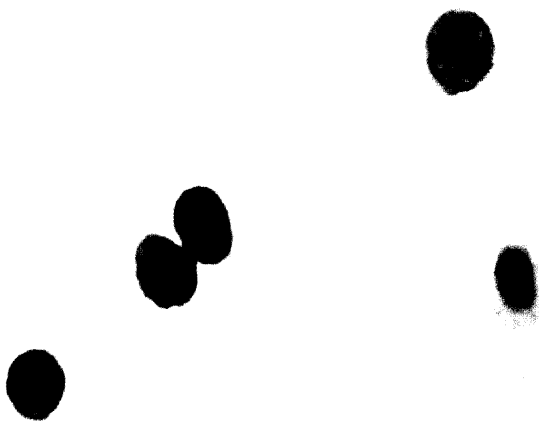


Figure-1: Numerous stripped or "naked" nuclei are seen during lactation(Papanicolaou stain),(X400).



Figure-4: Ductal carcinoma. Note the pronounced nuclear pleomorphism, multinucleated atypical cells, and nuclear atypia (Papanicolaou stain),(X250)

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