

Breast Lesions During Pregnancy Diagnosed by Fine Needle Aspiration Cytology

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ABSTRACT:

BACKGROUND:

The breast functions as a secretory gland during pregnancy due to the interaction of estrogen and progesterone, where the secretory unit is the lobule.

OBJECTIVE:

Is to highlight breast lesions during pregnancy and to show the importance of fine needle aspiration cytology in the diagnosis of these breast lesions.

PATIENTS AND METHOD:

This study was carried out within the Main Referral Training Center for Early Detection of Breast Tumors, Medical City Teaching Hospital, Baghdad (from the beginning of May 2006 till the end of August 2008). Fifty eight pregnant ladies presenting with different breast lesions were included, all were subjected to physical breast examination, ultrasonography of the breast and fine needle aspiration with 10 ml disposable syringe (20-22 gauge), spread on glass slides and fixed in 95% alcohol, stained with Pap stain and examined under light microscope.

RESULT:

Clinicopathological study of 58 pregnant ladies presented with breast lesions including the age (range between 17-42 years), chief complaint (pain 10(17.2%) cases, mass 30(51.8%) cases, discharge 3(5.2%) cases, painful mass 11(18.9%) cases, axillary mass 3(5.2%) cases and pain and discharge in 1(1.7%) case), site of the lesion (left side 24(41.4%) cases, right side 27(46.5%) cases and bilateral in 7(12.1%) cases.), the time of presentation during pregnancy (first trimester 19(32.8%) cases, second trimester 26(44.8%) and third trimester 13(22.4%) cases.) Our results show that breast lesions presented during pregnancy were benign in 54 (93.1%) cases, and malignant in 4 (6.9%) cases (all were breast carcinoma), the benign lesions include: fibroadenoma 15(25.9%) cases, inflammatory lesions 13(22.4%) cases, galactocele 8(13.8%) cases, fibrocystic changes 6(10.3%) cases, pregnancy related changes 5(8.6%) cases, lactating adenoma 3(5.2%) cases, 2(3.5%) cases lipoma, and papilloma one (1.7%) case, and one case was diagnosed as accessory axillary breast tissue.

CONCLUSION:

The majority of breast lesions during pregnancy are benign; however, a small percentage of these lesions prove to be malignant. Aspiration cytology has a place in the work up of abnormal areas found in pregnant breasts but an experienced cytologist with knowledge of the clinical setting is required.

KEYWORDS: breast lesions, pregnancy, cytological diagnosis, breast cancer.

INTRODUCTION:

During pregnancy the breast increases in volume, firmness and nodularity as the pregnancy continues a mass may then feel similar to normal hypertrophic thickness, or a mass may be deeper in the breast because of the generalized greater volume, causing it to be non palpable.^(1,2) Mammograms are not routinely performed

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because little information can be gained; where the increased vascularity, cellularity and water content of pregnant breast all contribute to generalized radiographic parenchymal density with loss of the contrasting fatty tissue. Breast ultrasonography is accurate and safe, as it is in nonpregnant, in determining whether a palpable mass is fluid-filled or solid.⁽³⁾ Pathophysiology

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When the epithelial cells of the lobule are stimulated by hormones, the cytoplasmic volume increases and lipid droplets become visible within the cytoplasm. Epithelial growth takes place principally during the first and second trimester therefore, growth proceeds slowly because of acinar expansion by secretion as well as hypertrophy of myoepithelial cells. Dilated acini are distorted by crowding and partial fusion. The mammary epithelial cells become hypersecretory. Extrusion of the contents 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. Exuberant hyperplastic foci may be mistaken for fibroadenoma. ^(1,4,5)

Needle aspiration for cytological analysis

Cytological interpretation of needle aspiration is notoriously difficult because of the hyperproliferative cellularity during pregnancy. Furthermore, 3-5 false-positive aspiration cytodiagnosis has been documented during gestation for benign breast tissue and is probably due to frequent mitosis, increased cellularity, anisonucleosis, prominent nucleoli and variable granular chromatin within a proteinaceous background. ^(6, 7)

Special consideration of biopsy in pregnant breast

In pregnant women local anesthesia is always safer than other anesthetic techniques. Monitored sedation or even general anesthesia with an experienced anesthesiologist is rarely required and is acceptable, especially in the later phases of pregnancy when teratogenesis is not of great concern. ^(5, 8, 9)

PATIENTS AND METHODS:

Retrospective study of fifty eight pregnant women who attended the Main Referral Training Center for Early Detection of Breast Tumors, Medical City Teaching Hospital, Baghdad (from the beginning of May 2006 till the end of August 2008).were examined clinically and radiographically using ultrasonographic study.

If the patient presented with a breast mass fine-needle aspiration done using 10ml disposable syringe (20-22gauge), the aspirate spread on slides and fixed in 95% alcohol then stained with Pap-stain and examined carefully under light microscope.

RESULT:

Clinicopathological study of 58 pregnant ladies presented with breast lesions including the age, chief complaint, site of the lesion whether left, right or bilateral, the time of presentation during pregnancy and the main cytological findings diagnosed by FNA.

1. The age:

as seen in table 1; five (8.6%) pregnant ladies present with breast lesions below 20 years, where the youngest age of presentation in those 5 cases was 17 years.

Between 20-30 years, 29(50%) pregnant ladies present with breast lesions, which is the main age of fertilization.

About 17(29.3%) pregnant ladies present with breast lesions between 30-40 years, while 7(12.1%) cases found between 40-50 years, where the oldest lady among those 7 cases aged 42 years.

Table 1: Age of 58 pregnant ladies with breast lesions

Age	Number of cases	%
<20 years	5	8.6
20-30 years	29	50
30-40 years	17	29.3
40-50 years	7	12.1
Total	58	100

2. Chief complaint:

In table 2; those 58 pregnant ladies presented with different complaint where, 10(17.2%) cases presented with breast pain; 30(51.7%) cases present with breast mass; 3(5.2%) cases presented with nipple discharge ; 11(18.9%)

cases presented with both breast mass and pain; 3(5.2%) cases presented with axillary mass and no breast lesions, and only one (1.7%) case presented with nipple discharge and pain.

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Table 2: Chief complaint in 58 pregnant ladies present with breast lesions

Chief complaint	Number of cases	%
pain	10	17.2
mass	30	51.8
discharge	3	5.2
Mass & pain	11	18.9
Axillary mass	3	5.2
pain& discharge	1	1.7
Total	58	100

3. Site of the lesion:

Twenty four (41.4%) cases presented with breast lesions on the left side, while 27(46.5%) cases presented with breast lesions mainly on the right side and 7(12.1%) cases presented with bilateral breast lesions; as shown in table 3.

Table 3: Site of breast lesions in 58 pregnant ladies

Site of the lesion	Number of cases	%
Left	24	41.4%
right	27	46.5%
bilateral	7	12.1%
Total	58	100

4. Time of presentation during pregnancy:

Pregnancy is divided into three trimesters, where the first trimester include the 1st three months of pregnancy, the 2nd trimester start from the 4th month to the end of the 6th month; and the 3rd trimester include the last three months. So according to table 4; 19 pregnant ladies (33%) present with breast lesions during the 1st trimester; 26cases (45%) present during the 2nd trimester and 13 cases (22.4%) present during the 3rd trimester.

Table 4: Time of presentation during pregnancy of 58 ladies with breast lesions

Time of presentation	Number of cases	%
First trimester	19	32.8
second trimester	26	44.8
third trimester	13	22.4
Total	58	100

5. Main cytological diagnosis:

The main breast lesions during pregnancy diagnosed by F.N.A cytological examination, are listed in table 5, theses include: 15(25.9%) cases fibroadenoma, 13(22.4%) cases inflammatory lesions; including: suppurative mastitis and breast abscesses, 8(13.8%) cases galactoceles, 6(10.3%) cases fibrocystic changes of the breast, 5(8.6%) cases pregnancy related changes (normal cytological changes during pregnancy), 4(6.9%) cases breast cancer, 3(5.2%) cases lactating adenoma, 2(3.5%) cases lipoma, 1(1.7%) case papilloma, and 1(1.7%) case as accessory axillary breast tissue. 54(93.1%) cases were diagnosed as benign lesions, and 4(6.9%) cases as malignant lesions.

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Table 5: Main cytological diagnosis in 58 pregnant ladies present with breast lesions

Cytological diagnosis	Number of cases	%
fibroadenoma		
Inflammatory lesions	13	22.4
Galactocele		
Fibrocystic changes	6	10.3
Pregnancy related changes		
Breast cancer	4	6.9
Lactating adenoma		
Lipoma	2	3.5
Papilloma	1	1.7
Accessory axillary breast tissue	1	1.7
Total		

DISCUSSION:

Breast disease is pregnancy associated if the diagnosis is made either during pregnancy or within one year following pregnancy.⁽¹⁰⁾

During pregnancy and lactation, striking changes take place in the mammary glands. The placenta causes hormone elevation by secreting estrogen and progesterone, the major hormones responsible for full breast development.⁽¹¹⁾

Breast masses can be diagnosed with a high degree of accuracy by combined physical, mammographic, and fine needle aspiration cytologic examination.^(12, 13)

A study by Gupta RK et al 1993⁽⁶⁾ showed that begin lesions during pregnancy diagnosed by fine needle aspiration cytology, in decreasing order of frequency include: fibroadenoma, lipomas, papillomas, fibrocystic changes, galactocele, and inflammatory lesions.

In our study we found that breast lesions presented during pregnancy were benign in 54(93.1%) cases and malignant in 4(6.9%) cases (all were breast carcinoma). The benign lesions include the following: fibroadenomas (25.9%), inflammatory lesions (22.4%), galactocele (13.8%), fibrocystic changes (10.3%), pregnancy related changes (normal cytological changes that occur during pregnancy) (8.6%), lactating

adenoma (5.2%), lipoma (3.5%), and papilloma (1.7%).

Fibroadenoma is the most common benign neoplasm of female breast.⁽¹⁴⁾ These estrogen sensitive tumors are found as early as puberty, have the highest incidence between the ages of 20-35 years, and may show acinar hyperplasia in women taking oral contraceptives. During pregnancy the lesion may develop secretory changes and after menopause sclerosis and regression occur. Less than 5% of women with fibroadenoma are older than 50 years or post menopause.⁽¹⁵⁾

Inflammatory lesions, especially breast abscesses develop in 5-11% of pregnant and lactating women; the predominant infectious organism is staphylococcus aureus, and often the penicillinase producing type. Peripheral breast abscesses have generally been associated with mastitis during breast feeding, but previous reports indicate that abscesses are common in non lactating women.⁽¹⁶⁾

Galactocele are the most common benign cystic breast lesions in pregnant and lactating women.⁽¹⁷⁾ They are true cuboidal epithelium lined cysts that contain milk like fluid, either with or without curd like material; the main

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predisposing factor for galactocele development is thought to be mammary duct obstruction, most likely due to inflammation or in rare cases tumors.⁽¹⁸⁾ Galactocele should be differentiated from other cystic breast lesions, most importantly intracystic carcinoma.⁽¹⁸⁾ From a galactocele a white grey fluid is aspirated, the aspirate is a relatively cellular, large rounded foam cells with abundant foamy granular or vacuolated cytoplasm and vesicular or hyperchromatic nuclei.^(7, 14)

Lactating adenoma is a mass that occurs in response to physiologic changes of pregnancy and during lactation. The nature of the neoplasm remains controversial, in many cases are discovered in the third trimester of pregnancy.⁽¹⁹⁾

Sumkin HJ et al 1998⁽¹³⁾ found 11 lactating adenomas in 9 patients aged 35-36 years, and stated that the ultrasonographic features of lactating adenoma although benign are not specific, tissue sampling with fine needle aspiration biopsy recommended. Core biopsy is necessary if a diagnosis can not be made with aspirate, but is not performed initially because of the possibility of milk fistula. Fine needle aspiration biopsy has proved to be an adequate method of diagnosing lactating adenoma.

The cytological features of lactating adenoma include: cellular smears poorly cohesive clusters of epithelial cells with granular and foamy to vacuolated cytoplasm, these epithelial cells contain nuclei with prominent nucleoli; the background is dirty with cytoplasmic fragments, secretory material and numerous epithelial nuclei without cytoplasm. The differential diagnosis of lactating adenoma includes fibroadenoma and carcinoma. Fibroadenoma shows marked myoepithelial cell proliferation seen as naked stromal nuclei, carcinoma is distinguished by nuclear enlargement and irregularities and hyperchromasia.⁽⁷⁾

Depending on the degree of lactational changes and occasional cytologic atypia, there is a small but real risk of false positive diagnosis of breast carcinoma with fine needle aspiration biopsy particularly later in pregnancy and the postpartum period.⁽²⁰⁾

Fibrocystic changes (fibrocystic disease) is the

most common lesion of breast and affects more than 50% of all women, the patient may experience localized, generalized, or bilateral lumpiness that may vary during the menstrual cycle.^(7, 14)

When the condition presents as a solitary or dominant mass, it might mimic carcinoma and prompt fine needle aspiration cytology.^(7, 14, 24)

Age incidence between 30 and 50 years, and peaking just before menopause reflects a hormonal relationship. Estrogen predominance over progesterone is considered causative in its development, stimulating proliferation of the epithelium and stroma.^(7, 14)

The cells derived from fibrocystic changes are polymorphic, they include the benign cellular components seen in tissue sections: epithelial cells, apocrine cells, adipose fragments, histiocytes, and other chronic inflammatory cells, most of the epithelial cells chiefly ductal in origin, appear as small clusters of uniform cells, with bland nuclei with no nucleoli.⁽⁷⁾

During pregnancy if fine needle aspiration cytology from a solid breast mass is cell-rich with diminished intercellular cohesion, with derbies and proteinaceous (milky) material constitute the background, unless the clinical impression is harmonious with a fibroadenoma or lactating adenoma, these aspirates should be reported as pregnancy-related changes.⁽¹⁴⁾ Here the epithelial cells form large tissue fragments, smaller sheets, acini, or isolated cells, and oval naked nuclei. The secretory stimulus creates indistinctly bordered cells with foamy or vacuolated cytoplasm. Anisonucleosis and eosinophilic macronucleoli may be prominent; these changes become more pronounced as gestation progress and enhanced during lactation.⁽⁷⁾

Palpable breast masses are frequently encountered during pregnancy, although infrequent, breast carcinoma may occur, with a reported prevalence of one case per 1,300 pregnancies to case per 6,200 pregnancies.⁽¹³⁾

The discussion of pregnancy associated breast cancer has been increasingly common over the past several years, perhaps because more women are becoming pregnant in their 30s and 40s, and the incidence of breast cancer increases with age.⁽²¹⁾

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Many studies reported a poor prognosis for patients with pregnancy associated breast cancer, more recently several investigations found that no statistically significant difference in the mortality rates of patients with pregnancy associated versus non-pregnancy associated breast cancer. ⁽²²⁾

Helewa M et al 2002 ⁽²³⁾ stated that all women should be encourage to practice breast self examination in pregnancy and during lactation. Clinicians should screen all pregnant patients for breast cancer for thorough breast examination early in pregnancy.

Physicians should be encourage to use ultrasonography, mammography, needle aspiration, or breast biopsies to asses suspicious breast masses in pregnancy and during lactation in the same timely fashion as for non-lactating women. ⁽²³⁾

Although pregnancy and lactational changes can present a diagnostic challenge, cytological interpretation of carcinoma at this time reliable in the presence of criteria of malignancy reflected in large numbers of well preserved cells in a smear of fine needle aspiration, cells rich aspirates are composed principally of dyshesive clusters of mammary epithelial cells with anisonucleosis, nuclear contour irregularity and macronucleoli. ⁽¹³⁾ During pregnancy and lactation, diagnosis of carcinoma must be based on all criteria of malignancy. ⁽²⁴⁾

CONCLUSION:

The majority of breast lesions during pregnancy are benign; however, a small percentage of these lesions prove to be malignant. Aspiration cytology has a place in the work up of abnormal areas found in pregnant breasts but an experienced cytologist with knowledge of the clinical setting is required.

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