Male Breast Lesions: A review of 124 cases diagnosed by Fine Needle Aspiration Cytology

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#### Summary

J Fac Med Baghdad Vol. 50, No. 3, 2008 Received: March 2008 Accepted: July 2008 **Background**:Gynecomastia and breast cancer are the two most common diseases of the male breast. Most other diseases found in male breast arise from the skin and subcutaneous tissues. Male breast cancer is relatively rare, in contrast to gynecomastia, which is relatively common. **Objectives:** The aim of this report is to determine the prevalence of the different breast lesions among males; based upon the findings of fine needle aspiration cytology.

**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 January 2003 till the end of November 2007). One hundred twenty four males presenting with different breast lesions were included; all were subjected to physical breast examination, ultrasonography of the breast and fine-needle aspiration.

Results: Pathologically, 112 cases (90.3%) were diagnosed as benign lesions, including: 103 cases (83.1%) of gynecomastia, and 9 cases (7.2%) of other miscellaneous benign lesions: six cases (4.8%) diagnosed as inflammatoty conditions [three cases of acute mastitis and three cases of suberolar abscess], two cases (1.6%) diagnosed as granlomatous mastitis, and one case (0.8%) as lipoma. On cytological examination, 14 cases (13.6%) of gynecomastia showed varying degree of cellular atypia. Breast cancer was diagnosed in twelve patients (9.7%); all were infilterative ductal carcinoma. The mean age of patients with gynecomastia was 20.3 years, while it was 61.8 years in breast cancer patients. Sixty six cases (53.2%) of male breast masses were located within the left breast, 47 cases (37.9%) were located within the right breast, while eleven cases (8.9%0) were bilateral (all were gynecomastia). The chief complaints of patients with gynecomastia were as follows: painless mass in 38 cases (30.7%), painful mass in 45 cases (36.3%), pain without mass in 13 cases (10.5), while evidence of bilateral swelling was observed in seven cases (5.6%). Ten patients (8.1%) with breast cancer presented with painless mass, while in only two (1.6%) the chief complaint was painful lump. On ultrasonographic examination of patients with gynecomastia, 58 conditions (46.7%) presented with proliferation of fibroglandular tissue (no definite mass), 35 conditions (28.2%) showed well defined discoid lesions, while in ten cases (8.1%) the findings revealed ill defined retroareolar masses. On the other hand, in patients diagnosed as having male breast carcinoma, the ultrasound findings showed ill defined eccentric masses in eight cases (6.5%) and multiple masses in four (3.2%).

Most cases of gynecomastia were idiopathic since patients gave no history of hormonal therapy or exposure to other relevant risk factors.

**Conclusions**: Most palpable masses in the male breast are due to gynecomastia followed by breast carcinoma. Because both present clinically as palpable masses, fine-needle aspiration cytology is extremely useful for the diagnosis.

Keywords: gynecomastia, male breast cancer, cytological diagnosis, ultrasonograpghy.

#### Introduction :

The male breast is similar to the breast of a preadolescent girl; consisting primarily of few branching ducts lined by flattened cells and surrounded by connective tissue.

\*lecturer, Baghdad Medical College \*\*Professor, Baghdad Medical College Although diseases of the male breast are uncommon, they engender a tremendous emotional response. Fortunately most diseases presented with a mass and are easily detected <sup>(1,2)</sup>. Gynecomastia and breast cancer are the two most commonly encountered pathological entities. Other diseases found in the male breast arise from the skin and subcutaneous tissue (e.g. fat necrosis, lipoma and epidermal inclusion cysts). <sup>(1, 2, 5)</sup>

Gynecomastia, the enlargement of the male breast, occurs secondary to hyperplasia and hypertrophy of both glandular and stromal tissues. It is mainly attributable to hormonal imbalance which could be either physiological (i.e., pubertal which could be present as bilateral swelling that regress spontaneously) or pathological.<sup>(3, 4, 5)</sup>

Many people are unaware that men can develop breast cancer. Although substantially less common than gynecomastia, it has been reported that it accounts for 1% of all cases of breast cancers and 0.17% of all cancer cases in men.  $^{(6, 7)}$  Most patients are diagnosed in their sixties, but the disease can strike younger or older men.  $^{(8, 11, 12)}$ 

Some authors reported that as many as 20% of the male breast cancer patients have a history of gynecomastia. <sup>(4)</sup>, where excessive estrogen has been identified as a possible factor.

Unlike gynecomastia which typically produces a swelling that is firm, well-defined and tender, a malignant breast lump is hard, irregular, and painless.  $^{(4, 6, 10)}$  Because both cases present with palpable masses, it is logical to believe that fine-needle aspiration cytology (FNAC) would be a useful diagnostic tool.  $^{(4, 7, 9)}$ 

This study was designed to determine the prevalence of different lesions which could be encountered in the male breast; based primarily upon the findings of fine needle aspiration cytology and ultrasonography.

## PATIENTS & METHODS:

The study was conducted within the Main Referral Training Center for Early Detection of Breast Tumors, at the Medical City Teaching Hospital from January 2003 till November 2007. Within that period, a total of 9393 subjects presented with different breast complains. Fine needle aspiration cytology was carried out for 2303 (24.5%) patients with palpable lumps of whom 124 (5.38%) were males (as shown in table 1).

Year	Number of patients presented to the center	Number of patients subjected to F.N.A.C	Number of male patients presented with breast mass and subjected to F.N.A.C		
2003	2495	556	18		
2004	1982	432	25		
2005	2251	530	27		
2006	1468	415	28		
2007	1197	370	26		
TOTAL	9393	2303	124		

# Table 1: Number of patients

The technique was performed using 22 or 23 gauge needles attached to 10-20 ml disposable plastic syringes, placed on a syringe holder. In cases where a well defined subareolar mass was encountered, the mass was fixed with two fingers, and the aspiration was performed by introducing the needle to the exact position, applying negative pressure and moving the needle forward and backward in a fan like direction until yielding a satisfactory material visible to eyes. On the other hand, in cases with no definite mass (i.e., generalized breast enlargement), more than one aspiration from different sites were attempted.

In most cases with gynecomastia, the aspiration material was scanty, while it was mainly bloody in nature in breast carcinoma.

Each aspirate was smeared on 4 slides which were fixed in absolute alcohol for at least 20 minutes, stained by Papanicolaou stain and examined under light microscopy.

### **RESULTS:**

One hundred and twelve cases (90.3%) out of 124 were diagnosed as benign lesions, including 103 cases (83.1%) diagnosed as gynecomastia, 9 cases (7.2%) as benign miscellaneous (three cases (2.4%) of acute mastitis, three cases (2.4%) of subareolar abscess, two cases (1.6%) of granulomatous mastitis, and one case (0.8%) of lipoma. Twelve cases (9.7%) were diagnosed as malignant lesions, all of which were ductal carcinoma.

## 1. Age distribution:

Age	Gynecomastia		carcinoma		Miscellaneous		Total	
(years)	No.	%	No.	%	No.	%	No.	%
10-19	29	23.4	-	-	1	0.8	30	24.2
20-29	25	20.2	1	0.8	2	1.6	28	22.6
30-39	18	14.5	2	1.6	4	3.2	24	19.4
40-49	13	10.5	-	-	-	-	13	10.5
50-59	11	8.9	3	2.4	2	1.6	16	12.9
60-69	7	5.6	6	4.9	-	-	13	10.5
Total	103	83.1	12	9.7	9	7.2	124	100

# Table 2: Distribution of the study population among Age.

The mean age in gynecomastia was 20.3; the peak frequency (23.4%) presented in the age group (10 - 19) years), while only 5.6% of the cases were detected over 60 years (Table 2).

The mean age for patients with breast cancer was 61.8 years; the highest frequency was recorded in the age group (60-69 years) (4.9% six cases). Two patients (1.6%) were observed in the age group (30-39 years) while one patient (0.8%) was diagnosed in the age group 20-29 years). The latter was a 23 year old medical student who had, in the examined FNAC specimen, changes consistent with gynecomastia as well.

Regarding the age distribution of patients presenting with other benign conditions: six cases with inflammatory conditions (acute mastitis and subareolar abscess) and two cases with granulomatous mastitis had an age range between (15-40 years), while one 27 year old male was diagnosed with lipoma.

2. Site:

Site	Gynecomastia		Carcinoma		Miscell	laneous	Total		
	No.	%	No.	%	No.	%	No.	%	
Bilateral	11	8.9	-	-	-	-	11	8.9	
Left	52	41.9	9	7.3	5	4	66	53.2	
Right	40	32.3	3	2.4	4	3.2	47	37.9	
Total	103	83.1	12	9.7	9	7.2	124	100	

## Table 3: Distribution of male breast lesions according to their sites.

Sixty six cases (53.2%) out of the total 124 cases of male breast lesions were located within the left breast, 47 cases (37.9%) were located within the right breast, while 11 cases (8.9%) presented as bilateral swelling; all of which were diagnosed as gynecomastia (Table 3). In breast cancer patients 75% of the masses were encountered in the left breast.

As displayed in Table 4, 49 patients (39.5%) presented as painless mass, including 38 cases (30.7%) of gynecomastia, and ten cases (8.1%) of breast cancer. Fifty five patients (44.3%) presented with well defined painful mass; this included: 45 cases (36.3%) of gynecomastia, and two cases of breast cancer. The two cases which were diagnosed as granulomatous mastitis and six cases with inflammatory conditions (acute mastitis and subareolar abscess) presented with retroareolar mass and pain, while the patient who was diagnosed cytologically as having a lipoma presented with a solitary painless mass.

Thirteen patients (10.5%) presented with pain only without mass; all of whom had gynecomastia while seven cases (5.6%) of gynecomastia presented with bilateral swelling without pain.

## 3. Clinical presentation:

# Table 4: Clinical presentation of male patients diagnosed with breast lesions.

Presentation	Gynecomastia		Carci	noma	Miscella	neous	Total	
	No.	%	No.	%	No.	%	No.	%
Painless mass	38	30.7	10	8.1	1	0.8	49	39.5
Pain	13	10.5	-	-	-	-	13	10.5
Painful mass	45	36.3	2	1.6	8	6.4	55	44.3
Bilateral swelling	7	5.6	-	-	-	-	7	5.6
Nipple discharge	-	-	-	-	-	-	-	-
Total	103	83.1	12	9.7	9	7.2	124	100

### 4. Ultrasonographic presentation:

### Table 5: Ultrasonographic presentation of male breast lesions.

Ultrasonographic	Gynecomastia		Carcinoma		Miscellaneous		Total	
presentation	No.	%	No.	%	No.	%	No.	%
Proliferation of fibroglandular tissue	58	46.7	-	-	-	-	58	46.8
Well defined mass (centric)	35	28.2	-	-	-	-	35	28.2
Ill-defined mass (centric)	10	8.1	-	-	4	3.2	14	11.3
Ill-defined mass (eccentric)	-	-	8	6.5	3	2.4	11	8.9
Cystic lesion	-	-	-	-	2	1.6	2	1.6
Multiple ill-defined masses	-	-	4	3.2	-	-	4	3.2
Total	103	83.1	12	9.7	9	7.2	124	100

Under ultrasound examination, 58 cases (46.8%) of gynecomastia showed evidence of glandular tissue proliferation, while 35 cases (28.2%) of gynecomastia presented as well defined masses; subareolar, centric, or discoid. In the remaining ten cases (8.1%) of gynecomastia the ultrasound revealed ill-defined centric subareolar masses.

In patients with carcinoma, eight cases (6.5%) presented as ill-defined subareolar eccentric mass while the remaining four cases (3.2%) presented as multiple ill-defined masses.

Two cases (1.6%) showed changes consistent with benign cystic lesions (those patients had inflammatory condition and abscess).

**5.** Cytologically, in general smears of patients diagnosed as gynecomastia revealed evidence of benign ductal cell proliferation, featuring various cellularities: cohesive ductal cells with bland morphology, presence of bipolar naked nuclei, and scattered single intact ductal cells. Fourteen cases (13.6%) were highly cellular with predominantly cohesive clusters of ductal cells arranged in flat sheets showing a mild degree of atypia with fragments of myxoid fibroadipose tissue (Figure 1).

The cytologic features in breast carcinoma were characterized by markedly enlarged pleomorphic cells, exhibiting pleomorphisim, a high nuclear-cytoplasmic ratio, hyperchromatic nuclei, smudged chromatin, and evidence of conspicuous nucleoli. All cases were diagnosed as ductal carcinoma (Figure 2).

6. **Family history:** It is note worthy mentioning that all patients with breast carcinoma had negative family history for breast cancer; nevertheless, nine had recalled a positive family history of other types of cancers (including colonic cancer (five cases), brain cancer (two cases), lymphoma and laryngeal carcinoma (single cases).

A 19 year old patient with bilateral gynecomastia had a family history of lung cancer (small cell carcinoma) where gynecomastia may represent a part of paraneoplastic feature that accompany lung cancer especially (small cell carcinoma) due to the secretion of hormones.

Another four patients presenting with bilateral gynecomastia gave a history of hormonal therapy. The remaining patients did not recall any significant relevant history.



Figure 1: FNAC showing changes of gynecomasia (note the well defined regular nuclear membrane of the benign epithelial mammary cells. Papanicolaou Stain (X 250)



**Figure 2:** Infiltrative ductal carcinoma of the male breast. Papanicolaou stained smear showing chromatin clumping in the nucleus with prominent nucleoli and high nucleocytoplasmic ratio. (FNAC X400).

## Discussion:-

Male breast masses are uncommon pathologic findings; they are rarely aspirated, resulting in limited cytopathologic experience. The current report describes the cytopathological findings in male breast lesions from data collected over a period of five years.

In our study, 83.1% of the patients had gynecomastia and 9.7% had mammary carcinoma. Siddiqui al 2002 <sup>(1)</sup> recorded a close figure for gynecomasia (82.6%) but lower frequency was displayed for patients with malignancy (5.2%); 47% of which were metastatic in origin. He encountered atypical suspicious changes in 10% of the examined smears.

The mean ages for patients with gynecomastia and carcinoma (20.3 years and 61.8 years respectively) were consistent with those reported in other studies (Das et al 1995<sup>(8)</sup> and Schiller al 2001<sup>(11)</sup>. Most of the cases being diagnosed in the left breast (Sirtoric and Veronesi 1957<sup>(12)</sup>).

In this report, the peak frequency in patients with gynecomasia (23.4%) presented in the age group (10 - 19 years). It has been reported that gynecomastia is considered to be normal physiological changes related to puberty and occuring most frequently during times of hormonal changes; resulting from an altered estrogenandrogen balance on the breast tissue, or from the increased sensitivity of this tissue to a normal estrogen level<sup>(2, 3)</sup>. Pubertal gynecomastia is thus regarded as a common condition with an overall incidence of 38% in 10 to 16 years of age, increasing to 65% at age 14, and dropping to 14% in 16 years old boys.<sup>(2)</sup> Fortunately, it has been demonstrated that pubertal gynecomastia often regresses spontaneously within six months, 75% within two years of onset and 90% resolve within three years of the onset.<sup>(3)</sup>

Felner and White  $2000^{(3)}$  found that during adolescence 75% of gynecomastia cases are bilateral, while bilateralism was encountered in only 5.6% of the cases studied in this report.

Unlike gynecomastia, which typically produce a swelling that is firm, well defined, and tender, a malignant breast lump is more likely to be hard, and painless. In both gynecomastia and breast cancer the lump can adhere to the areola, but a mass due to gynecomastia is not usually fixed to the underlying tissues, nor does it produce ulceration or other changes in the nipple and areola. <sup>(4, 6)</sup> Such changes as well as skin thickening, inflammation, nipple discharge (especially bloody), and enlarged axillary lymph nodes, are likely to be signs of malignancy. <sup>(4)</sup>

Clinical breast examination is the key in the evaluation of palpable masses in males. Hoffman Kohn scale, adapted from Mc Kinney and Simon <sup>(3,</sup>

<sup>4)</sup> was found useful in assessing the grade of the condition; where Grade I corresponds to: small breast enlargement with localized button of tissue that is concentrated around the areola.

Grade II: moderate breast enlargement exceeding areola boundaries with edges that are indistinct from the chest.

Grade III: moderate breast enlargement exceeding areola boundaries with edges that are distinct from the chest with skin redundancy present.

Grade IV: marked breast enlargement with skin redundancy and feminization of the breast.

If the physical breast examination strongly suggest gynecomastia, further evaluation may not be necessary. On the other hand, if the clinical features are equivocal, fine-needle aspiration guided by palpation &/or excisional biopsy are necessary to make the diagnosis. Fine-needle aspiration cytology should therefore be an integral part of the primary assessment of breast lumps in males. <sup>(13, 14, 15)</sup>

All cases of breast cancer were diagnosed cytologically as invasive ductal carcinomas in the current study with no false positive rates (i.e., 100% specificity). The corresponding histopathology confirmed our cytodiagnosis. It has been documented in the literature that the overwhelming histological subtype of breast carcinoma in men is ductal followed by papillary while lobular carcinoma is rare due to the scanty number of terminal lobules in the male breast. Estrogen receptors are present more commonly in males with breast cancer than in females, occurring in 75%-94% of males with cancer. <sup>(6, 7, 10, 11)</sup>

Cytological atypia remains a commonly encountered dilemma in cytological diagnosis. In our study 14 cases (13.6%) of gynecomastia cytologically with presented atypical or hyperplastic changes, Amrikachi et al 2001<sup>(16)</sup> recorded atypia in nine out of 100 cases of gynecomastia (9%), and reported that apocrine metaplasia and epithelial atypia are common findings in gynecomastia; adding that attention should be directed towards the pattern of cells. The presence of sheets of benign-looking ductal cells and the absence of atypical single scattered cells could point to the correct diagnosis.

Reported cases of gynecomastia progressing to carcinoma are rare, but gynecomastia with hyperplastic and atypical changes suggest that such progression may occur. <sup>(8, 9)</sup> Our study population included a <u>23 year old medical student who had, in the examined FNAC specimen, changes consistent with gynecomastia as well; indicating the possibility of unique etiological agents.</u>

Ultrasonography may be extremely useful in demonstrating a cyst in the male breast, but cysts are rare. Under ultrasonographic examination, 46.7% of gynecomastias did not reveal any cystic or

solid lesions, but presented as proliferation of fibroglandular tissue, while 28.2% presented as well defined retroareolar mass centric in position. The two cases which presented as cystic lesions had a benign inflammatory nature.

Most cases of breast carcinomas on the other hand, presented as ill-defined eccentric retroareolar masses. Others may show a hypoechoic mass with irregular, ill-defined, or circumscribed margins, and increased vascular flow. Similar findings may be observed in gynecomastia or in inflammatory conditions. Thus, ultrasonography alone is not a reliable method to distinguish male breast carcinoma from other etiologies, where false positive results may be seen in abscess, gynecomastia and fat necrosis. (17) Likewise, it has been reported that although some mammographic findings do suggest male breast cancer (i.e., eccentric speculated mass), yet the predictive value of mammography and ultrasonography as screening tools do not reach those recorded upon using clinical breast examination and fine-needle aspiration cytology.<sup>(7)</sup>

The etiology of gynecomastia is not yet known. There seems to be no increased incidence of malignancies in patients with idiopathic gynecomastia, however, patients with klinefelter syndrome exhibits an increased incidence of malignancy<sup>(17)</sup>. It has been shown that pathological gynecomastia is associated with both androgen deficiency and estrogen excess, both of which might be correlated to medication, diseases related to endocrinologic abnormalities, familial disorders, tumors. chronic diseases, chromosomal abnormalities, or miscellaneous other conditions.<sup>(3,</sup>

The presence of elevated estrogen and progesterone receptors in those patients provides a potential mechanism by which they may develop breast neoplasms<sup>(18)</sup>.

### **Conclusions:**

Most palpable masses in males are due to gynecomastia followed by breast carcinoma. Because both present clinically as a palpable mass, FNAC remains an important tool for the diagnosis yielding high sensitivity and specificity.

All diagnosed cases of male mammary carcinomas were ductal in origin, presenting mostly after the age of 50 years as a painless mass in the left breast. Nevertheless, 25% of breast carcinomas affected younger men under the age of 35.

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