A Panoramic View of Morphological Spectrum of Male Breast Lesions at a Tertiary Care Hospital in South India

Salony Mittal (salony.mittal@sharda.ac.in)  
Sharda University

Goyal Shefali  
Sharda University

Mittal Saumya  
Sharda University

Kini Hema  
Kasturba Medical College

Adiga Deepa  
Kasturba Medical College

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Abstract

Background:

Though male breast lesions are infrequently studied and documented, a wide variety of lesions afflict it. Conditions and entities that affect the female breast also occur in the male breast. However, lobular lesions are seldom seen in male breasts because of absence of terminal differentiation induced by progesterone. So far, there have been very few studies on the spectrum of male breast lesions and most of them are done either on aspiration smears or on biopsies. Therefore, in the present study, we aimed to analyse the spectrum of different types of male breast lesions at our tertiary care centre both on aspiration cytology smears and histological specimens as well as biopsies.

Objectives:

To study the spectrum of male breast lesions encountered in histopathology and cytology lab.

Study Design:

Data on male breast lesions between 2010 to 2015 were retrieved from the records of Kasturba Medical College, Mangalore. The cytological and histological features were studied and the number of benign and malignant cases recorded. Cytohistologic correlation, wherever available was done. Immunohistochemistry was studied in malignancies wherever available.

Results:

Out of 7700 breast lumps retrieved, 120 (1.55%) male breast lesions were identified. Of these, 54 were diagnosed by FNAC and 76 lesions on surgical specimens. On FNAC, 49 were benign and 5 malignant. The 76 cases diagnosed on histology had 70 benign and 6 malignant lesions. The benign lesions were gynecomastia, inflammatory masses, fibroadenoma and intraductal papillomas. Malignant lesions included infiltrating ductal carcinoma (NOS), papillary and metastatic carcinoma with 60% showing ER positivity. Ten of these cases had both cytology and histology.

Conclusion:

While gynaecomastia and invasive ductal cancer were the commonest lesions encountered in the male breast, there were other rarer benign and malignant lesions.

Introduction

Since ages, the epidemiology and morphological spectrum of female breast lesions are well studied in comparison to the male breast lesions. Conditions and entities that affect the female breast also occur in the male breast. However, lobular lesions are seldom seen in male breasts because of absence of
terminal differentiation induced by progesterone. Owing to their rare occurrence, the male breast lesions are infrequently studied and documented.

The delay in diagnosis is due to the fact that the male breast lumps remain unnoticed for years and also the patients are usually hesitant to seek medical advice especially in developing countries where poverty, illiteracy, ignorance and social stigma hinder medical advice. This limits our existing literature on male breast lesions.

Despite there has been constant advances in diagnosis and treatment of female breast lesions, our understanding of pathology of male breast lesions is still limited and thus, needs to be further explored.

So far, there have been very few studies on the spectrum of male breast lesions and most of them are done either on aspiration smears or on biopsies. Therefore, in the present study, we aimed to analyse the spectrum of different types of male breast lesions at our tertiary care centre both on aspiration cytology smears and histological specimens as well as biopsies. And to the best of our knowledge, it is the largest study, so far, in our Indian scenario on the morphological spectrum of male breast lesions where both cytopathology and histopathology cases were analysed.

**Material And Methods**

The medical records of all the patients who underwent Fine needle aspiration cytology, core biopsy, lumpectomy and Mastectomy from 2010 to 2015 at Kasturba Medical College, Mangalore were retrieved and the available data on the male breast aspirates were analysed after obtaining the Ethical clearance. The cytological diagnoses were classified into four major diagnostic categories such as benign, malignant, suspicious of malignancy and unsatisfactory aspirate. The unsatisfactory aspirates were looked for repeat cytopathology or histopathology if done or not. And the cases which were rendered unsatisfactory on cytology reports with no repeat aspiration done and those with no histopathological confirmation were excluded from the study. Histopathological specimens of post treatment cases and sections with autolytic changes were also excluded from the study. For the histopathologic diagnosis, the gross and microscopic findings were recorded and reviewed. Special stains and immunohistochemical stains wherever available were also studied. In addition, the cases with both cytological and histological data available were analysed to look for cytohistological correlation of the diagnoses. Finally, data were analysed using SPSS software for appropriate statistical methods wherever required.

**Results**

Out of total 7700 cases of palpable breast lumps, male breast cases were 130. Out of 130 cases, 24 cases had both cytology and histopathology done. So, the total number of cases analysed either in histopathology or in cytology were 118 (130-24/2) (1.5%). Out of these 130 cases of male breast lesions, 54 cases were diagnosed on FNAC and 76 cases on histological specimens. 24 cases out of 130 cases
had both cytology and histopathology records. To the best of our knowledge, our 5 year study is done on the largest number of male breast lesions till date.

The cytological diagnoses of 54 (49 benign and 5 malignant cases) are summarised in Table 1. The histopathological diagnoses of 76 (70 benign cases and 6 malignant cases) are shown in Table 2. The cytohistological correlation is summarised in Table 3.

**Table 1: Summary of cytological diagnoses**

<table>
<thead>
<tr>
<th>CYTOLOGY</th>
<th>BENIGN (49)</th>
<th>MALIGNANT (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gynaecomastia (Figure 1) (36)</td>
<td>Infiltrating ductal carcinoma (Not otherwise specified)</td>
</tr>
<tr>
<td></td>
<td>Benign non specific breast disease(6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inflammatory (4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibrocystic disease (2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibroadenoma (1)</td>
<td></td>
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</tbody>
</table>

**Table 2: Summary of histopathological diagnoses**

<table>
<thead>
<tr>
<th>HISTOLOGY</th>
<th>BENIGN (70)</th>
<th>MALIGNANT (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gynecomastia fibrous(Figure 2)[51]</td>
<td>Infiltrating ductal carcinoma (NOS)[4]</td>
</tr>
<tr>
<td></td>
<td>Tubercular mastitis[3]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibrocystic disease[2]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fibroadenoma[2]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Duct papilloma with florid hyperplasia (Figure 3)[1]</td>
<td></td>
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</table>

**Table 3: Cytohistological correlation**
BENIGN (n=20)  MALIGNANT (n=4)

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Gynecomastia fibrous type (12)</td>
<td>Infiltrating ductal carcinoma [NOS] (4)</td>
</tr>
<tr>
<td>Gynecomastia florid hyperplasia (2)</td>
<td></td>
</tr>
<tr>
<td>Granulomatous mastitis (2)</td>
<td></td>
</tr>
<tr>
<td>Breast abscess (2)</td>
<td></td>
</tr>
<tr>
<td>Fibrocystic disease (2)</td>
<td></td>
</tr>
</tbody>
</table>

No false positive, no false negative cases were identified in cyto- histo correlation (Table 3). Thus, the sensitivity and specificity in both benign and malignant cases was 100%.

The NMBR grading and immunohistochemical profile of malignant cases diagnosed on histopathology are shown in Table 4.

**Table 4: Summary of NMBR grading and immunohistochemical profile.**

<table>
<thead>
<tr>
<th>CASES</th>
<th>HISTOLOGICAL SUBTYPE</th>
<th>NMBR* GRADING</th>
<th>ER**</th>
<th>PR***</th>
<th>Her 2 Neu</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASE 1</td>
<td>IDC (NOS)****</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>CASE 2</td>
<td>IDC (NOS)</td>
<td>2</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CASE 3</td>
<td>Invasive papillary carcinoma</td>
<td>2</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CASE 4</td>
<td>IDC (NOS)</td>
<td>1</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CASE 5</td>
<td>IDC (NOS)</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>CASE 6</td>
<td>IDC (NOS)</td>
<td>3</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
</tr>
</tbody>
</table>

*Nottinghams Bloom Richardson grading **Estrogen receptor ***Progesterone receptor ****Infiltrating ductal carcinoma (Not otherwise specified)

Out of 78 cases of gynaecomastia, 72 cases had unilateral gynaecomastia while 6 cases had bilateral involvement. Amongst 78 unilateral cases, 70 cases had left breast involvement while right breast was involved in 8 cases. The age ranged from 19 to 80 years for benign cases and 55 to 68 years for malignant cases. Among 56 cases diagnosed as gynecomastia on histopathology, 5 cases showed the features of florid type of hyperplasia.

**Discussion**

The male breast diseases are less common compared to female breast. This is attributable both to hormonal changes during peripubertal period as well as scant available literature on male breast lesions. In males, rise in testosterone levels causes atrophy and involution of ducts. Moreover, the absence of
progesterone\textsuperscript{[19, 20]} in males compared to peripubertal females, inhibits differentiation of terminal ductal-lobular units (TDLU) in males. On the contrary, in females, the peripubertal rise in oestrogen levels stimulates proliferation of ducts and progesterone initiates differentiation of TDLUs thus, accounting to common occurrence of proliferative lesions in female breast. However, the transient rise in estradiol during puberty may cause proliferation of mammary ducts and stroma. But as the male child reaches adulthood, the rising levels of testosterone combats the effects of estradiol. The components of an adult male breasts are skin, subcutaneous tissue, involuting ducts and stroma. Coopers ligament is also absent in male breasts. Owing to lack of progesterone, the terminal differentiation of TDLUs is absent in male breasts. This accounts to extremely rare occurrence of lobular proliferative diseases like lobular carcinoma in male breasts.

The common benign lesions afflicting male breasts are lipoma, sebaceous cyst, subareolar abscess, fat necrosis, intraductal papilloma, etc.

Male breast lesions constitute less than 2% of the total cases in large FNAC studies of breast lumps.

In the present study out of total 7700 cases of palpable breast lumps, male breast cases were 130.24 cases out of 130 cases had both cytology and histopathology done. So, the total number of cases analysed were 118 (130 – 12)(1.5%). This data was consistent with the studies done by Westend\textsuperscript{[1]} and Wauters et al\textsuperscript{[2]}, who found male breast lesions comprising 1.5% and 1.7% respectively of all breast lump cases.

Out of 106 cases 99 (93%) cases were benign and 7 cases (7%) were malignant. This was slightly more than the findings of Jagannath Jatav (2015)\textsuperscript{[3]} and Kirana Pailoor et al (2014)\textsuperscript{[4]} which can be attributed to our large sample size as compared to these authors. Interestingly, our results were close to the studies done by Siddiqui MT (2002)\textsuperscript{[5]}, Maclntosh et al (2008)\textsuperscript{[6]} Westend et al (2002)\textsuperscript{[7]} and Wauters et al (2009)\textsuperscript{[8]}. 

Gynecomastia was the most common cytological as well as histological diagnosis. This was concordant with the studies done by Singh R (2012)\textsuperscript{[9]} Jagannath Jatav (2015)\textsuperscript{[3]} and Kirana Pailoor et al (2014)\textsuperscript{[4]}. FNAC features of gynecomastia included mild to moderately cellular smears showing cohesive clusters of benign ductal epithelial cells alongwith bare bipolar nuclei. Almost all cases (100%) in the present study showed mild to moderate cellularity consistent with the results of Russin and associates (1989)\textsuperscript{[10]} (86%) and Das et al., (96.2%) \textsuperscript{[11]}

Nuclear atypia was not seen in any of the gynecomastia cases in the present study. This was against the findings of Das et al \textsuperscript{[11]} (1995), and Gupta et al (1988)\textsuperscript{[12]} who found atypia in 5.3% and 9.3% of the cases respectively.

Out of 78 cases of gynaecomastia, 72 cases had unilateral while 6 cases had bilateral gynaecomastia. This was concordant with studies of Martin Bates \textsuperscript{[13]} and Russin et al., \textsuperscript{[10]}. Amongst 78 unilateral cases,
72 cases had left breast while right breast was involved in 6 cases. This was concordant to the studies conducted by Das et al. and Martin-Bates et al. who observed it more in the left breast.

The most important pitfall that has been reported for FNAC of the male breast is overdiagnosis of florid hyperplasia in gynaecomastia\textsuperscript{[14]}. However, in the present study, 2 cases of florid gynecomastia cytology was available and both were accurately diagnosed as benign lesion on cytology with no false positive results for malignancy.

Among the malignant lesions invasive ductal carcinoma was the commonest tumour. Among the malignant cases, one case was papillary carcinoma while the other was metastatic with unknown primary.

Our results correlated with those of Haagensen CD\textsuperscript{[15, 21, 23]} who reported a single case of papillary carcinoma out of 16 carcinoma of the male breast.

FNAC was found to be 100% sensitive and 100% specific in both the benign as well as malignant cases. On review of literature\textsuperscript{[3, 4, 11, 16, 17, 22]} similar findings were noted.

Among the malignant cases 3 out 5 cases including invasive papillary carcinoma showed Luminal Subtype A features on immunohistochemistry while 1 case showed Luminal subtype B and there were no basal like subtype in the present study. The nuclear grades were low in all the cases. These findings were close to the results of Yimin et al\textsuperscript{[18]}

**Conclusions**

Gynecomastia is the commonest breast lesion in males. It is more common on left side. Other benign lesions in males are abscess, fibrocystic disease, granulomatous mastitis and fibroadenoma. Infiltrating ductal carcinoma is the commonest malignancy among male breasts.

FNAC is a sensitive and specific tool to diagnose male breast lesions which can avoid unnecessary biopsies.

Male breast carcinomas are usually low-grade tumours. Lobular lesions are uncommon in males. Papillary lesions, though uncommon, can be found in male breasts.

The diagnosis of male breast lesions is usually delayed as they go unnoticed for years. This probably explains male breast carcinoma presenting at a more advanced stage compared to female breast carcinoma.

In conclusion, this study has attempted to establish a baseline of histomorphological spectrum of male breast lesions. This may provide an excellent workup for future population targeted studies on male breast lesions. The differences in histology and histomorphological spectrum of male breast lesions from those of female breasts further may raise many research questions in inquisitive minds on whether there
is any difference in immunohistochemical expression, molecular expression and thus, the therapy of cancers in both the sexes.

The emphasis on further studies on male breast lesions will ensure accurate timely diagnosis, appropriate treatment and will also avoid unnecessary invasive procedures. And nevertheless will also sensitise male patients of breast lumps in both the developing and underdeveloped countries.

Declarations

Conflicts of Interest: None

Funding: None

Declarations:

1. Ethical Approval: Done by ethical committee, KMC Mangalore, India.
2. Authors contributions: Mittal Salony- Performed the study

Goyal Shefali-Paper writing

Kini H- Brainchild of this study

Mittal Saumya-Paper writing and data compilation

Adiga Deepa- Ethical approval and data compilation

3.Availability of Data and materials: Complete dataset is available and can be accessed whenever required.

References


Figures

Figure 1
Cytology smears showing fibrofatty fragments with few benign ductal epithelial cells. Gynaecomastia fibrous type (100x)

Figure 2

Photomicrograph showing benign ducts surrounded by fibrous stroma. Gynaecomastia fibrous type (500x)
Figure 3

Photomicrograph showing Intraductal papilloma (100x)