A panoramic view of morphological spectrum of male breast lesions at a tertiary care hospital in South India

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ABSTRACT:

Background: Although 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. 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 histolopathology. **Objectives:** To study the spectrum of male breast lesions encountered in the histopathology and cytology lab. **Study Design:** Five years data of male breast lesions 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. **Results:** Out of 7700 breast lumps retrieved, 120 cases were of male breasts. Of these, 54 were diagnosed by FNAC and 76 lesions on histopathology. 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, 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.

KEYWORDS: Male breast lesions, gynaecomastia and male breast disease.

INTRODUCTION: Since age, 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 the absence of terminal differentiation induced by

progesterone. Owing to their rare occurrence, male breast lesions are infrequently studied and documented.

The delay in diagnosis is due to the fact that male breast lumps remain unnoticed for years and 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 have been constant advances in then diagnosis and treatment of female breast lesions, our understanding of the 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 of 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, cases with both cytological and histological data available were analysed to look for the cytohistological correlation of the diagnoses. Finally, data were analysed using SPSS software using appropriate statistical methods wherever required.

RESULTS:

Out of the 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

CYTOLOGY	BENIGN (49)	MALIGNANT (5)
	Gynaecomastia (36)	Infiltrating ductal carcinoma (Not otherwise specified)
	Benign non-specific breast disease(6)	
	Inflammatory (4)	
	Fibrocystic disease (2)	
	Fibroadenoma (1)	

Table 2: Summary of histopathological diagnoses

HISTOLOGY	BENIGN (70)	MALIGNANT (6)
	Gynecomastia fibrous(51)	Infiltrating ductal carcinoma (NOS) (4)
	Gynecomastia florid hyperplasia (5)	Invasive papillary carcinoma(1)
	Breast abscess (6)	Metastatic (1)
	Tubercular mastitis (3)	
	Fibrocystic disease (2)	
	Fibroadenoma (2)	
	Duct papilloma with florid hyperplasia (1)	

Table 3: Cytohistological correlation

BENIGN (n=20)	MALIGNANT (n=4)
Gynecomastia fibrous type (12) Gynecomastia florid hyperplasia(2)	Infiltrating ductal carcinoma[NOS](4)
Granulomatous mastitis (2)	
Breast abscess (2)	
Fibrocystic disease (2)	

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.

CASES	HISTOLOGICAL SUBTYPE	NMBR* GRADING	ER**	PR***	Her 2 Neu
CASE 1	IDC (NOS)****	2	-	-	+
CASE 2	IDC (NOS)	2	+	+	-
CASE 3	Invasive papillary carcinoma	2	+	+	-
CASE 4	IDC (NOS)	1	+	+	-
CASE 5	IDC(NOS)	2	-	-	+
CASE 6	IDC(NOS)	3	Not done	Not done	Not done

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

Out of the 78 cases of gynaecomastia (Figure 1, Figure 2), 72 cases had unilateral gynaecomastia while 6 cases had bilateral involvement. Amongst 78 unilateral cases, 70 cases had left breast involvement while the 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 the 56 cases diagnosed as gynecomastia on histopathology, 5 cases showed features of florid type of hyperplasia. One case revealed duct papilloma with florid hyperplasia (Figure 3)

Figure Legends:

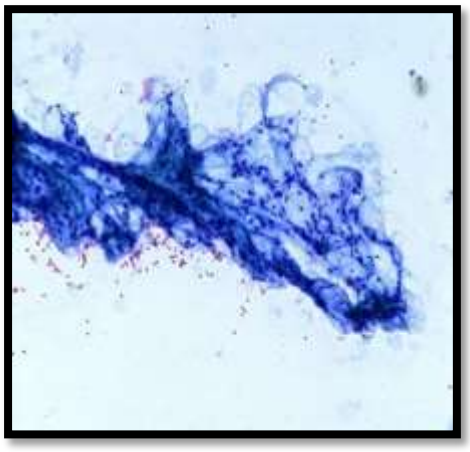

Figure 1: Cytology smears showing fibrofatty fragments with few benign ductal epithelial cells. Gynaecomastia fibrous type(100x)

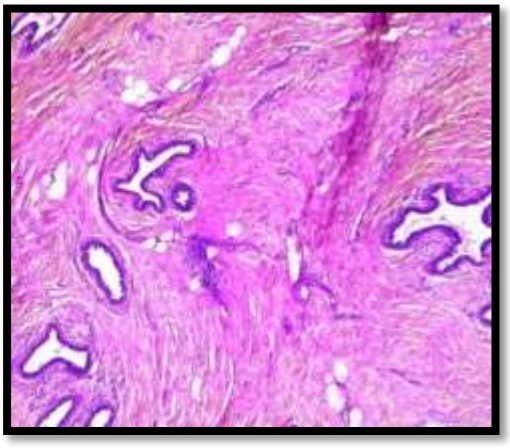

Figure 2: Photomicrograph showing benign ducts surrounded by fibrous stroma. Gynaecomastia fibrous type (500x)

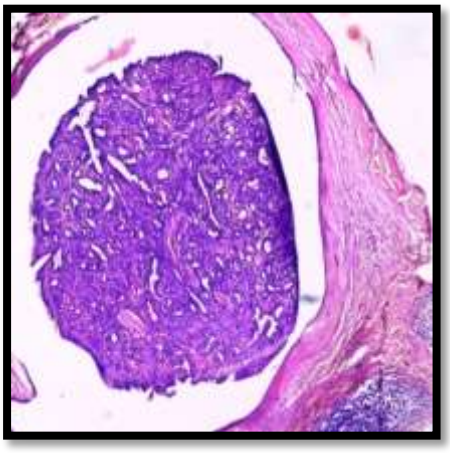

Figure 3: Photomicrograph showing Intraductal papilloma (100x)

DISCUSSION:

Male breast diseases are less common compared to female breast. This is attributable both to hormonal changes during the peripubertal period as well as the scant available literature on male breast lesions. In males, the rise in testosterone levels causes atrophy and involution of the ducts. Moreover, the absence of progesterone[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 the differentiation of TDLUs, thus accounting for the common occurrence of proliferative lesions in the 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 combat the effects of estradiol. The components of adult male breast are skin, subcutaneous tissue, involuting ducts, and stroma. Cooper ligament is also absent in male breasts. Owing to the lack of progesterone, the terminal differentiation of TDLUs is absent in male breasts. This accounts for the 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[1] and Wauters *et al*[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) [3] and Kirana Pailoor *et al* (2014)[4] which can be attributed to our large sample size compared to these authors. Interestingly, our results were close to the studies done by Siddiqui MT (2002)[5] , MacIntosh *et al* (2008)[6], Westend *et al* (2002)[7] and Wauters *et al* (2009)[8].

Gynecomastia was the most common cytological as well as histological diagnosis. This was concordant with the studies done by Singh R (2012)[9] , Jagannath Jatav (2015) [3] , and Kirana Pailoor *et al* (2014)[4] . FNAC features of gynecomastia included mild to moderately cellular smears showing cohesive clusters of benign ductal epithelial cells along with 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)[10] (86%) and Das *et al*., (96.2 %) [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* [11] (1995)., and Gupta *et al* (1988) [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 the studies of Martin Bates [13] and Russin *et al*.[10]. Amongst the 78 unilateral cases, 72 cases had a left breast while the right breast was involved in 6 cases. This was concordant with 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 the overdiagnosis of florid hyperplasia in gynaecomastia [14]. However, in the present study,2 cases of florid gynecomastia cytology were available and both were accurately diagnosed as benign lesions 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 [15,21,23] who reported a single case of papillary carcinoma out of 16 carcinomas of the male breast.

FNAC was found to be 100% sensitive and 100% specific in both benign as well as malignant cases. On review of literature [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 subtypes in the present study. The nuclear grades were low in all cases. These findings were close to the results of Yimin *et al* [18]

CONCLUSIONS:

Gynecomastia is the commonest breast lesion in males. It is more common on the 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, although 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 the 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 cancer in both 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 with breast lumps in both developing and underdeveloped countries.

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.

4. Conflicts of Interest: None

5. Funding agencies: No funding was used in this study

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