Histopathological Spectrum of Unusual Breast Lesions: A Seven Year Retrospective Review

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Abstract

Background: Breast lesions are the heterogeneous diseases that encompass several distinct entities with remarkably different characteristics. While the more common forms of breast cancers are well recognized and understood better, there are many important unusual lesions and malignancies that are less known and less appreciated.

Aims and Objectives: To highlight the spectrum, histomorphology and prevalence of unusual breast lesions in our tertiary care hospital.

Material and Methods: The clinicopathological records of resected breast lesions submitted to histopathology department over the period of seven years from Jan 2009 to December 2015 were reviewed retrospectively. It was observational, retrospective and descriptive analysis of 473 resected breast lesions including excised, lumpectomy and modified radical mastectomy (MRM) specimens. The most common lesions like infiltrating ductal carcinoma (IDC) and infiltrating lobular carcinoma in malignant category and fibroadenoma, fibrocystic disease in benign category were excluded from the study. We encounter unusual breast lesions that were included in our study.

Results: Out of total 473 resected specimens of breast, benign lesions accounted for 336 (71.05 %) and malignant 136 (28.75%). The unusual findings were 5.48% in malignant category and 1.12% in benign category and one in intermediate/ borderline category. In unusual malignant category, we found 8 types of rare tumors out of 12 unusual variants. In benign and intermediate lesions, we found 4 cases of unusual pathologies.

Conclusion: This study highlights the importance of histopathology in breast lesions not only in diagnosing the lesion but also in predicting the prognosis. There are more than a dozen variants of breast cancer which are less common. Our study highlights the spectrum, histopathology and prevalence of such unusual lesions in our centre.

Keywords: Breast lesions, Unusual, Histopathological type, Cancer variants.

Access this article online

Quick Response Code:

Website: www.innovativepublication.com

DOI: 10.5958/2394-6792.2016.00086.7

Introduction

In India, breast cancer forms the second common malignancy after cervical cancer and is detected in 20 per 1, 00,000 women.[1,2] Breast lesions are the leading cause of morbidity and mortality among women worldwide with few cases being reported in males. Due to lack of breast screening practice in developing nations, patients present with palpable lumps.[3] However there are more benign breast lesions than the malignant breast lesions.[1,2]

Breast cancer is a heterogeneous disease which can be characterized into clinical, morphological and biological meaningful groups.[4] The high mortality associated with breast cancer is linked to aggressiveness of the tumor which depends to a large extent on the histopathological types and stages.[5]

Most of the tumors are derived from mammary ductal epithelium, principally the terminal duct lobular unit (TDLU) and upto 75% of the diagnosed infiltrating duct carcinoma, not otherwise specified (IDC-NOS). The second most common epithelial type is invasive lobular carcinoma which comprises 5-15% of the lumps. However, there are more than dozen variants which are less common but still very well defined by world health organization (WHO) classification.[6] They comprises less than 10% of the breast tumors. Their behavior can differ greatly. So it is important to know their main characteristics in order to make the best treatment choice and foresee prognosis.[7] The same is true for unusual lesion in benign and intermediate category. Therefore, we have conducted this research with the aim to highlight the spectrum, histopathology and prevalence of the unusual breast lesions in our set up. As the most common forms of breast lesions and cancers are well understood and recognized, there are many important rare/unusual lesions and malignancies that are less appreciated.

Material and Methods

This was a retrospective descriptive analysis of all unusual or rare breast lesions submitted to the Hi-tech

Diagnostic Centre, Dhule and Department of Pathology, KIMS, Karad and over a period of 7 years from Jan 2009 to Dec 2015. All records of patients with Clinico-pathological data of breast lesions were retrieved from the Pathology registers and stored records. During this study, we came across uncommon and interesting lesions which were studied in detail. Some of the uncommon lesions were presented as case reports also included in our study. We received a total of 473 specimens in form of biopsy, lobectomy, lumpectomy and modified radical mastectomy (MRM). Histopathologically, the most common lesions were IDC-NOS and infiltrating lobular carcinoma of breast in malignant category and fibroadenoma, fibrocystic disease of breast in benign category. Both these lesions were excluded from the study. The uncommon/rare and interesting lesions in malignant and benign / borderline category were included in the study. Paraffin-embedded sections were studied with the routine Hematoxylin and eosin method. Immunohistochemistry (ER, PR, HER 2/neu) and special stains were performed whenever required and as per availability.

Observations and Results

During the period of 7 years from Jan 2009 to Dec 2015, a total of 473 breast specimens were received. Out of these, there were 336(71.05%) benign and remaining 136 (28.75%) were malignant. We diagnosed one case of borderline category as giant borderline Phyllodes tumor. Of the 473 cases, 472 were females and one was male. The age ranged from 12-80 years. The commonest presenting symptom was lump in breast in both benign and malignant groups.

In the benign group, out of 336 cases we encounter 03 unusual and interesting diagnosis as crystallizing galactocele, hydatid cyst and bilateral giant juvenile fibroadenomas, constituting 1.12% of unusual histopathological diagnosis. Remaining all were fibroadenoma and fibrocystic diseases. We found one case of borderline lesion as giant borderline phyllodes tumor.

In the malignant group, we found IDC-NOS and infiltrating lobular carcinoma was the commonest histo-diagnosis. In unusual category of malignant tumors, we found one case each case of metaplastic carcinoma, intracystic papillary carcinoma in male and female patients, invasive micropapillary carcinoma, tubulolobular carcinoma, medullary carcinoma, mucinous carcinoma, and adenoid cystic carcinoma respectively.(Table 1) Out of 136 cases in malignant category, unusual entities were 08(5.48%) and left side of breast was the most common site of the lesion as compared to the right one.

Table 1: List of Unusual breast tumors

Sr No	Unusual malignant tumors	No of cases
1	Metaplastic Carcinoma with extensive cartilaginous differentiation	01
2	Invasive Intracystic papillary carcinoma(Male)	01
3	Invasive Papillary carcinoma(Female)	01
4	Micro papillary carcinoma	01
5	Tubulolobular carcinoma	01
6	Medullary carcinoma	01
7	Mucinous/Colloid carcinoma	01
8	Adenoid cystic carcinoma	01
9	Apocrine carcinoma	Nil
10	Non Hodgkin Carcinoma	Nil
11	Invasive cribriform Carcinoma	Nil
12	Secretory breast Carcinoma	Nil
13	Neuroendocrine Carcinoma	Nil

Findings in the present study with reference to unusual breast lesions were tabulated. (Table 2)

Table 2: Distribution of Breast lesions

Total lesions (%)	Benign lesions (%)	Malignant lesions (%)	Borderline lesion (%)
473 (100)	336 (71.05)	136 (28.75)	01(0.2%)
Unusual lesions(%)	1.12	5.48	--

Discussion

Breast lesions pose health and cosmetic hazards predominantly in females. The anxiety and fear associated with increased awareness, breast cancers have significantly improved the health seeking behavior of the patients with breast lumps. This might partially explain the increasing incidence of benign breast neoplasms.[8]

In the present study, 473 cases were studied over a period of seven years. Benign lesions constituted 336 (71.03%) of cases whereas malignant were 136 (28.75%) with the one case of borderline /intermediate category. Regarding unusual lesions of the breast, in benign category, we found 3 (1.12%) cases and in malignant 8 (5.48%) unusual cases were diagnosed. In our study, females dominated the study as 99% of the cases with single case in male. The age group varied from 12-80 years in our study.

The spectrum of breast lesion in our study showed 71.03% benign lesions and 28.75% malignant lesions with one case of intermediate category. Our study was in concordance of study by Desai[1], Malik R and Bharadwaj VK.[9] Desai studied 212 cases over a period of 7 years. She reported benign lesions in 81.13 % and malignant lesions in 18.87%. Malik R and Bharadwaj VK[9] in their study of 1724 cases over a period of 20 years reported benign lesions in 72.97% and malignant in 27.03% which tallies with our incidence.

Uncommon and interesting cases studied in the benign groups were crystallizing galactocele, hydatid cyst and bilateral giant juvenile fibroadenomas. In borderline category, we diagnosed one case of borderline giant borderline Phyllodes tumor. Metaplastic carcinoma, intracystic papillary carcinoma in male and female patients, invasive micropapillary carcinoma, tubulolobular carcinoma, medullary carcinoma, mucinous carcinoma, and adenoid cystic carcinoma were the unusual cancers in malignant category. In the present study, we studied these cases in detail and uncommon findings of lesions were compared with other researchers (Table 3).

With the drawback of limited case series regarding unusual lesions in breast, handful of 2/3 studies were found in literature by Desai[1], Malik and Kulkarni S et al[10] and Dayanand V et al[11]. Danda AM et al[12] in his seven year retrospective review on Nigerian population, found 10.2% of unusual or special types of breast cancers.(Table 3)

Table 3: Comparison of Unusual breast lesions with other researchers

Unusual lesions (%)	Desai M[1]	Malik R & Bharadwaj VK[9]	Kulkarni S et al [10]	Dayanand V et al [11]	Danda AM el al[12]	Present study
Benign	1.17	-	0.72	-	--	1.12
Malignant	-	13.0	15.15	13.9	10.2	5.48

In benign category

Case 1: Bilateral Giant Juvenile Fibroadenomas of Breasts[13]

The incidence of giant juvenile fibroadenoma is found to be only 0.5% of all fibroadenomas. To the best of our knowledge, we published the fifth case of bilateral giant juvenile fibroadenoma in a 12 year old prepubertal girl.[13] A 12 year old girl presented with rapidly growing bilateral breast lumps. Pre-operative FNAC was done and both resected specimens were sent for histopathological confirmation (Fig. 1a). Cut surface showed well circumscribed, capsulated, gray white multiple nodules with myxoid appearance and occasional slit like spaces (Fig. 1b). Light microscopy confirmed the diagnosis of bilateral Giant Juvenile Fibroadenoma of breasts. To best of our knowledge, only four case reports are available in the English literature.[14-17]

Case 2: Crystallizing galactocele

We have diagnosed unusual lesion on FNAC as crystallizing galactocele in a 27 year old female.[18] FNAC resulted in aspiration of thick, milky material with reduction in size of the lesion. The smear studied showed numerous, semitransparent to dark blue crystals on H and E and retractile crystals with defined borders of variable shapes and sizes on Leishman stain (Fig. 1c). In view of the clinical history of lactation and the cytology, a diagnosis of crystallizing galactocele was made. To the best of our knowledge, ours was the second case report.[18] The cytodiagnosis of crystallizing galactocele was only reported by Raso DS et al[19] in 1997. Histologically, the diagnosis was confirmed on lumpectomy specimen.

Case 3: Hydatid cyst of breast

Hydatid cyst in the breast is very unusual and rare with reported incidence of 0.27% in the English literature. A 60 year old female presented with painless, slow growing lump in the left breast mimicking breast tumor clinically. FNAC was advised and we found benign ductal epithelial cells, granular debris and scattered retractile hooklets. Lumpectomy specimen showed cystic mass with whitish membranous material(Fig. 1d). Microscopy confirmed the diagnosis of hydatid cyst of breast in view of cyst wall of outer laminar layer with inner germinal centre with luminal scolices and hooklets. Final diagnosis of hydatid cyst of left breast was rendered.[20] Breast may be primary site or may be part of disseminated hydatidosis[21].

Case 4: Giant borderline Phyllodes tumor of the Breast: (Borderline /Intermediate category)

Phyllodes tumors appear with the frequency of 0.4% of all the breast tumors. Giant phyllodes tumor constitutes 20% of phyllodes tumor category[22,23,24]. A 60 year old female presented with huge irregular nodular lump in the left breast measuring 28x25x16 cms. FNAC is inconclusive in most of the time in phyllodes tumor. Hence we published this case which was diagnosed on FNAC.[22] Cytology of giant phyllodes revealed spindle shaped tumor with elongated vesicular to hyperchromatic nuclei with occasional prominent nucleoli, anisonucleosis and atypia. The MRM confirmed the final diagnosis as Giant borderline Phyllodes tumor of the breast. Grossly, we received giant multinodular mass with pushing margin and leaf like areas (Fig. 1e). Sections showed circumscribed tumor with pushing margins with hypercellularity of atypical stromal-spindle shaped tumor cells arranged in storiform, fascicular, sheets and clusters with mitosis[22].

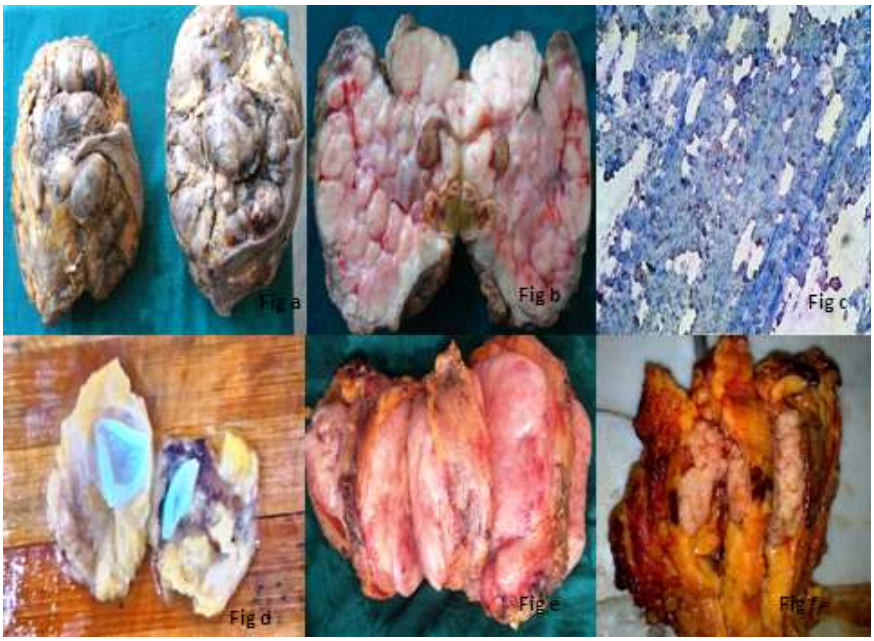

Fig. 1: Gross features of unusual findings in breast specimens

a. Lumpectomy specimen of giant juvenile bilateral fibroadenomas
b. Specimen on cut section with whitish nodules with few slit like spaces
c. Blushish crystals on proteinaceous background of galactocele patient on cytology
d. Hydatid cyst of breast showed cystic mass filled with whitish membranes
e. Phyllodes tumor showing giant, multinodular mass
f. Intracystic papillary tumor on c/s of MRM

In malignant category

Case 1: Metaplastic carcinoma of left breast with extensive chondroid differentiation

Metaplastic carcinoma is general term referring to a heterogeneous group of neoplasms characterized by an infiltrate admixture of adenocarcinoma with dominant areas of spindle cells, squamous and of mesenchymal differentiation.[7] The incidence of metaplastic breast carcinoma is in range of 0.2-0.6% and the median age of presentation is 47-61 years.[25-27] We reported a case of 33 year old female with lump in left breast since 6 months measuring 5x3 cms in lower inner quadrant.[28] MRM was done and histologically, tumor composed of glandular, lobular, whorls and nest with malignant cartilage forming tumor as basophilic cartilaginous matrix (Fig. 2a). When evaluating metaplastic carcinomas, extensive sampling is a need of hour, to differentiate from sarcoma and phyllodes tumor due to treatment implications.[29] IHC showed cytokeratin, vimentin, S-100 protein positivity in metaplastic carcinoma.

Case 2: Intracystic papillary carcinoma of male breast without invasion

Breast carcinoma is uncommon in male and represents 0.6% of all breast carcinomas and less than 0.1% of all malignancies in male. We report a case of intracystic papillary carcinoma (ICPC) of breast in 80 year old male patient.[30] ICPC accounts for 5–7.7% of all breast cancers[31]. An 80 year old farmer presented with 7x6cm well circumscribed mobile mass in left upper outer quadrant of breast. Simple mastectomy was done. Cut surface showed large cyst measuring 5x4 cms containing dark fluid and tumor (Fig. 1f) in it. Tumor measured 4x4x3 cm and showed multiple papillary excrescences with grayish white solid friable mass. Microscopy showed large cystic cavity filled with papillary neoplasm. ICPC composed of numerous delicate, branching papillary folds lined by neoplastic epithelial cells with mild pleomorphic, hyperchromatic nuclei with high N:C ratio (Fig. 2d). In our case, ER and PR were positive in the tumor cells with erb B2 negativity.[30]

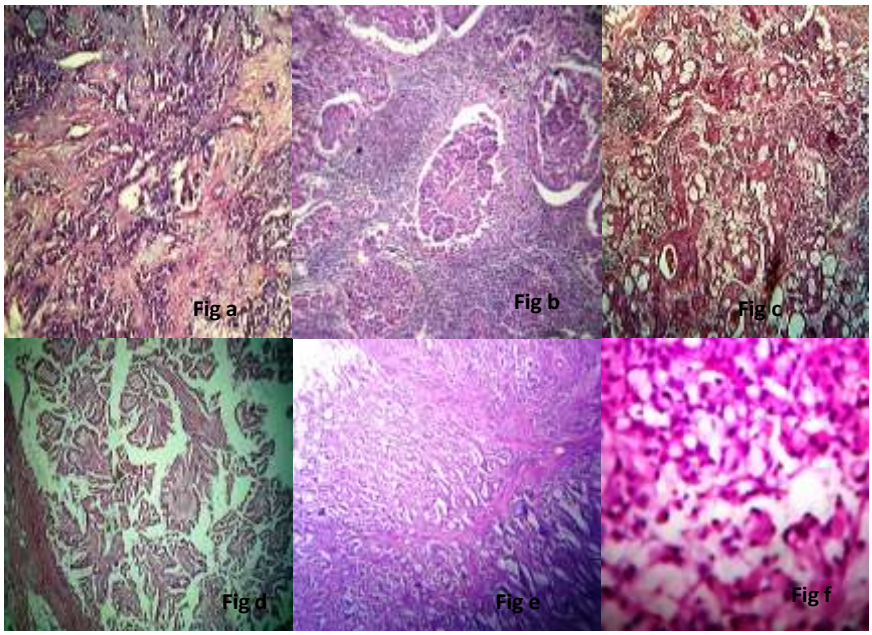

Fig. 2: Unusual findings on histopathology

a. Metaplastic carcinoma with chondroid differentiation (H&E, x100).
b. Medullary carcinoma with characteristic pushing margins, lymphocytic infiltration and round to oval tumor cells (H & E, x400).
c. Adenoid cystic carcinoma with cribriform pattern and cystic spaces containing basophilic material (H & E, x100).
d. ICPC with multiple branching fronds lined by neoplastic cells. (H & E, x100)
e. Mixed pattern of Tubulolobular carcinoma showing small rounded tubules and single cells pattern of lobular carcinoma in fibrous stroma (H & E, x100)
f. Mucinous carcinoma showing signet ring cells in lakes of mucin. (H & E, x400)

Case 3: Intracystic papillary carcinoma of female breast with invasive component.

A 55 year old post-menopausal woman presented with lump in right breast measuring 6x4x2cms. MRM showed tumor arranged in papillary pattern with solid and trabecular areas with individual pleomorphic hyperchromatic nuclei with prominent nucleoli and variable mitosis. Histopathological diagnosis was ICPC with invasive component.[32] IHC revealed ER, PR negativity Her 2neu and SMA revealed absence of myoepithelial cell layer. Although rare, ICPC has an excellent prognosis.

Case 4: Tubulolobular carcinoma

Tubulo-lobular carcinoma is a rare variant of mammary carcinoma that displays an admixture of invasive tubules and lobule like cells. It accounts for 1% of breast cancers.[33] A 60 year old female presented with lump in right breast since 4 months. MRM showed 4x3x2cms grayish white tumor with infiltrating border on cut section. Light microscopy showed tumor composed of neoplastic cells arranged in sheets, cords, tubules, cribriform, lobules and solid pattern. The tumor cells exhibit intermixed pattern of small, rounded tubules with lobule like single cells infiltrating in the duct in fibrous stroma (Fig. 2e). Tumor showed ER and PR positivity. We published this case in view of its rarity and unique variant with favorable prognosis.[34]

Case 5: Medullary carcinoma

It is well circumscribed carcinoma, composed of poorly differentiated cells arranged in large sheets with no glandular patterns, scant stroma and a prominent lymphoplasmocytic infiltrate (Fig. 2b). Medullary carcinoma represents 1-7% of all breast carcinoma.[7] We have diagnosed a medullary carcinoma in 51 year old female presented with 4x4 cm lump in left breast since 8 months. Histologically, confirmed as medullary carcinoma due to its characteristic morphology on gross and microscopy.

Case 6: Mucinous or colloid carcinoma

Pure mucinous carcinoma represents 1-4 % of all the breast cancers.[7,34] In this type of cancer, the tumor is formed from abnormal cells that floats in the pools of mucin.[7](Fig. 2f) We evaluated a case of 69 year old female presented with well-defined lobulated lesion measuring 5x3 cms in left breast. Mucinous carcinoma has a favorable prognosis.[7] IHC showed ER and PR positivity with HER-2 negativity.

Case 7: Invasive micropapillary carcinoma

It is a carcinoma composed of small clusters of the tumor cells lying within the clear stromal spaces. The

pure variant is extremely rare.[6] Hollow aggregates of malignant cells and lymphatic invasion are common features of this tumor. Carcinoma with micropapillary features have poor survival.[6] We have found a mixed feature of invasive micropapillary carcinoma with papillary carcinoma in a 80 year old male in view of its pure form is very rare[30].

Case 8: Adenoid cystic carcinoma

Primary adenoid cystic carcinoma (ACC) of the breast is an uncommon histological form of breast cancer accounting for 0.1% of all mammary neoplasm.[7] The differentials are benign collagenous spherolosis and cribriform carcinoma.[7] We published a case of adenoid cystic carcinoma in a 38 year old female, who presented with painless mass in right breast since 9 months.[35] We received right side MRM specimen measuring 20x10x5 cms. Microscopy showed tumor composed of neoplastic cells arranged in solid, cribriform, tubular and trabecular pattern with cystic spaces. Cystic space contain characteristic eosinophilic basement membrane material (Fig. 2c) Hence proper and early diagnosis of ACC on histopathology always wanted, in view of its favorable diagnosis.

Summary

Unusual breast lesions are a heterogeneous group of benign and malignant etiologies with different behaviors and varied prognosis. Histopathology has been gold standard for the diagnosis and predicting the prognosis. In this paper, several rare and unusual lesion of breast have been discussed. Understanding of these unusual and less appreciated lesions is important in today's era of varied differentials and different prognosis of the lesion. We have summarized, the unusual lesions encountered by us over a period of seven years. These features will be useful in the management of patients as well as carries prognostic value. Using information gained from case reports and small several series presented here, the predicting clinician will be able to counsel, design management and treatment plans of patient with these unusual breast lesions with better confidence.

Source of funding: Nil

Conflicts of interest: Nil

Ethical consideration

Permitted, in view study done on specimen sent to private Hi-Tech Diagnostic center, Dhule and KIMS, Karad-where all written consent were taken from patients.

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