Original Article

# Fibroadenoma: A harbor for various histopathological changes

**K. Geethamala, B. R. Vani[1], V. Srinivasa Murthy[1], M. Radha[1]**

Department of Pathology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda District, Telangana, [1]Department of Pathology, ESIC Medical College and PGIMSR, Rajajinagar, Bengaluru, Karnataka, India

## ABSTRACT

**Background:** Fibroadenomas (FAs) are the most common benign tumor of the female breast constituting approximately one-third of all benign breast lesions. Epithelial elements of FA can exhibit spectrum of proliferative changes similar to those found in normal breast counterparts. **Objective:** To study and analyze various histopathological changes within FAs. **Materials and Methods:** A 3 years retrospective study conducted in the Department of Pathology Employee's State Insurance Corporation (ESIC) Medical College and Postgraduate Institute of Medical Sciences and Research and ESIC Model Hospital, Rajajinagar. Bengaluru. 372 diagnosed cases of FAs were retrieved and examined for various changes associated within it. Relevant clinical data were analyzed. **Results:** FAs were commonly encountered in the age group of 21–30 years (63.2). 42.5% of FAs had associated pathological entities. Complex FAs were 1.5%, 0.9% of infarcts and 0.3% of FA with extensive squamous metaplasia. 24.3% of FA with fibrocystic disease, 12.3% of FA with varied degrees of hyperplasia and 0.3% of invasive carcinoma was noted. Incidental detection of even single case of carcinoma within FA emphasizes the need for comprehensive histopathological examination of all FAs. **Conclusions:** The present study highlights various gamut of nonproliferative and proliferative lesions seen in amalgamate within FAs. Early detection enables further management and surveillance of the concerned patients.

**Key words:** Fibroadenoma, histopathological changes, infarct, invasive carcinoma, proliferative lesions

## INTRODUCTION

Breast is a glandular organ influenced by hormones with various structural changes giving rise to different types of lesion.[1,2] Of these lesions fibroadenomas (FAs) are the most common benign tumor of the female breast constituting approximately one-third of all benign breast lesions. They can occur in women of any age, but the peak incidence is seen in second and third decade of life.[1-5]

Fibroadenoma is a biphasic benign stromal tumors arising from monoclonal intralobular stromal mesenchymal cells and reactive polyclonal hyperplasia of intralobular ductular and acinar epithelium with subsequent compression of ducts and acini into slit like spaces resulting in final picture of FA.[1-5] Etiology for FA is unknown, however both epithelial and stromal cells exhibit estrogen and progesterone receptor. Hence, these proliferate during reproductive age and undergo atrophic changes in menopause.[1-5]

Epithelial elements of FA exhibit spectrum of proliferative changes similar to those found in normal breast counterparts.[3,6] Dupont *et al*. described complex FA that has an increased risk of malignancy.[7] Breast carcinoma is an aggressive malignancy with a grim prognosis, the 5 years survival for Indian women is being 60%. In addition, it is the most common cancer among women in the urban Indian population and second only to cervical cancer in the rural population attributing to 22–28% of all cancer deaths.[8-10] Our hospital-based cancer registry also shows breast carcinoma being commoner 37.4% followed by cervical cancer 13.4%. In this background detection of even a single case of carcinoma within FA, justifies cautious histopathological examination of all FAs, even when preliminary diagnosis was just FA. There are very few literatures regarding various

Access this article online

Quick Response Code:

Website: www.ccij-online.org

DOI: 10.4103/2278-0513.148949

**Address for correspondence:** Dr. K. Geethamala, Department of Pathology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda District, Telangana, India. E-mail: drgeethamala@gmail.com

nonproliferative and proliferative changes occurring within FAs. In this communication, the study was undertaken to analyze various histopathological changes within FAs. The objective is to study and analyze various histopathological changes occurring within FAs.

## MATERIALS AND METHODS

The present study was conducted in the Department of Pathology Employee's State Insurance Corporation (ESIC) Medical College and Postgraduate Institute of Medical Sciences and Research and ESIC Model Hospital, Rajajinagar, Bengaluru, India over a period of 3 years from Jan 2010 to Jan 2013.

A total of 372 female patients diagnosed as FA on histopathology were taken up for the study. Clinical data of patients regarding the age and side of the breast involved were retrieved from the medical records.

Hematoxylin and Eosin stained slides were archived and studied for histopathological details. FAs were clustered as pericanalicular or intracanalicular, when 90% of tumor was of a particular pattern if neither then mixed. Associated epithelial and stromal morphological variants were evaluated and tabulated. Among the proliferative epithelial changes, the most advanced lesion was taken for grouping. Those FAs with one or more complex features like epithelial calcifications, apocrine metaplasia, sclerosing adenosis and cysts larger than 3 mm were categorized as complex FA. FA with tubular adenoma was considered when a focus of densely packed uniform round uncompressed bilayered ducts with negligible stroma noted. Stromal expansion with increased cellularity and leaf-like pattern characteristic of phylloides if present focally was termed as FA with phylloides tumor.

### Statistical analysis

The data was analyzed using Statistical Package for the Social Sciences software version 18.0 (SPSS Inc, Chicago). Obtained parameters were evaluated using descriptive statistical analysis and presented in terms of percentage.

## RESULTS

Total surgical specimens during 3 years period were 8808, of which 372 (4.2%) were FA. 235 (63.2%) females were in 2nd and 3rd decade of life with a mean age being 25.5 years. Right side of the breast were affected in 51.4% and left side in 47.4%. Majority had unitary FA 362 (97.3%) while multiple were noted in 10 (2.7%) cases. Of the total study group 214 (57.5%) of females had exclusive FAs while 158 (42.5%) had FAs associated with other pathological entities.

Table 1 depicts various epithelial and stromal histopathological metamorphoses occurring in FA. Most consistent microscopic associated entity was fibrocystic disease (FCD) 92 (24.3%). Forty seven (12.6%) cases of proliferative epithelial hyperplasias were detected, of which one was invasive carcinoma in a clinically unsuspected young lady with FA. Infarcts in FAs were 0.9% wherein all three cases showed residual pericanalicular and intracanalicular pattern in the margins of the lesion. Lactational changes were seen in two cases of infarcts. Five cases of complex FAs and one case of FA with multiple keratinous cysts, extensive metaplasia in a 29 years lady was seen.

## DISCUSSION

Fibroadenoma is the commonest benign breast disease in young females. In the present study majority of cases were in 2nd and 3rd decade of life similar to the studies by Bewtra[4] and *et al*.[11] Bilateral breast FAs were perceived in 7.2% of cases comparable to a study by Onuigbo.[12] Right side of the breast was affected in 51.4% and left side in 47.4% analogous to a study by Vijaykumar *et al*.[1] and Kumar.[2] Predominant right sided the involvement of breast may be due to physical and social grounds.[2] However, side of the breast involved has no clinical or prognostic significance. Proliferating fibromyxoid stroma surrounding ducts in pericanalicular pattern was chief histologic feature in 50.9% cases, rest were intracanalicular 39.7%, and mixed 9.4% similar to a study by Kuijper *et al*.[6] Nevertheless this distinction has been observed to have no clinical outcome.

Extensive search of the literature revealed 48–50% of associated pathologies in FA,[3,11] while in the present study it was 42.5% (158 cases) [Table 1]. Morphological variants in FA in the present study were one case (0.3%) each of hyalinization and squamous metaplasia with

**Table 1: Histopathological changes within FAs (158 cases)**

| Histopathological change | Number (*n*=158) | Percentage |
|---|---|---|
| FA with morphologic variants | 10 | 3 |
| Hyalinization | 1 | 0.3 |
| Squamous metaplasia | 1 | 0.3 |
| Infarction | 3 | 0.9 |
| Complex FAs | 5 | 1.5 |
| FA with fibrocystic change | 92 | 24.3 |
| FA with tubular adenoma | 5 | 1.4 |
| FA with phylloides | 1 | 0.6 |
| FA with lactation changes | 3 | 0.9 |
| FA with proliferative changes | 47 | 12.6 |
| Mild hyperplasia | 25 | 6.8 |
| Moderate hyperplasia | 10 | 2.6 |
| Florid hyperplasia | 06 | 1.6 |
| Atypical ductal hyperplasia | 5 | 1.3 |
| Invasive carcinoma | 1 | 0.3 |
| Total | 158 | 42.5 |

FAs: Fibroadenomas

keratinous cyst. The squamous changes in the breast begin within the myoepithelial cell layer. Further involving the entire ducts, acinus and leading on to the formation of epidermal cyst [Figure 1]. Awareness of this rare entity within FA is essential for it, not to be misdiagnosed as squamous cell carcinoma.[13,14] Three cases (0.9%) of infarcts were noted in the present study. Delaure and Redon were the first to describe spontaneous infarction in FA in 1949 with the incidence of 0.5–1.5% of all FAs. Infarcts occur due to vascular failure and thrombosis of vessels during hypermetabolic status of pregnancy and lactation, while in young patients etiology though obscure possible trauma and fine needle aspiration cytology induced could be considered.[15,16] In the present study, two patients were in reproductive age group, and other was an elderly patient with the clinical diagnosis of malignancy. Hence, stresses the paramount of histopathology in all cases of FAs.

In the present study, 1.5% cases of complex FAs were noted in women aged more than 40 years. Dupont *et al.*, reported 22% of complex FAs and opined, complex FA have 3.1 times the increased risk of invasive breast carcinoma in comparison to women with exclusive FA in the general population.[7] In a study by Sklair-Levy *et al.*,[5] 15.7% were complex FAs seen in older patients with a mean age of 47 years. This increased number of complex FAs may be due to a longer period of study and a large number of cases. Documented literatures on management for complex FA are very few. However study, by Greenberg *et al.*,[17] recommends complete excision after diagnosis of a complex FA. FA with focus of tubular adenoma, lactational changes and phylloides tumor were noted in 1.4%, 0.6% and 0.9% respectively. Noguchi *et al.*,[18] have documented progression of FA to phylloides by clonal expansion of the stromal compartment. Phylloides have a tendency to recur and hence entails the necessity for wide excision of the lesion.

Among various morphological lesions FCD was the commonest associated pathology accounting to 24.3% that in contrast was 6.8% in a study by Shabtai *et al.*[11] Proliferative epithelial hyperplasias in FAs were seen in 47 patients. Average age of incidence of proliferative hyperplasia was 27 years, 38 years, 39 years and 38 years in mild, moderate, florid and atypical ductal hyperplasia respectively favoring the fact that progressive epithelial proliferative lesions could be a forerunner for invasive carcinomas [Figure 2]. In a study by Kuijper *et al.*,[6] found hyperplasia being commoner associated lesions accounting to 43.9% in all age groups. And added hyperplasia within FA behaves in equivalence with otherwise normal breast parenchyma attributing to increased risk for progression to invasive carcinoma. Women with FAs harboring associated complex changes or hyperplasia need further surveillance especially if they have a strong family history of malignancy.[3,6,19]

In the present study, out of 372 cases of FAs, carcinoma within FA was 0.3%.It is in concordance with other studies who observed a range of 0.01–5.4% [Table 2].[6,11,20-23] Literature studies reveal carcinomas within FA usually being incidental histologic detection in routinely excised FA specimens.[24,25] Also imaging lacks characteristic signs, and cytology may have sampling error for precise diagnosis.[26,27] Two-third of invasive carcinomas within FA are lobular and one-third each of ductal or mixed lobular and ductal. Carcinomas *in situ* either ductal or lobular have equal frequency.[22,24] Although malignant transformation in FA is rare, high index of suspicion is mandatory in middle and elderly aged women with FA, especially those who are associated with strong family

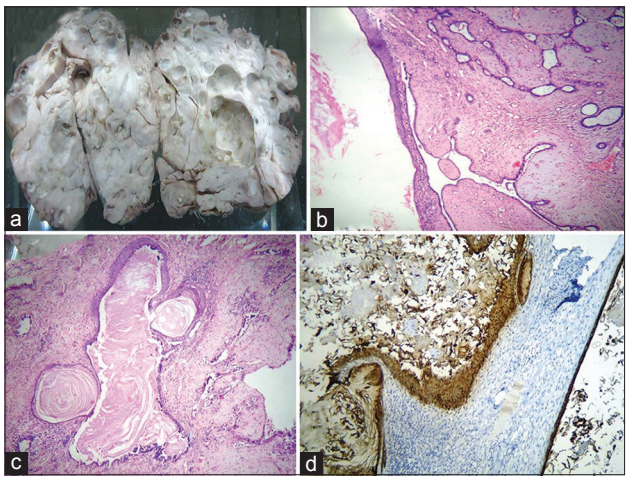


**Figure 1:** (a) Gross-cut surface shows numerous cysts filled with pultaceous material and (b and c) H and E section-showing pericanalicular and intracanalicular fibroadenoma, few cystically dilated spaces and large ducts lined by multilayered squamous epithelial cells-squamous metaplasia of the ductal epithelium (×4), (d) Immunohistochemistry showing squamous epithelium cytokeratin positive

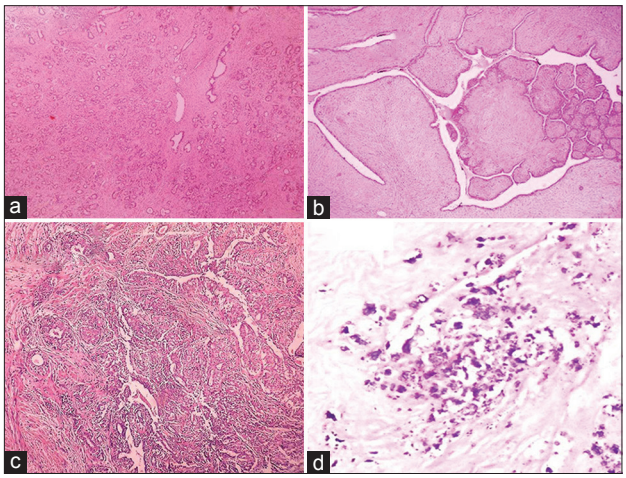


**Figure 2:** H and E section (a) Fibroadenoma with tubular adenoma, (b) with phylloides, (c) atypical ductal hyperplasia, (d) calcification (×4)

**Table 2: Invasive carcinoma within FAs**

| Author-studies | Invasive carcinoma in FA (%) |
|---|---|
| Ooe *et al.*[22] | 0.01-0.3 |
| Ozzello and Gump[21] | 0.3 |
| Deschênes *et al.*[20] | 1 |
| Shabtai *et al.*[11] | 5.4 |
| Present study | 0.3 |

FAs: Fibroadenomas

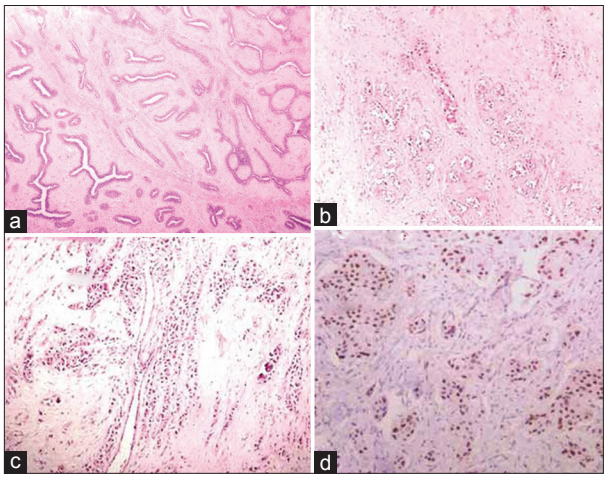


**Figure 3:** H and E section (a) Fibroadenoma (b and c) malignant cells in cords surrounds the ducts, fibromyxoid stroma (×4), (d) Immunohistochemistry diffuse estrogen nuclear staining (×100)

history of malignancy in first degree relative and mutations like BRCA-1 and BRCA-2.[3,6,19] In the present study, invasive ductal carcinoma within FA expressing hormone receptor positivity by immunohistochemistry was identified in a 32 years lady. The patient did not have any family history or other associated risk factors [Figure 3].

Current management of patients with FA varies among authors, few of whom suggest wait and watch policy in younger age group patients and excision only in women more than 40 years to rule out malignancy.[1,3,6,28,29] In the present study, a case of malignancy within FA was identified incidentally in a young lady and hence we emphasize the necessity for surgical excision of all FAs and subsequent histopathological examination irrespective of age. Early and prompt diagnosis enables imparting appropriate treatment, improving patient's morbidity and mortality.

## CONCLUSION

Fibroadenomas are the commonest benign biphasic fibroepithelial neoplasms occurring in 2nd and 3rd decade of life. The present study highlights various gamut of nonproliferative and proliferative changes seen in amalgamate within FAs, which may need further management and surveillance of the concerned patients. Hence, pathologist must conscientiously quest through all FAs and its various histopathological changes within them.

## REFERENCES


1. Vijaykumar A, Ajitha MB, Shivaswamy BS, Srinivasan N. A systematic study on fibroadenoma of the breast. Eur J Surg Sci 2012;3:80-5.
2. Kumar R. A clinicopathologic study of breast lumps in Bhairahwa, Nepal. Asian Pac J Cancer Prev 2010;11:855-8.
3. Guray M, Sahin AA. Benign breast diseases: Classification, diagnosis, and management. Oncologist 2006;11:435-49.
4. Bewtra C. Fibroadenoma in women in Ghana. Pan Afr Med J 2009;2:11.
5. Sklair-Levy M, Sella T, Alweiss T, Craciun I, Libson E, Mally B. Incidence and management of complex fibroadenomas. AJR Am J Roentgenol 2008;190:214-8.
6. Kuijper A, Mommers EC, van der Wall E, van Diest PJ. Histopathology of fibroadenoma of the breast. Am J Clin Pathol 2001;115:736-42.
7. Dupont WD, Page DL, Parl FF, Vnencak-Jones CL, Plummer WD Jr, Rados MS, *et al.* Long-term risk of breast cancer in women with fibroadenoma. N Engl J Med 1994;331:10-5.
8. Pakseresht S, Ingle GK, Bahadur AK, Ramteke VK, Singh MM, Garg S, *et al.* Risk factors with breast cancer among women in Delhi. Indian J Cancer 2009;46:132-8.
9. Murthy NS, Chaudhry K, Nadayil D, Agarwal UK, Saxena S. Changing trends in incidence of breast cancer: Indian scenario. Indian J Cancer 2009;46:73-4.
10. National Cancer Registry Programme. Indian Council of Medical Research, Two-year Report of the Population Based Cancer Registries, 1999-2000. Incidence and Distribution of Cancer, Bangalore, India, 2005.
11. Shabtai M, Saavedra-Malinger P, Shabtai EL, Rosin D, Kuriansky J, Ravid-Megido M, *et al.* Fibroadenoma of the breast: Analysis of associated pathological entities – A different risk marker in different age groups for concurrent breast cancer. Isr Med Assoc J 2001;3:813-7.
12. Onuigbo W. Breast fibroadenoma in teenage females. Turk J Pediatr 2003;45:326-8.
13. Cha EJ, Choi KM, Yain HJ, Kim DS, Moon WS. Extensive squamous metaplasia mimicking squamous cell carcinoma in fibroadenoma. J Korean Surg 2009;76:56-60.
14. Devi PM, Singh LR, Gatphoh ED. Fibroadenoma with squamous metaplasia. Singapore Med J 2007;48:682-3.
15. Singh N, Sharma S, Ishar T, Gupta RK. Infarction in fibroadenoma breast during pregnancy with skin necrosis and fungation. JK Sci 2008;10:140-1.
16. Hsu SD, Hsieh H, Hsu GC, Lee HS, Chen K, Yu JC. Spontaneous infarction of a fibroadenoma of the breast in a 12 year old girl. J Med Sci 2005;25:313-4.
17. Greenberg R, Skornick Y, Kaplan O. Management of breast fibroadenomas. J Gen Intern Med 1998;13:640-5.
18. Noguchi S, Yokouchi H, Aihara T, Motomura K, Inaji H, Imaoka S, *et al.* Progression of fibroadenoma to phyllodes tumor demonstrated by clonal analysis. Cancer 1995;76:1779-85.
19. El-Wakeel H, Umpleby HC. Systematic review of fibroadenoma as a risk factor for breast cancer. Breast 2003;12:302-7.
20. Deschênes L, Jacob S, Fabia J, Christen A. Beware of breast fibroadenomas in middle-aged women. Can J Surg 1985;28:372-4.
21. Ozzello L, Gump FE. The management of patients with carcinomas in fibroadenomatous tumors of the breast. Surg Gynecol Obstet 1985;160:99-104.
22. Ooe A, Takahara S, Sumiyoshi K, Yamamoto H, Shiba E, Kawai J. Preoperative diagnosis of ductal carcinoma *in situ* arising within a mammary fibroadenoma: A case report. Jpn J Clin Oncol 2011;41:918-23.

23. Iyengar KR, Peh SC, Yip CH, Vijayananthan A. Infiltrating duct carcinoma within a fibroadenoma. Indian J Cancer 2009;46:244-6.
24. Gashi-Luci HL, Limani RA, Kurshumliu FI. Invasive ductal carcinoma within fibroadenoma: A case report. Cases J 2009;2:174-7.
25. Jahan F, Ghosh PK, Rahman S, Khanam R. Fibroadenoma with foci of infiltrating ductal carcinoma. J Med 2012;13:115-7.
26. Rao S, Latha PS, Ravi A, Thanka J. Ductal carcinoma in a multiple fibroadenoma: Diagnostic inaccuracies. J Cancer Res Ther 2010;6:385-7.
27. Baker KS, Monsees BS, Diaz NM, Destouet JM, McDivitt RW. Carcinoma within fibroadenomas: Mammographic features. Radiology 1990;176:371-4.
28. Memon A, Parveen S, Sangrarasi AK, Malik AM, Laghari A, Talpur AH. Changing pattern of benign breast lumps in young females. World J Med Sci 2007;2:21-4.
29. Rosen PP. Pathological examination of breast specimens. In: Rosen PP, editor. Breast Pathology. Philadelphia, PA: Lippincott-Raven; 1997. p. 837-72.

**Cite this article as:** Geethamala K, Vani BR, Murthy VS, Radha M. Fibroadenoma: A harbor for various histopathological changes. Clin Cancer Investig J 2015;4:183-7.

**Source of Support:** Nil, **Conflict of Interest:** None declared.