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CLINICO-HISTOMORPHOLOGICAL VARIATIONS IN FIBROADENOMA

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ABSTRACT

Introduction: Fibroadenomas (FAs) are the most common benign tumor of the female breast constituting approximately one-third of all benign breast lesions. Although often considered a benign tumour, it can undergo a variety of histological variations.

Objectives: The aims of the study -

1. Evaluation of the histomorphological variations in fibroadenoma, frequency of their occurrence and to find out the unusual variants if any.
2. Assessment of myoepithelial cell layer integrity.

Materials and Methods: A 5 year retrospective study was conducted in the Department of Pathology, Bhopal Memorial Hospital and Research Centre. A total of 53 cases with clinical and gross impression of fibroadenoma were included in the study. Several clinico-histopathological parameters like age at presentation, size, number, laterality, growth pattern, apocrine metaplasia, adenosis, fibrocystic changes, leaf like pattern, hyperplasia & others, were studied. Smooth Muscle antibody (SMA) was done for myoepithelial cell layer.

Results: Most common age group affected was 11-20 years (43.4%). Majority of them presented with right side breast lump (62.3%). Size ranges from 2-18cms. Multiple fibroadenomas were found in 15.1%. Mixed growth pattern (41.5%) was predominant. Most common histopathological variation found was epithelial hyperplasia (79.2%).Other findings include myxoid change and collagenisation (67.9%), inflammation (47.2%), papillary hyperplasia (43.4%), adenosis (32.1%), apocrine change (22.6%), stromal overgrowth (16.98%). Multiple fibroadenomas were more in the patients below 20 years age group. Rare variations found in our study were presence of stromal giant cells (3.8%), foci of tubular adenoma (1.9%), foci of squamous metaplasia (1.9%) and calcification (1.9%). Myoepithelial cell layer was intact in all the cases.

Conclusion: Fibroadenomas display a characteristic morphology, although several epithelial and stromal variations exist which may pose diagnostic difficulty. Therefore, a thorough knowledge of these changes is necessary for accurate diagnosis of fibroadenoma.

KEYWORDS : apocrine, breast, fibroadenoma, histopathology, hyperplasia.w discrepancy

INTRODUCTION:

Fibroadenoma (FA) are the most common benign breast tumours occuring mainly in adolescent and young women. Mostly they present as a sharply demarcated, firm mass, usually not more than 3 cm in diameter. The cut surface is solid, grayish white, and bulging, with a whorl-like pattern and slit-like spaces1. It is a biphasic tumor and arises from the epithelium and stroma of the terminal duct-lobular unit of breast2. The epithelial component as well as stroma of fibroadenoma can display a variety of morphological variations which can pose diagnostic difficulty.

There are very few literatures regarding various histopathological variations occurring within fibroadenomas. This study was undertaken to analyze and report various histopathological changes in fibroadenoma.

Material and Methods:

A retrospective study of 5 years data is done in the department of Pathology in Bhopal Memorial Hospital and Research Centre. Lumpectomy specimens of 63 patients with clinical impression and gross features suggestive of fibroadenoma breast were included. Specimens were sectioned, processed and subjected for Haematoxylin and Eosin (Hand E) staining and IHC stain SMA routinely. Special stains like PAS, Masson trichrome and IHC like ER, PR and Ki-67 were done wherever required. Different histological parameters studied included pattern of growth whether pericanalicular, intracanalicular or mixed; apocrine metaplasia, adenosis, epithelial hyperplasia, leaf like pattern, fibrocystic changes, stromal growth, atypical ductal hyperplasia and other changes like myxoid degeneration, collegenisation or fibrosis. The following criteria were used in the present series:

1. Fibroadenomas were classified as pericanalicular or intracanalicular when 90% of the tumour displayed that particular type of growth pattern. If neither type could be assigned to a tumour, we diagnosed it as mixed histologic type.

2.Leaf-like pattern (enhanced intracanalicular pattern) characterized by the projection of cellular stroma into clefts of cystic spaces.

3.Stromal overgrowth was defined as the presence of stroma without epithelium in atleast one microscopic field at 40x total magnification (10x ocular objective and 4x microscopic lens objective)[3].

4. Epithelial hyperplasia, if present, was categorized as the usual type (mild, moderate and severe) or atypical ductal hyperplasia as per Rosen[3].

5. Stromal collegenisation was categorized as focal, periductular or (marked) throughout the tumour.

6. Adenosis was categorized as focal or marked, if present through out the tumour.

7. SMA positivity will be seen in myoepithelial cells surrounding the glands.

OBSERVATIONS AND RESULTS:

A total of 63 cases with clinically and gross impression of fibroadenoma were analysed for studying various histopathological changes. Out of these 63 patients, 10 patients were excluded due to different histopathological diagnosis other than FA. These are summarized in table below.

Table 1. Final histopathological diagnosis of 10 cases with clinical and gross impression of fibroadenoma

Histopathological diagnosis	Number of cases
Benign Phylloides	3
Acute on chronic mastitis with granulomatous reaction	2
Granulomatous mastitis	1
Sclerotic breast disease	1
Reactive follicular hyperplasia with sinus histiocytosis	1

Metaplastic carcinoma	1
Normal tissue (negative for malignancy)	1

Fifty three cases histologically diagnosed as fibroadenoma breast were analyzed for the frequency of occurrence of fibroadenoma in different age groups. Various parameters were studied according to the age, location, multiplicity and microscopic histopathological variants.

Maximum number of cases (n=33, 62.3%) were found in less than 30 years of age. One case was reported as fibroadenoma in male patient in left axillary region. Location wise right breast was most frequently involved. Lumpectomy size varied from 2-18cms. The largest size that we found of 18cm is an unusual presentation. It was reported as Giant fibroadenoma.

Eight patients presented as multiple fibroadenoma. Various histopathological parameters were studied like pattern of growth, epithelial and stromal changes. These are summarized in tables below.

Table 2: Age Distribution of Fibroadenoma

S. No	Age (in years)	Total No. of cases	Total percentage of cases
1	Less than 10	0	0%
2	11-20	23	43.4%
3	21-30	10	18.9%
4	31-40	12	22.6%
5	41-50	6	11.3%
6	51-60	2	3.8%

Table 3: Location wise distribution

Site	Total no. of cases	Total percentage of cases
Left Breast	17	32%
Right Breast	33	62.3%
Bilateral	2	3.8%
Others(left axilla)	1	1.9%

Table 4: Size wise distribution

Size (in cms)	Number of cases	Percentage
Less than 5	49	92.4%
6-10	2	3.8%
11-15	1	1.9%
16-20	1	1.9%

Table 5: Histological changes according to growth pattern

Histological changes (Predominantly Growth Pattern)	Total No. of Cases	Total percentage of Cases
Pericanalicular	15	28.3%
Intracanalicular	16	30.2%
Mixed	22	41.5%

Table 6: Histopathological features seen in fibroadenoma

S.No.	Histopathological features	No. of cases	% of cases
1	Epithelial hyperplasia	42	79.2%
2	Collegenisation	36	67.9%
3	Myxoid change	36	67.9%
4	Inflammation	25	47.2%
5	Papillary metaplasia	23	43.4%
6	Adenosis	17	32.1%
7	Leaf like pattern	15	28.3%
8	Apocrine change	12	22.6%
9	Cystic dilatation	11	20.7%
10	Stromal overgrowth	9	17%
11	Haemorrhage	9	17%
12	Infarction	4	7.5%
13	Congested blood vessels	4	7.5%
14	Atypical ductal hyperplasia	2	3.8%
15	Stromal giant cells	2	3.8%
16	Squamous metaplasia	1	1.9%
17	Tubular metaplasia	1	1.9%
18	Calcification	1	1.9%

Table 7: Clinicohistomorphological parameters comparision in two age groups (<=20 years and >20 years).

S.No.	Clinicohistological parameters	Subcategory	<=20 years (n=23)	>20 years (n=30)
1	Multiple fibroadenoma		5	3
2	Growth pattern	Intra Mixed Peri	8 11 4	8 11 11
3	Apocrine change	Present	5	7
4	Leaf like pattern	Present	7	8
5	Stromal overgrowth	Present	2	7
6	Myxoid change	Mild Marked	13 0	21 2
7	Collegenisation	Mild Periductular Marked	6 4 4	11 7 4
8	Stromal Giant cells	Present	1	1
9	Infarction	Present	3	1
10	Papillary metaplasia	Mild Marked	10 1	10 2
11	Adenosis	Focal Marked	6 0	8 3
12	Haemorrhage	Mild Marked	7 2	0 0
13	Tubular change	Present	1	0
14	Atypical ductal hyperplasia	Present	1	1
15	Calcification	Present	1	0
16	Cystic dilatation	Present	5	6
17	Inflammation	Present	13	11
18	Congested blood vessels	Present	2	2
19	Epithelial hyperplasia	Mild Moderate Florid	19 1 1	19 0 2

SMA was done on all the slides to look for myoepithelial cell integrity. It was found positive in all the cases, thus ruling out the possibility of in-situ carcinoma.

DISCUSSION

Fibroadenoma of the breast is relatively frequently occurring tumour. The age distribution for FAs ranges from childhood to more than 70 years of age with a mean age of about 30 years3. In our study, it ranged from 14-56 years with a mean of 27.2 years. Majority of them occurred below 30 years of age (n=33, 62.3%). Patients with Juvenile fibroadenoma tend to be younger than average age for adult fibroadenoma, with majority younger than 20 years of age3. In our study, 2 cases were diagnosed as Juvenile fibroadenoma, out of which one was less than 20 year old.

Rare examples of fibroadenoma have been reported in men4,5,6. Most have been associated with treatment with various medications such as estrogen or hormone modulators or spironolactone. In this study, a single case of male fibroadenoma presenting as left axillary swelling was found.

Location wise, we found predominantly right side involvement(n=33, 62.3%). Bilateral fibroadenoma were involved in 2 (3.8%) cases. Our results are in concordance with the study done by Geetha et al7, and in discordance with Rosen3 who found left breast to be more frequently involved, however no clinical or prognostic significance is found in laterality of fibroadenoma.

Multiple FAs occur in about 15% of patients3. In our study we found multiple fibroadenoma in 8(15.1%). These were found more frequently in younger age group similar to study done by Thakur et al2.

Most fibroadenomas are not larger than 3 cms. FAs larger than 4cm are frequent in patients less than 20 years than in older ones3. In our study, we found one FA as large as 18 cms, diagnosed as Giant FA. This is an unusual presentation and very few cases have been reported in literature till now. Thakur et al2 found greatest size of 16 cms in their study.

Pattern of growth is termed as intracanalicular when the leisonal stroma stretches the lobular units and ducts into elongated tubular structures and compresses the glandular lumens. When the lesional stroma is expanded but does not bulge into glandular lumen , and latter maintains a round outline, the growth pattern is described as pericanalicular. In our study we found mixed growth pattern as predominant histologic type (n=22, 41.5%), followed by intra and pericanalicular type.

The so-called complex features like adenosis, apocrine metaplasia, cystic dilatation and calcifications were found in 17 (32.1%), 12 (22.6%), 11(20.7%) and 1(1.9%) respectively. Kuijper et al found similar changes in 49 (12.4%), 111(28%), 20(5.1%) and 15 (3.8%) respectively. Taken together, 54.7% (n=29) of our patients had complex fibroadenoma. Dupont et al8 found that cumulative risk of invasive breast carcinoma in women with complex fibroadenomas was 3.1 times that of women in the general population, compared with a relative risk of 1.89 times in women with non-complex fibroadenomas.

Foci of tubular adenoma was found in single case in our study and worth special mention. The so called tubular adenoma is a variant of pericanalicular FA with exceptionally prominent or florid adenosis like proliferation3. Our findings are comparable with the studies done by Kuijper et al9 who found tubular adenoma like foci in 0.5% of cases, however Zakaria et al10 found it in 8% of cases.

Proliferative epithelial changes including mild, moderate, florid and atypical ductal hyperplasia was found in 38 (71.69), 1(1.8%), 3(5.66%), and 2(3.77%) respectively. Zakaria et al10 found it in 26%,2%, 1% and 1% respectively. In a study done by Kuijper et al9, hyperplasia was the commoner associated lesions accounting 43.9% in all age groups. And added hyperplasia within fibroadenoma behaves in equivalence with normal breast parenchyma attributing to increased risk for progression to invasive carcinoma. According to Rosen3, mild epithelial hyperplasia includes cell thickness of 3-4 layers with no change in duct diameter. Moderate hyperplasia includes cell layer thickness of more than 3 layers, with mildincreased in duct diameter. Florid epithelial hyperplasia includes complete filling of duct lumen with cells with increased duct diameter.

Squamous metaplasia sometimes develop in moderate and florid hyperplasia. It was found in single case in our study i.e. 1.88%. Similar findings were got by Geetha et al7, where they found squamous metaplasia with keratinous cyst. Awareness of this rare entity within fibroadenoma is essential for it not to be misdiagnosed as squamous cell lesion within small needle biopsies.

Stromal changes like stromal overgrowth, myxoid changes, collegenisation, giant cells, infarction, haemorrhagic foci, inflammatory foci and congested blood vessels were seen as shown in table.

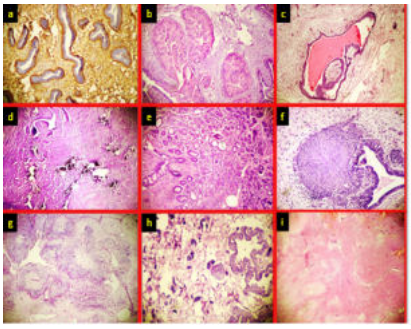
Stromal giant cells found in two of our cases worth special mention as it is an unusual feature. Jaiswal R et al11 found it in single teenage patient benign breast disease. In 1979, Rosen3 first described the presence of multinucleated stromal giant cells (MSGCs) in the breast. He concluded that these cells represent a nonneoplastic and possibly repairative process12. These cells are CD68, CD34, and Vimentin positive. These cells have ultrastructural features consistent with fibroblasts.

Fibroadenomas are prone to develop foci of infarction, during pregnancy. We also got infarction in four of our cases, however, no predisposing cause could be identified.

Conclusion:

This is a study reviewing various demographic, gross and histopathological features in 53 cases of fibroadenoma, thus contributing to prevent the diagnostic difficulties commonly encountered in rare histopathological variants. The study also contributed in analyzing various histopathological variants in relation to age and frequency of occurrence.

Figure 1: Photomicrographs of Fibroadenoma showing (a) SMA positive myoepithelial cell layer, (b) Apocrine change (c) Cystically dilated gland (d) Calcification (e) Foci of tubular change (f) Squamous metaplasia (g) Myxoid change (h) Stromal giant cells (i) Infarction



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