

FIBROADENOMATOID MASTOPATHY: ANOTHER DISTRACTIVE BREAST LESION?

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Summary

Although most anatomical pathologists have encountered breast lesions with the composite histological features of fibroadenoma (FA) and fibrocystic change (FC), referred to as fibroadenomatosis or fibroadenomatoid mastopathy (FAM), little is known about its prevalence or clinico-pathological significance. In a retrospective histological review of 400 consecutive breast lesions, among both East and West Malaysians, coded either as FA or FC in the files of the Department of Pathology, University of Malaya, we found 45 (11.3%) cases of FAM. Typically, FAM lesions showed fibroadenomatoid foci in a background of fibrocystic change. The finding of FAM among lesions coded as FC was higher (18.5%) than among FA (4%). The mean age of patients with FAM (32.1 years) was similar to FC (35.1 years) but significantly older than that of FA (26.1 years).

The notion that FA and FC are lesions at two ends of a spectrum of growth disorder of breast related to oestrogen-progesterone interplay, and that FAM occupies a position intermediate between the two, may explain its morphological and age patterns, but remains speculative. It is hoped that increasing awareness of this condition will lead to better understanding of breast pathophysiology. Nevertheless, until its biological nature, histogenesis and malignant potential are more clearly understood, defining FAM as a distinct form of breast disease may not be meaningful to patient management.

Keywords: Fibroadenomatosis, fibroadenomatoid mastopathy, fibrocystic change, fibroadenoma, breast, tumour.

INTRODUCTION

Benign breast disease encompasses a wide range of disorders, a large proportion of which are fibroadenoma and fibrocystic change. The latter is also known by a variety of designations such as fibroadenosis, benign mammary dysplasia, fibrocystic condition and cystic mastopathy. Anatomical pathologists are well acquainted with fibroadenoma and fibrocystic change, which are generally regarded as separate entities! Fibroadenoma (FA), a benign neoplasm, is typically a well-circumscribed firm lesion that occurs in young women between 15 - 35 years of age, with a peak incidence in the third decade of life. In contrast, fibrocystic change (FC) is a less well-circumscribed, often cystic, lesion that occurs more often in women older than 30 years, with a peak incidence at 40 - 45 years.² However, lesions with the composite histological features of fibroadenoma and fibrocystic change have recently been recognised, and have been referred to as fibroadenomatoid hyperplasia,¹ fibroadenomatosis,³ fibroadenomatoid mastopathy⁴ or simply as mixed lesions.² There is scanty documented information about its prevalence or clinicopathological significance, particularly among Asian subjects. We undertook this study to assess its prevalence and position among the commoner benign breast lesions in a Malaysian population.

MATERIALS AND METHODS

100 consecutive cases coded as fibroadenoma and another 100 as fibrocystic disease from East Malaysian subjects were retrieved from the files of the Department of Pathology, University of Malaya. The same retrieval system was carried out for West Malaysian subjects. These excisional biopsies were received within a three year period. All histological sections were reexamined. In addition, recuts were made from the relevant paraffin blocks when necessary. Lesions were reclassified according to the following histological criteria. Fibroadenomata were circumscribed lesions exhibiting ductular proliferation within a proliferative fibroblastic or myxomatous stroma, typically forming intracanalicular or pericanalicular patterns. Fibrocystic change was diagnosed when the lesion exhibited a combination of fibrosis, cyst formation, adenosis and epithelial hyperplasia. Lesions were categorised as fibroadenomatoid mastopathy (FAM) when hyperplasia of stroma and small ducts gave rise to 'microfibroadenomata,' whether single or multiple, within a background of diffuse fibrocystic change. Relevant clinical and demographic data were obtained from histopathology request forms that accompanied the excision specimens. The student's 't-test', Chi-square and Fisher's exact

tests were used to analyse significance between variables.

RESULTS

Prevalence and demographic profile

FAM was identified in 45 (11.3%) of the 400 cases studied (Table 1). It was more commonly encountered in lesions originally coded as FC (37 cases) compared to FA (8 cases). The three conditions occurred in patients over a wide age range, being 17-52 years for FAM, 12-51 years for FA and 14-73 years for FC (Table 2). The mean age at presentation of FAM was 32.1 years which was statistically not different from that (35.1 years) for FC. It was, however, significantly different ($p < 0.001$) when compared to that of FA which had a younger mean age of 26.1 years at presentation.

There was no difference in prevalence of FAM among East and West Malaysian cases (Table 3). It is noteworthy that more FAM cases were encountered among the Chinese and Ibans compared with the Malays, Indians and Kadazans (Table 4).

Presentation

The majority (26/45) of FAM presented with signs and symptoms which led to a clinical diagnosis of fibrocystic change. In 11 of the 45 cases of FAM, the lesions were multiple of which 4 were bilateral.

Pathology

Grossly, the diameter of FAM lesions averaged 2.1 cm (range = 1.0 cm to 4.0 cm). The average diameter of FA lesions was 3.0 cm (range = 0.8 cm to 12 cm) while that of FC lesions was 2.0 cm (range = 0.5 cm to 9.0 cm). FAM lesions originally coded as FA generally appeared solid but lacked the typical bulging or lobulated appearance of the latter. In general, FAM lesions were difficult to differentiate from FC by naked eye examination.

Histologically, FAM lesions closely resembled FC, showing a combination of stromal fibrosis, cyst formation, adenosis, apocrine metaplasia and epithelial hyperplasia of varying severity. On this background, fibroadenomatoid foci characterised by an overgrowth of stroma associated with collapsed or compressed ducts are intermingled with areas of FC, often without clear lines of demarcation (Fig. 1).

DISCUSSION

Although our investigation involved only Asian subjects, the finding of FAM in 11.3% of the cases studied is comparable to a similar study among Western patients. In our study, there was no significant difference in the mean ages at presentation of FAM and FC patients. The mean age of FA patients, by contrast, was younger. Arguments can be put forward to

TABLE 1
FIBROADENOMATOID MASTOPATHY:
FREQUENCY IN FIBROADENOMA & FIBROCYSTIC CHANGE

	Fibroadenoma	Fibrocystic change	Total
No reviewed	200	200	400
No. positive	8	37	45
% positive	4.0	18.5	11.3

TABLE 2
FIBROADENOMATOID MASTOPATHY : COMPARISON OF AGE DISTRIBUTION

	Fibroadenomatoid mastopathy	Fibroadenoma	Fibrocystic change
No. of cases	45	192	163
Age range (yr)	17-52	12-51	14-73
Median age	31	23	36
Mean age	32.1	26.1*	35.1

* $p = < 0.001$ (student t-test)

TABLE 3

**FIBROADENOMATOID MASTOPATHY:
FREQUENCY IN EAST & WEST
MALAYSIAN SUBJECTS**

	E. Malaysian	W. Malaysian
No. reviewed	200	200
No. positive	22	23
% positive	11.0	11.5

explain these lesions on the grounds of hormonal interplay at different ages. In recent years, the position of FA as a true neoplasm has been questioned, and there are advocations of it being the result of localised hyperplasia of breast lobules, inclusive of ducts and stroma.⁵ Some studies have implicated endogenous hormones, particularly estrogen, in its aetiology. The presence of estrogen receptors within FA⁶ lends further support to this hypothesis. Its more frequent occurrence among younger women is thought to be related to the higher incidence of anovulatory cycles, and hence unopposed

TABLE 4
FIBROADENOMATOID MASTOPATHY: RACIAL DISTRIBUTION

Race	No. reviewed	No. positive	% positive
Chinese	201	30	14.9*
Malay	88	4	4.5
Indian	37	3	8.1
Kadazan	21	2	9.5
Iban	34	6	17.6**

* p = < 0.05 (Chi square test)

** p = < 0.05 (Fisher's exact test)

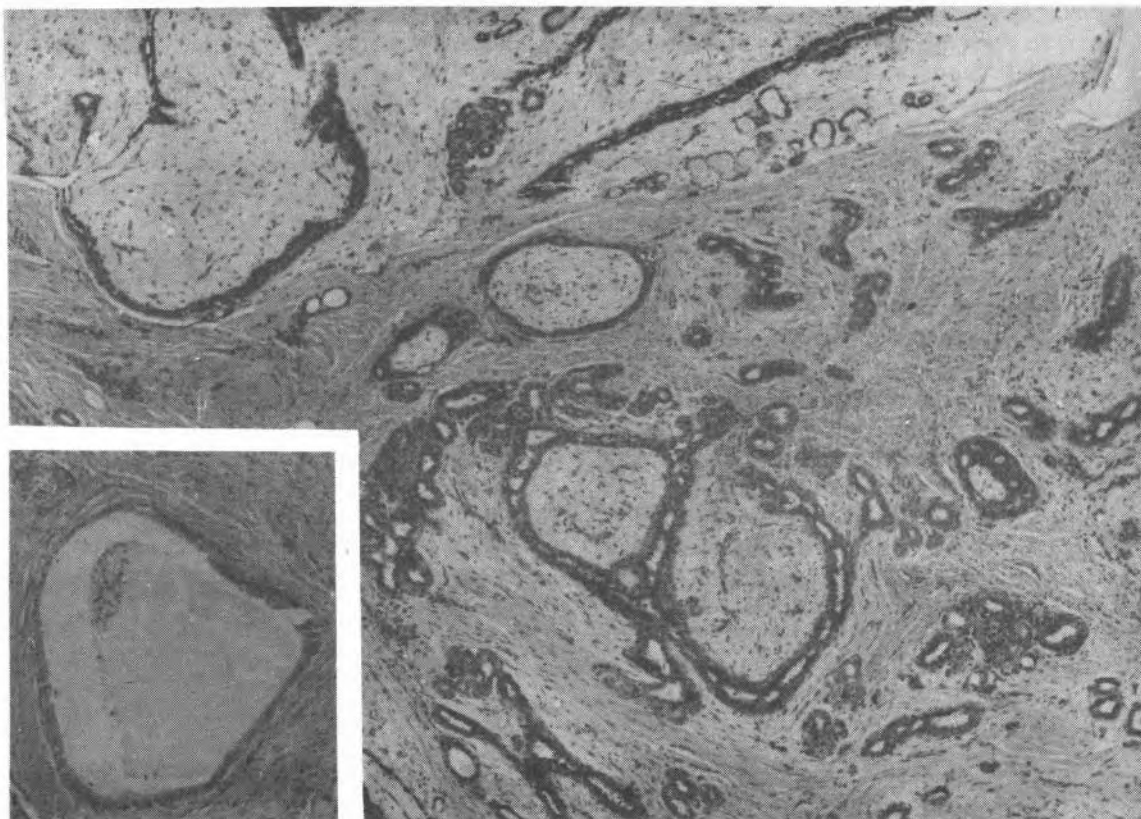


FIG. 1. Small fibroadenomatoid foci occurring in a background of fibrosis, adenosis and small cyst formation. Inset shows apocrine metaplasia of the lining of a cyst elsewhere in the lesion. H&E X 300.

oestrogen activity, in early reproductive life.⁶ In contrast, FC is considered as essentially a disordered growth of breast epithelium and stroma that occurs more commonly in perimenopausal women in whom dysovulation is common, being at the end of the reproductive life span. A variety of endocrine alterations have been postulated but imbalance between oestrogen and progesterone activity is believed to be a major concern in its pathophysiology.⁷ That the pathophysiology of FAM can be considered more similar to FC by mere similarity in age at presentation is an attractive consideration that should nevertheless be viewed with caution. One may argue that the age range of FAM patients, for instance, is more similar to FA than FC. The question then raised is whether FAM encompasses a position intermediate between FC and FA, and reflects episodes of oestrogen stimulation (fibroadenomatoid lesions) in a background of oestrogen-progesterone imbalance (fibrocystic change). This notion, admittedly, is mainly speculative.

That a larger proportion of cases initially coded as FC rather than FA were reclassified as FAM is not surprising in view of the closer resemblance between the histopathological features of FAM and FC. It is understandable that pathologists would attach more importance to the fibrocystic changes in FAM than to the 'microfibroadenomata' because epithelial changes tend to be of greater concern in the assessment of a possible cancer risk.

The significance of the more frequent finding of FAM among the Chinese and Ibans compared with other ethnic groups in this study is unclear. The marked discrepancy in actual numbers between the ethnic groups precludes any statistical conclusions.

Whether FAM deserves to be considered an entity distinct from FC and FA remains a moot point. As early as 1928, Semb recognised the existence of 'fibroadenomatosis' and used the term for a process that might have preceded a circumscribed fibroadenoma.¹ Curtis et al⁴ suggested that fibroadenomatoid mastopathy might be an early stage in the morphogenesis of fibroadenoma with which it shared similarities in age incidence and histology. There are others who do not share that sentiment.² It would appear that until more is known about its biological behaviour,

particularly its malignant potential, recognising FAM as a distinct entity may not be meaningful to patient management. Current thinking leans towards categorising benign breast lesions into three prognostically relevant groups: (1) non-proliferative, (2) proliferative without atypia and (3) atypical hyperplasia, with group 3 showing the highest risk of malignancy and group 2 an intermediate risk.⁸ According to this concept, FAM should be categorised according to its epithelial characteristics. We are inclined to agree with this approach because of its more practical applicability. It would appear that the case for recognising FAM as a distinct entity can only be made when its biological nature and histogenesis is more clearly defined. Nevertheless, it is hoped that increasing awareness of this condition will lead to better understanding of breast pathophysiology.

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