

# Histopathological Study on Mammary Dysplasia

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## INTRODUCTION

In 1829, Cooper described the condition, such as proliferative and cystic changes in the breast. But early nomenclature included such terms as "abnormal involution of the breast" (Warren, 1837), "cystic disease of the breast" (Reclus, 1883), "chronic cystic mastitis" (König, 1893), "chronic cystic mastopathia" (Aschoff, 1939).

Though the term "mammary dysplasia" has the advantage of being noncommittal, the term "fibrocystic disease" is currently in vogue. Taylor (1936) suggested adenofibrosis which is similar to the term "fibroadenomatosis cystica mammae" adopted by Semb. In the past, the surgeon consulting the literature is confronted with a multitude of conflicting opinions on the nature of this and with contradictory advice as to the nature of proper treatment. Since the publication of lectures by Sir Astley Cooper(1829) and Brodie (1846), and the classic observation made by Reclus(1883), numerous reports have appeared in the literature on the relationship of fibrocystic disease to carcinoma of breast. Convincing proof that this disease is pathologically related to carcinoma has not been established(Frants, 1951; McDivitt, 1968; Reed, 1948; Haagensen, 1971). This study was undertaken in order to further analyze morphologically the subtypes of mammary dysplasia, some of which may be precancerous lesions, and in order to evaluate the frequency of each type among Koreans.

## MATERIAL AND METHOD

A review of 180 biopsies, diagnosed as mammary dysplasia and fibroadenoma in the Department of Pathology, College of Medicine, Seoul National University Hospital in a period of 5 years(from 1974 to 1978), disclosed a total of 102 cases satisfied the criteria for mammary dysplasia(Haagensen, 1971; Robbins, 1979). The specimens were fixed in 10% buffered formalin, embedded in paraffin and cut at 5  $\mu$ m for viewing by optical microscopy. Sections were stained by hematoxylin-eosin and, if necessary, Masson-trichrome stains.

## RESULTS

### 1. Clinical summary

All patients were female, their ages ranging from 16 to 60 years (Table 1). In group of fibrosis, the average age was  $35.7 \pm 7.7$ (SD) years, in group of adenosis, it was  $29.7 \pm 7.1$  (SD) years, in group of cystic disease  $41.1 \pm 16.4$ (SD) years, and in group of epithelial hyperplasia  $33.6 \pm 12.7$ (SD) years.

### 2. Pathological findings

The pathological classification of mammary dysplasia is mostly adopted from that of Robbins(1979), because it is relatively simple covering all the pathologic features. In the cases of mixed form, we classified them according to the predominant component. Their incidence distribution is summarized in Table 2.

1) Fibrosis (64 cases): This is characterized principally by stromal fibrous tissue overgrow-

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**Table 1.** Distribution of mammary dysplasia by age group

Histopathological classification	Fibrosis	Adenosis	Cystic disease	Epithelial hyperplasia
Age(years)				
16~25	5	8	2	3
26~35	25	11		2
36~45	26	3	2	1
46~55	8	1	2	2
56~65			1	
Average age ±S.D.	35.7 ±7.7	29.7 ±7.1	41.1 ±16.4	33.6 ±12.7

**Table 2.** Histopathological classification of mammary dysplasia

Histopathological classification	No. of dysplasia
Fibrosis	64
Adenosis	23
Cystic disease	7
Epithelial hyperplasia	8
Total	102

th unaccompanied by prominent epithelial hyperplasia. Microscopically, the typical fibrous form shows broad hyaline connective tissue replacing the entire interductal breast substance. In some areas, the overgrowth of collagenous stromas engulfs the epithelial structures revealing flattened or atrophic ones.

- 2) Adenosis(23 cases): There is diffuse fibrosis, with permeation of the lobules by prominent bundles of fibrous tissue. Many ducts are moderately dilated and are either empty or containing varying amount of clear fluid. The ductal epithelium is definitely hyperplastic, and extends into the lumen as fine small papillary projection. In areas, this variety gives an impression of invasiveness. This is the lesion of the breast more frequently confused with carcinoma.
- 3) Cystic disease(7 cases): This is characterized by formation of cysts, sometimes accompanied

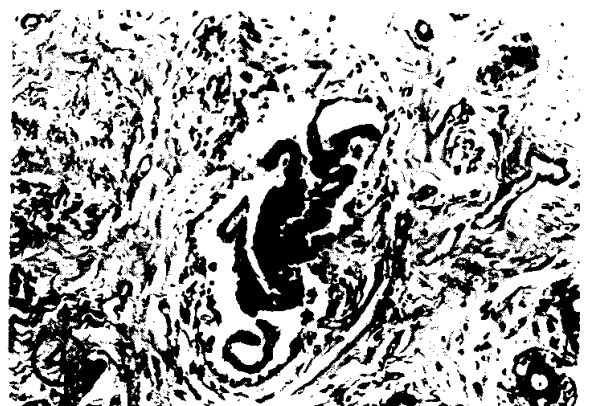
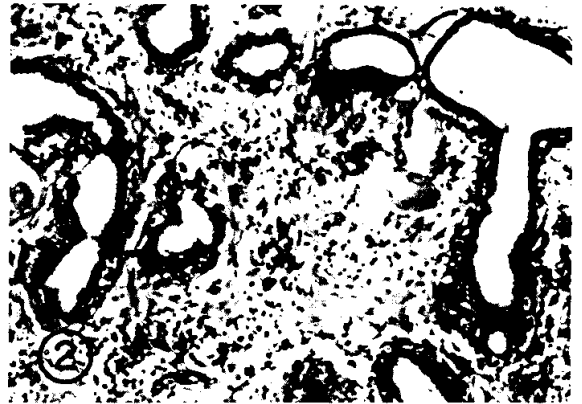
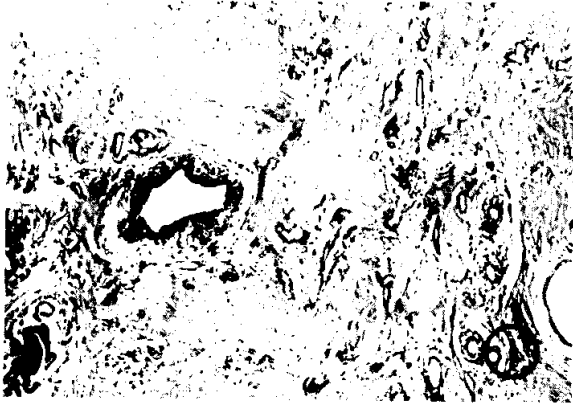
by stromal and epithelial hyperplasia. But histological hallmark is the cystic dilation of ducts. The epithelium lining the larger cyst is often flattened and atrophic. In smaller cysts, the epithelium is more cuboidal to columnar and is multilayered in focal areas. Also the cysts are sometimes filled with basophilic material. Apocrine metaplasia is observed. We could see stromal lymphocytic infiltration, especially around the cyst.

- 4) Epithelial hyperplasia(8 cases): This form of epithelial hyperplasia has a papillary pattern. There is irregular projection of the epithelium into the duct lumen, which coalesce to form a lace-like pattern partially filling the duct.

### COMMENT

Fibrocystic disease of the mammary glands is the commonest of all breast lesions and primarily affects females but may occur in males (Hodge, 1959). It is characterized clinically by pain or a lump in the breast and pathologically as a fibroglandular hyperplasia, localized or generalized, cystic or noncystic. However, it has great clinical importance for two reasons (Robbins, 1979); first, they produce masses in the breast that require differentiation from carcinoma, second, they may predispose to the subsequent development of carcinoma. So definite distinction is made by only certain way of biopsy and pathologic examination.

There are many reports in the literature concerning the important relationship of fibrocystic disease of the breast to carcinoma. A number of authorities (Foote, 1945) believed that fibrocystic disease was a precursor to cancer. Especially, Warren(1940) stressed the incidence of breast carcinoma in patient who had been operated upon for fibrocystic disease to be higher than in women with no previous history of



#### LEGENDS FOR FIGURES

- Fig. 1.** Fibrosis: Stromal fibrous tissue overgrowth. Ducts and glands are compressed and atrophic. H&E  $\times 40$ .
- Fig. 2.** Adenosis: Ductal epithelial overgrowth in glandular pattern. Lining cells are slightly distorted but not atypical. H&E  $\times 100$ .
- Fig. 3.** Cystic disease: Marked cystic dilatation with basophilic material in lumen. H&E  $\times 100$ .
- Fig. 4.** Epithelial hyperplasia: Duct exhibits hyperplastic epithelium in papillary pattern with multi-layering of lining epithelium. H&E  $\times 200$ .

chronic mastitis. Benign proliferative breast lesions have an increased incidence of breast cancer. This risk of developing breast cancer is reported to be from 1.7 to 4.5 times that of the general female population(Kern, 1969).

Of interest is the fact that women with cystic disease of the breast are somewhat more likely to develop carcinoma of the breast than women in general. Cystic disease of breast may be considered to be of two types; the cystic type, with one or more fairly large cyst of the blue-domed variety, lined by thin epithelium; and the adenocystic type, with many small cysts, lined by hyperplastic epithelium which gives the impression of marked activity. In our case, all cases are cystic types. Although it is difficult to decide which of the many histologic features of cystic disease are the most important in determining the precancerous potential, some authors stressed this cystic disease to be frequently coexist with carcinoma. A study of follow-up in 284 women with cystic disease who had local excision only revealed the patients with epithelial hyperplasia had relatively more recurrences and a higher incidence of subsequent carcinoma than those without hyperplasia(Davis, 1940).

Proliferative cystic disease complex is common in both noncancerous and cancerous breast. McDivitt(1973), and Frantz(1951) and associates having opportunity to examine the breast at autopsy, reported cystic disease in 53% of "normal breast". These cases, however, were weighed with older age groups, so do not represent a true sample of general population (Robbins, 1979).

In 1956, Haagensen reported a total of 205 ward patients with clinically evident cystic disease. Follow-up was possible in 163; of these patients, 4.9%, subsequently developed carcinoma. The shortest interval between the original diagnosis of cystic disease and the diagnosis of carcinoma was  $7\frac{1}{2}$  years; the longest interval

was 16 years. Also he concluded incidence of carcinoma developing in the women operated upon for the cystic disease of the breast was 4 times the expected incidence.

Klose et al. believed chronic cystic mastitis as a precancerous lesion, so they recommended mastectomy for treatment. But Warren et al. opposed this and mastectomy is not justified as a prophylactic measure. Bloodgood (1931) strongly stressed that microscopically various stages of chronic mastitis, encapsulated and non-encapsulated cystic adenoma, old fibroadenoma, rapidly growing intracanalicular myxoma, all forms of tubercles and pyogenic mastitis must be looked upon as borderline breast lesions, because many well-trained pathologists, when confronted with the microscopic picture either in frozen sections or later in permanent sections, are inclined to the diagnosis of malignancy and advise at least the removal of breast (Bloodgood, 1931). But a large number of authors oppose the view that fibrocystic disease is precancerous. Benign intraductal papillomatosis is so infrequently followed by carcinoma, a significant connection between duct papillomatosis and papillary carcinoma has not been demonstrated in large series of cases (McDivitt, 1968). Lewis et al. (1938) studied two groups totaling 1,048 cases of chronic cystic mastitis. There were 523 cases that were followed for five years or more, and 4 of them, less than 1% developed carcinoma. Reed(1948) studied twenty-six patients with chronic cystic mastitis of various types treated according to their principles and followed for from ten to seventeen years after operation. But carcinoma of the breast did not develop in a single instance. Carcinoma very rarely develops in the epithelium of a blue-domed cyst. Endocrine imbalance is probably the cause. A theory is presented in which overactivity of the anterior pituitary associated with deficient inhibition by the ovaries, is considered responsible for cystic

disease of the breast (Davis, 1941). It is interesting to note that apocrine metaplasia, sclerosing adenosis, and inflammatory changes were more common in benign, than in cancer-containing breast, whereas duct papillomatosis is slightly more prevalent in the cancer-containing specimen (Foote, 1945).

We could not find breast ducts within a nerve in all submitted specimen, which is sometimes detected from a patient without other evidence of carcinoma (Taylor, 1967), and no convincing relationship can be bound between epithelial hyperplasia and development of carcinoma possibly due to sparsity of cases.

### CONCLUSION

A light microscopic study of breast tissue specimen from 102 cases of mammary dysplasia collected during a period of 1974 to 1978 at Seoul National University Hospital was carried out. These cases were classified into four subgroups of mammary dysplasia; fibrosis (64 cases), adenosis(23 cases), cystic disease(7 cases) and epithelial hyperplasia(8 cases).

The mean age of the respective subgroups were as followings; fibrosis  $35 \pm 7.7$  (SD) years, adenosis,  $29.7 \pm 7.1$  years, cystic disease  $41.1 \pm 16.4$  years, and epithelial hyperplasia,  $33.6 \pm 12.7$  years. The much higher incidence of fibrosis in our study reflects we gave the emphasis to the most prominent component for the pathologic classification. Though we had tremendous attention to the epithelial hyperplasia concerning the development of carcinoma, no suggestions were made here due to sparsity of cases and follow-up long term studies are recommended to evaluate their relationship.

### 국 문 초 록

#### 乳房異形成症에 關한 病理組織學的 檢索

서울大學校 醫科大學 病理學교실

李 尙 國 · 李 賢 淳 · 朴 泰 東

1974년 1월부터 1978년 12월까지 서울대학교 의과대학 병리학교실에서 유방이형성증으로 진단된 102 예의 병리조직학적 검색분류에서 다음의 결과를 얻었다.

1. 유방이형성증의 4가지 아형의 분포는 섬유화형(64례), 선증형(23례), 낭포형(7례), 상피성증식형(8례)이었다.

2. 이들의 평균 연령별 분포는 섬유화형( $35.7 \pm 7.7$  (SD)세), 선증형( $29.7 \pm 7.1$ 세), 낭포형( $41.1 \pm 16.4$ 세), 상피성증식형( $33.6 \pm 12.7$ 세)이었다.

반생빈도에서 섬유화형이 가장 높은 빈도를 보이는 것은 병리학적 분류상 가장 두드러진 성분을 강조한 때문으로 해석되며 상피성증식형과 유암과의 관계는 뚜렷이 입증할 수 없었다.

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