FIBROADENOMA OF THE FEMALE BREAST: A CRITICAL CLINICAL ASSESSMENT

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In a study of 70 patients with 75 histologically proven fibroadenomas of the breast, a biphasic peak incidence was recorded, initially in their late 20s to early 30s with a second unexpected peak in their late 40s to early 50s. These lesions averaged 2.8 cm in diameter, two thirds were located in the lateral quadrants of the breast, and 10 percent were multiple. There was a significantly higher incidence among nonwhite than white women when compared to census figures and hospital admission data. The corrected recurrence rate was 17 percent. An inordinately high number of patients under 40 years of age in this series were nonwhite. Family history demonstrates a significantly high incidence of breast disease of all types in first-degree relatives.

Fibroadenoma is the most frequent breast tumor in women under 25 years of age. These tumors are multiple (15 to 20 percent) in the same or both breasts, sharply demarcated and in time may calcify and become extremely hard.[1-12] Characteristically, this tumor increases in size during pregnancy and undergoes resolution following delivery. The intracanalicular and pericanalicular varieties of this tumor seldom undergo malignant degeneration to sarcoma. This tumor is twice as common in black as in white women and 12 percent are bilateral.[11] These tumors are radioresistant and do not respond to hormone therapy. Of 5,604 consecutive breast biopsies in one series covering all age groups, 18 percent were fibroadenomas.[13] A critical assessment of the clinical and epidemiologic aspects of fibroadenomas was undertaken at the authors' institution with particular reference to age, site, size, multiplicity, bilaterality, parity, trauma, family history, recurrence, oral contraceptives, and racial distribution. A histologic distinction between intracanalicular and pericanalicular fibroadenoma was not made since both types are often present within a single specimen.

CLINICAL DATA BASE

In this retrospective study 70 patients with histologically proven fibroadenoma of the breast occurring between 1970 and 1977 were observed for a minimum of three years following surgical excision. Three patients were found at initial examination to have two tumors each and one patient had three tumors. In all four patients, both breasts were involved. In the 70 patients, 75 fibroadenomas were clinically detectable at the initial examination.

Age

The age distribution curve in this series initially peaked in the late 20s to the early 30s with a sec-

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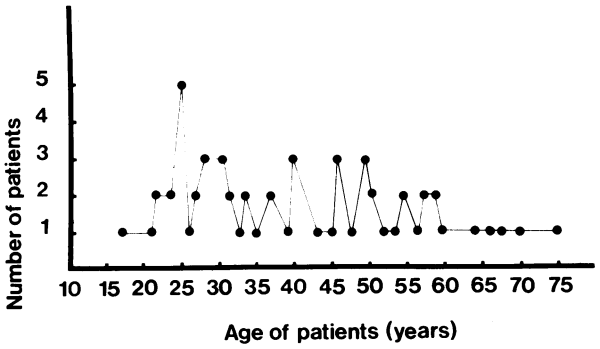

Figure 1. Age distribution curve (entire series)

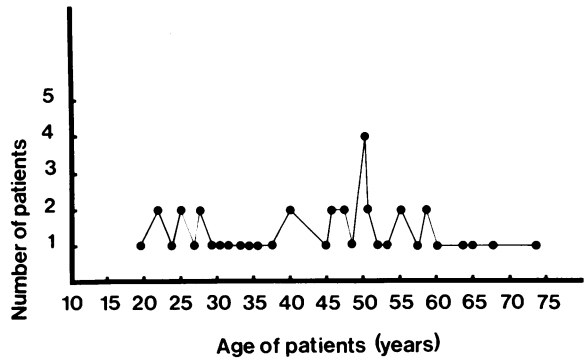

Figure 2. Age distribution curve (white patients)

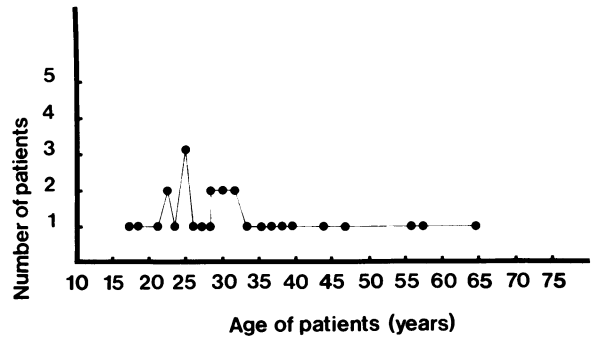

Figure 3. Age distribution curve (nonwhite patients)

ond peak between the late 40s and early 50s (Figure 1). Based on this biphasic curve, these patients were divided into two groups, Group A consisting of patients less than 40 years of age (n = 42) and Group B of patients over 40 years of age (n = 28).

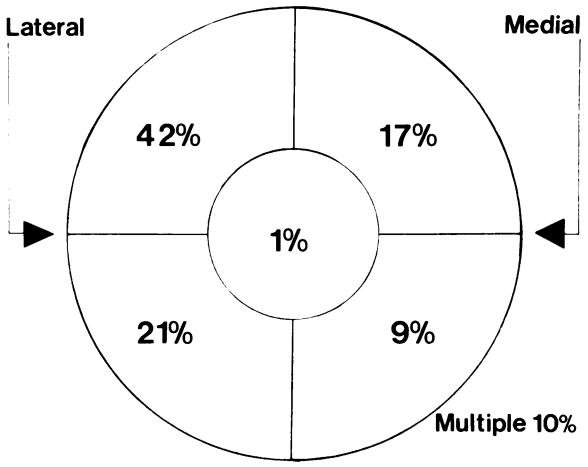

Figure 4. Location of fibroadenomas

The second peak in Group B consisted mainly of white patients (Figures 2 and 3).

Site and Size

Sixty-three percent of the fibroadenomas were located in the lateral quadrants of the breast, 26 percent in the medial quadrants, and 1 percent subareolar (Figure 4). In 10 percent, multiple adenomas were present in one or both breasts at the initial examination. The average size of the fibroadenomas was 2.8 cm, varying from 2.2 to 12.8 cm. Only 18 patients had had mammography, all in Group B and all after 1974. Calcification was present in eight (33 percent) of these patients. This distribution bears some resemblance to that of malignant neoplasms of the breast.

Parity

Previous investigators have noted a statistically significant relationship between parity and fibroadenoma.[3] Seventy-four percent of patients in Group A had one or more children (average 1.5) as compared with 93 percent of the older patients in Group B (average 3.4 children). Of the 70 patients only 13 (18 percent) were nulliparous. Three patients had fibroadenomas diagnosed during pregnancy.

One grew to an enormous size (12 × 16 cm) and had regressed miraculously three months postpartum.

Nipple Discharge

In response to close questioning a history of nipple discharge was elicited from only 11 percent of this population, none of whom were in Group B. No common characteristics of the discharge were noted.

Family History

Data relating to the incidence of breast disease in mothers and sisters (first-degree relatives) were significant. Evidence of breast disease of any type was pursued, the medical records were reviewed, and histologic confirmation was obtained. This was the most difficult aspect of such a retrospective study. A history of breast disease in first-degree relatives was confirmed in 57 percent of the cases consisting of fibrocystic disease, fibroadenoma, and cancer. Carcinoma of the breast accounted for 24 percent of the confirmed breast disease. This is alarmingly higher than in a random sample of women of corresponding ages. Twenty-seven percent of those with a family history of breast disease had a confirmed fibroadenoma, the vast majority of whom were in Group A.

Recurrence

The recurrent rate of fibroadenoma including multiple recurrences in the same breast was 34 percent. The disease-free interval ranged from four to 15 years with an average of 3.3 and 4.0 years for Groups A and B, respectively. One 23-year-old black woman had three recurrences within a 16-month period in the same breast but in distinctly different areas. It is difficult, if not impossible, in such a retrospective study to determine whether the recurrence was another primary tumor or a "true recurrence" of the same tumor, particularly if the same breast is involved. The differentiation between bilaterality and recurrence may be difficult. It is logical to assume that the disease process is multifocal in both breasts with clinical expressions at different times. Such a concept would more readily explain the higher recurrence in Group B. In both groups, a higher recurrence rate existed among nonwhite than white patients.

Hormones and Oral Contraceptives

Contraceptives in which estrogen was the main component were taken by 42 patients (60 percent of the total series). Only five (7 percent) had taken oral contraceptives whose main component was progesterone. Forty-three of 47 patients (91 percent) using oral contraceptives were in Group A. Seventeen patients (24 percent), all in Group B, were using estrogen as replacement therapy.

Racial Distribution

The percentage of nonwhite patients in the series (41 percent) was significantly higher than in the general population for this metropolitan area (15 percent) and disproportionate to the number of admissions to this major metropolitan hospital (7 percent). A majority of the nonwhite patients, mostly black, were in Group A (83 percent). (Native Americans were the second largest nonwhite group.) Groups A and B differed strikingly in the proportion of nonwhite patients (83 and 17 percent respectively) whereas the distribution of white patients was more equal in both sets (59 and 55 percent) (Figure 5).

DISCUSSION

The biphasic peak distribution of fibroadenomas in this group of patients is difficult to explain based upon current knowledge. The authors were unable to identify specific hormonal, genetic, or epidemiologic factors to account for the increased incidence [second peak] in Group B. This late biphasic peak should be considered in the

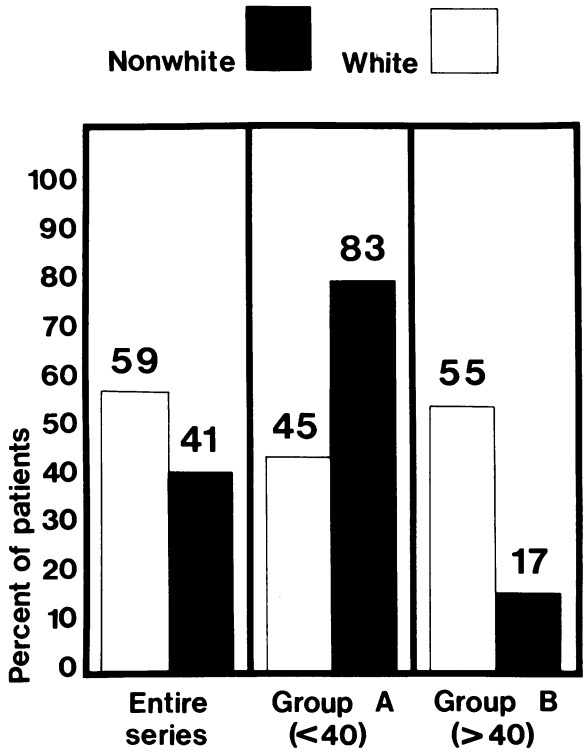

Figure 5. Racial distribution

differential diagnosis of breast tumors in this age group. The surprisingly high incidence of breast disease in first-degree relatives is striking and will be the subject of continuing review and investigation. This could represent a phenotypic expression that will be clarified with future detailed genetic investigation.

The possible relationship between exogenous estrogen usage and breast disease received a flurry of attention following a 1970 DDA report alluding to their etiologic role. This is not a new concept. In 1896 Beatson[6] advocated and utilized surgical ablation of the ovaries in several cases of advanced breast cancer. Allen and his co-workers[5] in 1923 suggested that estrogens were able to stimulate the female genital tract. Wiegenstein[7] in 1971 noted a positive correlation between hormonal contraceptives and fibroadenoma. However, Oberman[8] questioned the validity of this correlation with further substantiation by Taylor,[9] who offered electron and microscopic evidence to support Oberman's concern. In 1973, Hilf and associates[10] concluded that on the basis of measurements of inducible enzymes specifically associated with cancer, female hormones did not induce these substances or cause a principal change in fibroadenoma of the breast.

The recurrence rate of 34 percent in this series includes lesions appearing in the same or contralateral breast. When these data are corrected to include what were subjectively determined to be "strict recurrences," the rate is still 17 percent, a figure higher than the random incidence of fibroadenoma of the female breast. The size, intramammary distribution, and parity are consistent with previous reports.[1,3,4] What is intriguing is the alarmingly high incidence among nonwhite females. In-depth hormonal, genetic, and epidemiologic study is certainly warranted. No sweeping conclusions are recommended from the present study since the data base is small. However, a larger multi-institutional review with closer attention to familial and hereditary patterns should be undertaken.

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