Cystosarcoma Phyllodes in Adolescent Females

A Report of Seven Patients

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Cystosarcoma phyllodes, a relatively uncommon breast lesion, was first described and named by Müller in 1838. These tumors generally occur around the fourth and fifth decades of life, but they have been encountered in prepubertal females and in women in their late seventies.

Several large series of cystosarcoma phyllodes have been reported.[4, 5, 7, 11, 12] These reports, some from the same institution,[7, 11, 12] reflect differences in opinions relating to classification of benign and malignant lesions and also the therapeutic approach to be followed. Because of the rarity of this tumor and the experience encountered with seven adolescent females in the past 8 years, the following report is made.

Material

Seven patients between the ages of 10 and 17 years with cystosarcoma phyllodes were admitted to Grady Memorial Hospital between 1961 and 1969. The criteria for the diagnosis of cystosarcoma phyllodes were the presence of epithelial hyperplasia and a greater degree of stromal hyperplasia than is usually seen in fibroadenomas. Large tumors that showed only the microscopic features of fibroadenoma, generally termed giant fibroadenoma, were excluded. Histologic slides in this review were restudied with the pathologist of the hospital.

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Case Reports

Case 1. A. J. (C64722), a 10-year-old Negro girl was admitted March 7, 1968. Breast development began at the age of 8 years. One day before admission she experienced pain in the left breast, a mass having been present in this breast for approximately one month. An 11 × 8 cm. multilobulated mass was excised through an inframammary incision. Histologically marked stromal cellularity and epithelial hyperplasia were seen. The pathologic diagnosis was benign cystosarcoma phyllodes.

Follow-up examination one year later revealed symmetrical breast development with no evidence of recurrent breast masses.

Case 2. M. A. L. (C67467), a 12-year-old Negro girl was admitted in January, 1966, with a mass in the right breast of 3 months' duration. A 10 × 5 cm. multinodular mass weighing 99 grams was excised. Necrotic cystic areas were found on sectioning the tumor. Histologically there was typical leaf-like arrangement with hypercellularity of the stroma. Pathologic diagnosis was benign cystosarcoma phyllodes.

A 3-year follow-up showed normal breast development with no evidence of recurrence.

Case 3. C. S. (C75819), a 13-year-old Negro girl was admitted in May, 1966, with bilateral mammary masses of 1 month duration. An 8 × 6 cm. lesion was excised from the right breast and a 2 × 2 cm. mass was removed from the left breast. The large lesion showed typical cellular changes of benign cystosarcoma phyllodes and the smaller lesion proved to be a fibroadenoma.

Follow-up examination 3 years later revealed no recurrent breast lesions.

Case 4. J. C. (C120137), a 13-year-old Negro girl was admitted October 14, 1961, with a 4 × 2 cm. mass in the right breast of 1-month duration. This lesion was excised and histologically showed increased stromal cellularity and epithelial hyperplasia. It was interpreted as a benign cystosarcoma phyllodes. At a 7-year follow-up, breast develop-

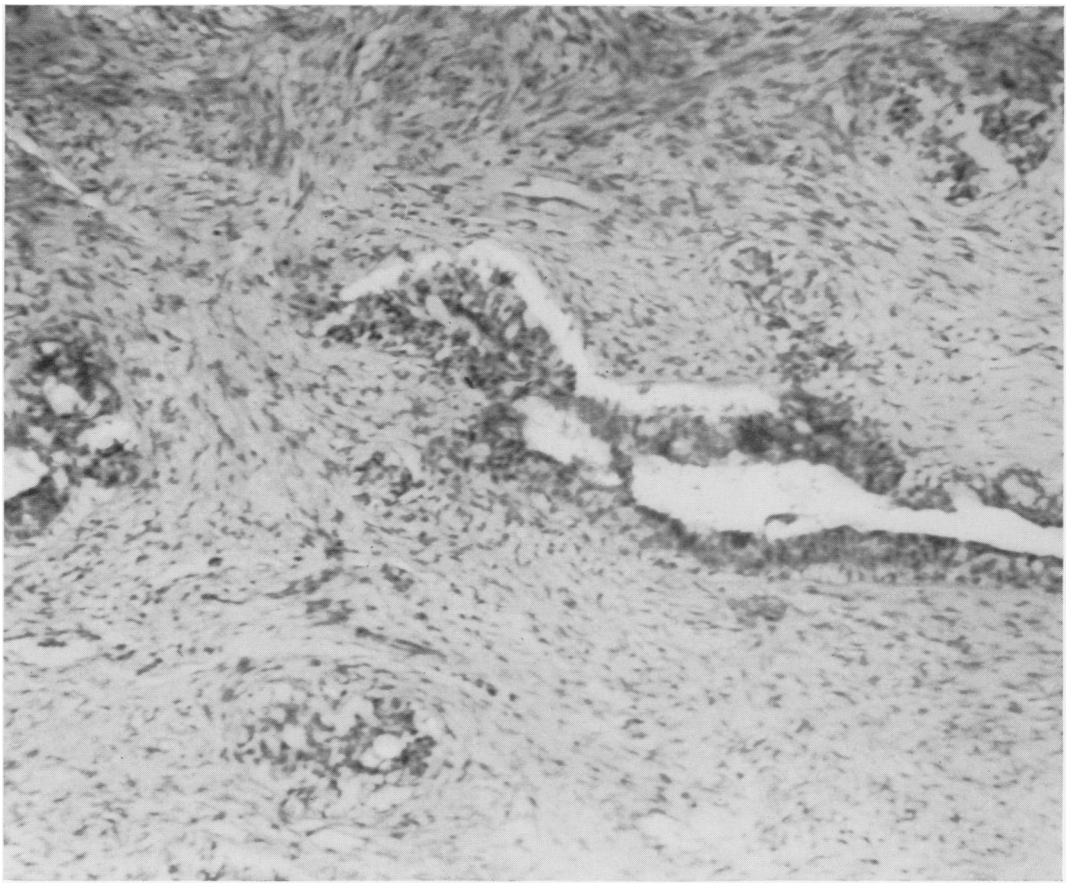

FIG. 1. Case 1: Photomicrograph of tumor showing increased stromal cellularity and epithelial hyperplasia (Hematoxylin-eosin, ×75).

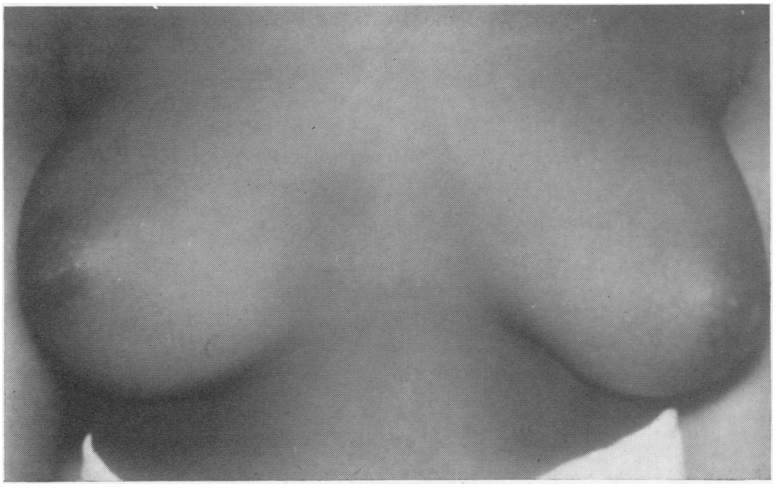

FIG. 2. Case 1: Frontal view of patient 1 year after removal of 11 × 8 cm. tumor from left breast.

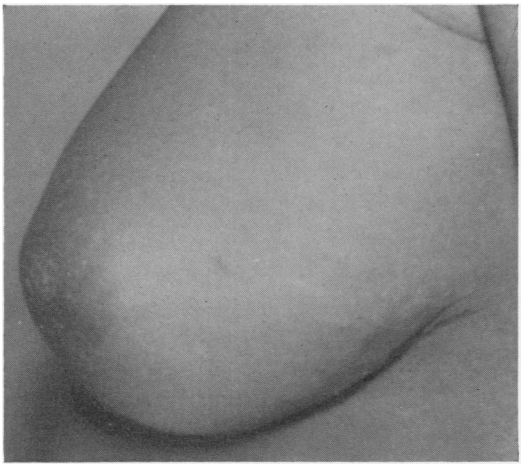

FIG. 3. Case 1: Left lateral view 1 year after removal of breast tumor. Note submammary incision scar.

ment was normal. In 1967, the patient delivered and nursed a normal infant.

Case 5. S. J. H. (C160165), a 14-year-old Negro girl was admitted in October, 1963, with a 14 × 13 cm. mass in the left breast of 1 year duration. There was no evidence of skin involvement although the overlying skin was taut and desquamating. In the subareolar area a small discoid area of breast tissue was palpated. Mammography showed a homogenous mass with a smooth outline. Excision of this lesion was performed leaving the subareolar breast tissue intact. Suction drainage was employed beneath the redundant breast skin.

Histologically there was an active stroma with rare mitotic figures. This lesion was interpreted as a benign cystosarcoma phyllodes. A 6-year follow-up showed no evidence of recurrence. The right breast was pendulous in comparison with the left breast. The patient delivered a normal infant in January, 1969, and lactated from both breasts.

Case 6. S. M. (C77932), a 16-year-old Negro girl was admitted May 2, 1968, with a history of enlargement of the left breast for 1 year. A multilobulated 14 × 13 cm. mass was excised. Marked stromal cellularity and epithelial hyperplasia were demonstrated histologically. Pathologic diagnosis was benign cystosarcoma phyllodes. Examination 1 year later revealed no recurrent breast lesions.

Case 7. G. D. (C105754), a 17-year-old Negro girl was admitted August 5, 1968, with bilateral mammary masses of 1 year duration. The right breast lesion measuring 7 × 6 cm. was excised. This lesion contained a 2 cm. cystic area and histologically showed characteristic findings of cystosarcoma phyllodes. The left breast lesion was excised and proved to be a fibroadenoma on histologic study.

Examination 6 months later revealed no breast abnormalities.

Discussion

Mammary lesions occurring at the time of puberty or during adolescence are relatively uncommon. In a recent study of 237 females between the ages of 10 and 20 years, fibroadenomas accounted for three-

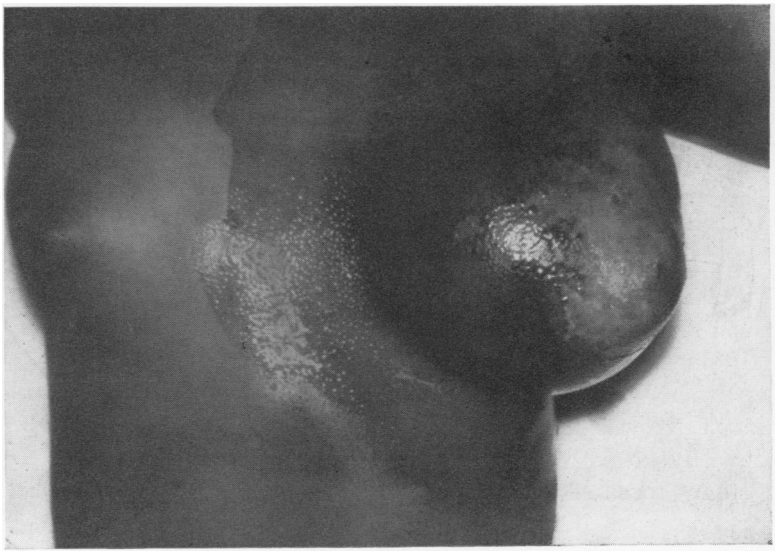

FIG. 4. Case 5: Frontal view of patient with large lesion of left breast. Note depigmentation of overlying skin.

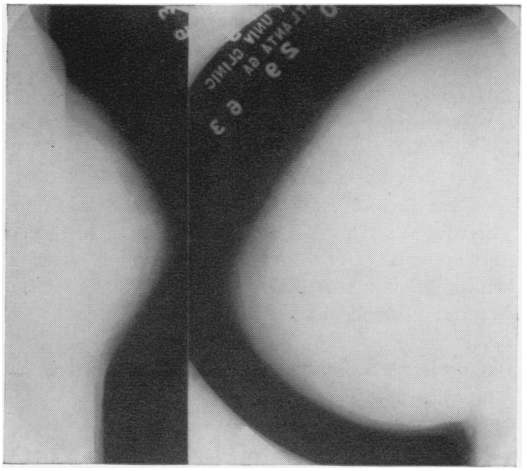

FIG. 5. Case 5: Mammogram comparing large left breast mass with normal right breast.

fourths of the lesions. Malignant lesions occurred in 1.3% and the remainder consisted of various mastopathies and inflammatory processes.[3] There were no instances of cystosarcoma phyllodes in this study.

Of 355 cases of cystosarcoma phyllodes summarized from four large studies in the American literature[4, 5, 7, 12] seventeen (5%) were in patients under the age of 20 years. All the lesions in this group were interpreted as benign. The tumors ranged from 6 to 18 cm. in size. Four patients underwent simple excision with no recorded recurrence. Simple mastectomy was performed in four and bilateral simple mastectomy was performed in two. In only one patient, an 18-year-old woman with bilateral lesions (bilateral simple mastectomy) was recurrence recorded at age 25 years. The patient was free of tumor at age 39 years.

In 1966, Gibbs reported a 12-year-old Filipino girl with a 15 × 12 cm. breast lesion.[2] A radical mastectomy was performed. Histologically the lesion was malignant and all axillary nodes were negative. One year later there was no evidence of recurrence.

A 14-year-old girl underwent simple mastectomy for a histologically benign cystosarcoma phyllodes at Massachusetts General Hospital.[6] Naryshkin and Redfield reported a case of malignant cystosarcoma in an 18-year-old woman who refused anything but simple excision of the lesion.[9] A 3 cm. recurrence was removed 6 months later and the patient was apparently free of tumor 42 months after initial operation.

Thus, a total of 20 cases of cystosarcoma phyllodes, two "malignant" and eighteen "benign," in prepubertal and adolescent females have been reported in the American literature. Only two of this group were reported to have local recurrences, one with a "malignant" primary and one with a "benign" primary. There have been no reported instances of distant metastasis or deaths from cystosarcoma in this age group in the series reviewed.

In a recent report of 40 cases of cystosarcoma phyllodes from Japan, 12 (30%) were 19 years of age or younger.[8] Of 12 cystosarcoma phyllodes seen at Grady Memorial Hospital since 1953, seven were 17 years of age or younger. Whether this reflects an increasing incidence of this lesion in the adolescent age group or a more de-

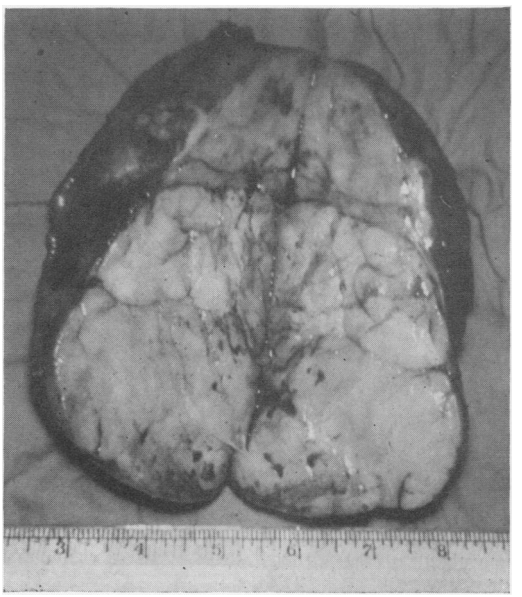

FIG. 6. Case 5: Large multilobulated tumor excised from left breast.

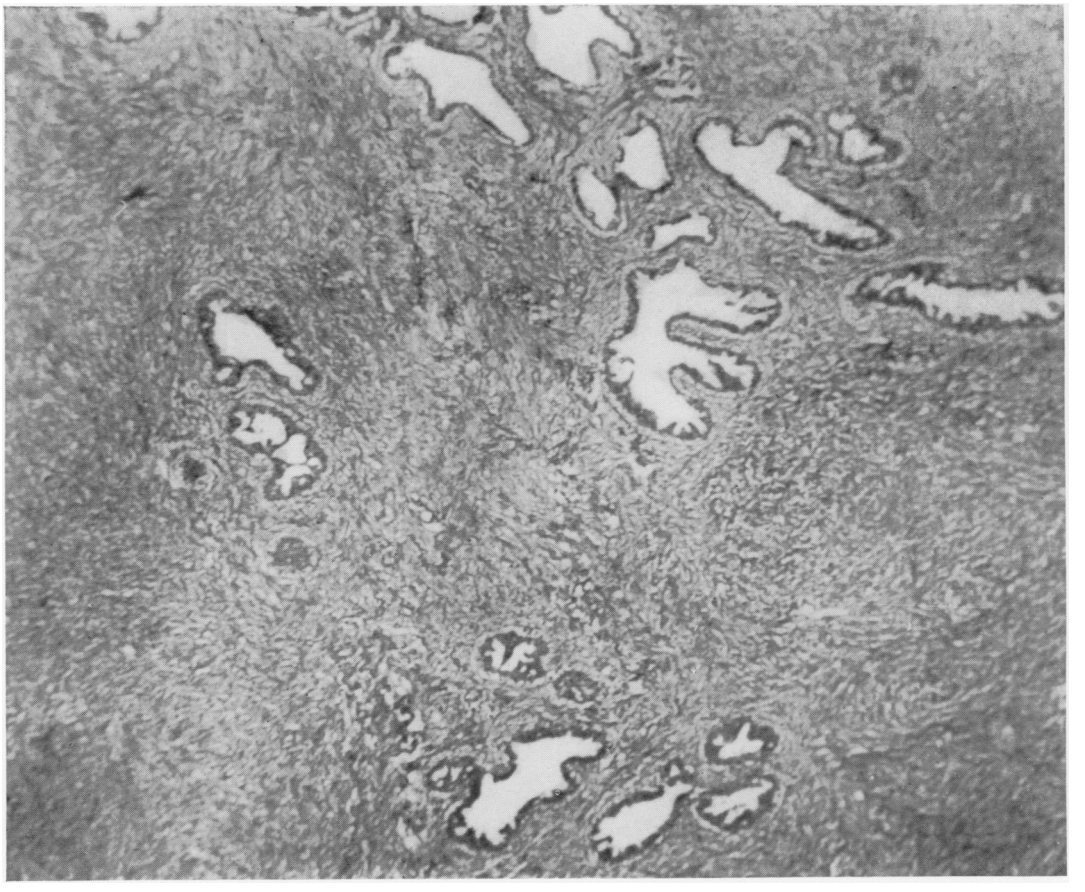

FIG. 7. Case 5: Photomicrograph of tumor showing marked increase in stromal cellularity (Hematoxylin-eosin, ×100).

finitive interpretation of histologic characteristics of fibroepithelial breast tumors removed is unknown. In the past, the term "giant fibroadenoma" has been synonymous with benign cystosarcoma phyllodes.

The clinical findings in cystosarcoma phyllodes besides the presence of a mass in the breast may include discoloration of the skin, ulcerations, fixation or retraction of the skin, discharge from the nipple, and dilated tortuous superficial veins. Overlying skin involvement is uncommon and in only one patient in this report was there evidence of skin involvement. This was primarily desquamation and depigmentation secondary to the rapid growth of the breast tumor. Mammary masses may be multiple or bilateral. Bilateral masses have prompted bilateral simple mastectomy in previously reported cases. Two patients in this report had masses in the opposite breasts which upon excision and study proved to be fibroadenomas.

Grossly cystosarcomas vary greatly with respect to size, consistency and cystic changes. Resected lesions have ranged from less than 1 cm. to 45 cm. in diameter.[4] The tumor surface may have a cauliflower or bosselated appearance suggesting lobulation or it may be entirely smooth in outline. Many contain firm fibrous areas alternating with soft fleshy areas or cystic areas. Benign lesions were found to be more frequently cystic according to the study of McDivitt and Urban.[7] About one-half of the lesions are grossly incapsulated.

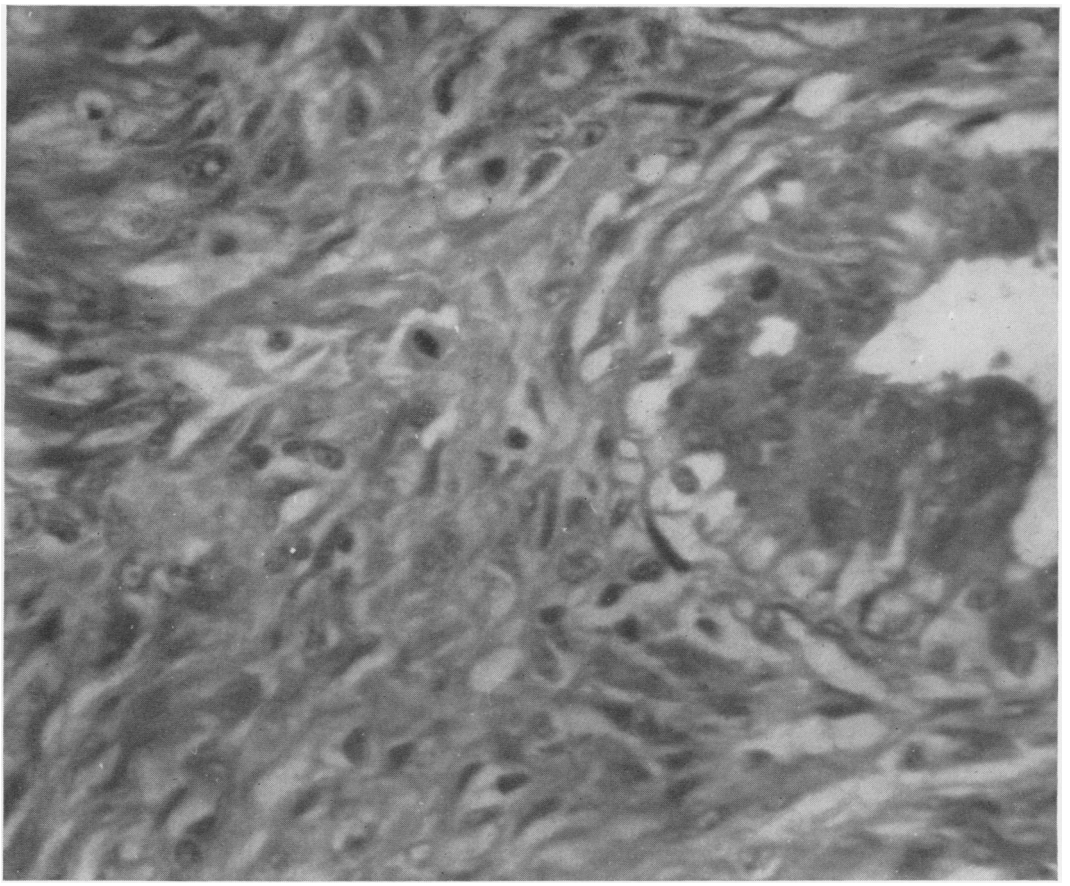

FIG. 8. Case 5: Photomicrograph of tumor showing epithelial hyperplasia and mitotic activity in stromal elements (Hematoxylin-eosin, ×250).

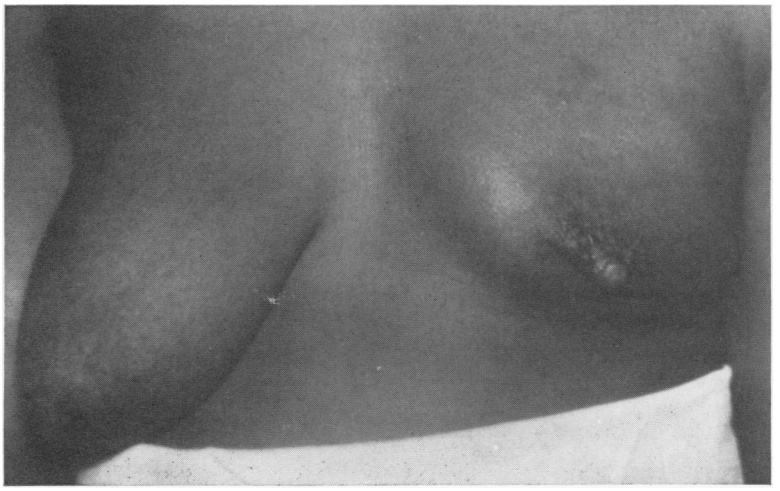

FIG. 9. Case 5: Frontal view of patient 6 years following removal of 14 × 13 cm. tumor from left breast.

TABLE 1. *Cystosarcoma Phyllodes*

Patient	Age Years	Size Cm.	Duration of Lesion	Therapy	Follow-up
A. J.	10	11 × 8	1 Month	Excision	1 Year N.E.D.*
M. A. L.	12	10 × 5	3 Months	Excision	3 Years N.E.D.
C. S.	13	8 × 6	1 Month	Excision	3 Years N.E.D.
J. C.	13	4 × 2	1 Month	Excision	7 Years N.E.D.
S. H.	14	14 × 13	1 Year	Excision	6 Years N.E.D.
S. M.	16	14 × 13	1 Year	Excision	1 Year N.E.D.
G. D.	17	7 × 6	1 Year	Excision	6 Months N.E.D.

* No evidence disease (tumor).

Histologically cystosarcomas are composed of epithelial elements and increased stromal cellularity when compared with fibroadenomas. The degree of increased stromal cellularity along with cellular atypism and mitotic activity have distinguished benign and malignant lesions. In an effort to relate histologic features of this tumor to its ultimate behavior, Norris and Taylor described the various patterns that may be encountered.[10] Cellular atypism and mitotic activity associated with the type of tumor margin (infiltrating or pushing) are the three criteria involved in distinguishing between the benign and malignant potential of cystosarcomas. Utilizing these criteria all seven patients in this report had "benign" lesions.

The therapy for cystosarcoma phyllodes in the adolescent age group varied from simple excision to radical mastectomy. Local recurrences are reported to be four times more frequent following local excision. However, deaths from metastatic tumor in the adult group were twice as common in patients initially treated by mastectomy.[10] Axillary lymph nodes involvement is reported to be rare.[7, 10, 12] In agreement with Wulsin,[13] one should hesitate to sacrifice the breast of an adolescent female for this lesion. Cystosarcomas encountered in this age group may not behave like the lesions seen in older age groups. Those described in adolescents tend to grow rapidly to a large size in a short period and this growth is probably related to the hormonal stimulus of puberty.[1, 13] Giant fibroadenomas and juvenile fibroadenomas which also grow to large sizes are best managed by excision. Likewise, mastectomy for the cystosarcomas of adolescence should be avoided if possible. When the lesion is large, it can be removed through a curved incision at the lateral or inferior border of the breast.

Summary

Experience with cystosarcoma phyllodes in seven adolescent females treated with local excision is reported. A review of the literature relating to the occurrence of this lesion in this age group is summarized. Local excision rather than sacrifice of the adolescent breast is advocated as therapy for this lesion even though the lesions rapidly

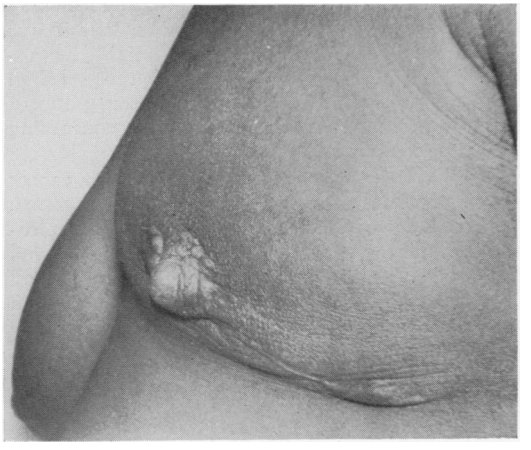

FIG. 10. Case 5: Left lateral view 6 years after operation. Note submammary incision scar.

grow to a large size. Early removal of fibroadenomas in the adolescent age group may further decrease the low incidence of this unusual breast tumor.

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Discussion

Dr. Warren H. Cole (Asheville): We have not had much new data presented regarding benign breast lesions for many decades; you might also say, from the standpoint of malignant lesions.

It would seem that this large series of 1,085 patients who have been on estrogen for 9 years probably represent a record of cases in that category, and it should allow us to determine the relationship of estrogen therapy to cancer.

You recall that he reported he had 20 patients with cancer in that series. That would appear only slightly above normal; but he implied that it was a little higher than normal, and might be approaching statistical significance. You heard him say that he is sending the material to a group of mathematicians for their interpretation concerning statistical significance.

This relationship of estrogen therapy to cancer was first called to our attention over 50 years ago by Leo Loeb of St. Louis, whom I had the pleasure of knowing when I was a student. He showed that when you gave estrogen to mice for a period of several months, a very high percentage of them would develop carcinoma; but we have not been able to transfer this experimental data onto the human being particularly since we have only slight clinical evidence to that effect.

He mentioned cystic mastitis, which is an important part of his paper. Dr. Rossiter and I studied cases of cystic mastitis at Illinois several years ago, and we find and conclude that there is a higher incidence of cancer developed in the hyperplastic type of mastitis than in patients with normal breasts; but not in the nonhyperplastic type. When we found extreme hyperplasia on biopsy, we found two or three instances which developed into carcinoma. If you would ask your pathologist if he finds such hyperplasia in patients with cancer of the breast, he will tell you this hyperplasia is found in the ducts surrounding the cancer in a high percentage of cases. So we get the idea that this relationship is rather acute, when you study the slides.

After studying this relationship I became worried if we found a slide showing hyperplasia of the extreme degree, and we would recommend excision of the breast through a submammary approach, preserving the fat and the nipple to protect against the development of cancer later. Such an operation is not very deforming, because most of these women with cystic mastitis have flat breasts anyway.

When Dr. Humphrey and Dr. Davis studied our series still further at Illinois, they found that when the hyperplasia was present in the large ducts, the danger of development of cancer was greater.

There are other features of a benign breast lesion, namely, the relationship of multiplicity of benign lesions such as cysts and adenosis to cancer. Is there any relationship of those lesions to cancer of the breast? There have been three or