Large Breast Tumors in Adolescent Females *

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THE CLINICAL entity of large, bulky, well delineated tumors of the breast has been extensively studied in several excellent reviews from large institutions.[6, 7, 12, 15] The striking characteristics and the relative rarity of these tumors have prompted many physicians to report individual case histories and often to add a new diagnostic term to the confusing list already in use. Among the more common names encountered are giant fibroadenoma, giant intracanalicular myxoma, and cystosarcoma phyllodes with benign and malignant variants.

Cystosarcoma phyllodes, as a diagnostic term, has assumed greater importance in recent years, particularly since the detailed reports of Treves and Sunderland [15] and Lester and Stout.[7] Whereas most authors have described only a few personal cases, the first series included 77 cases and the second, 36. In effect these authorities have significantly broadened the scope of cystosarcoma as a diagnostic entity by including any fibroepithelial tumor—large or small—which shows a characteristic cellularity of the stroma. Thus tumors, which many pathologists would call fibroadenoma, have been placed in the category of cystosarcoma. Surgeons must be aware of this changing trend in pathological interpretation and understand the current terminology in order to be guided in proper therapy.

The above cited authors not only separate cystosarcoma from fibroadenoma on the histological quality of the fibrous stroma, but they further subdivide cystosarcoma into benign and malignant types. The malignant variety, which is rare fortunately, is diagnosed chiefly from microscopic features, but occasionally it occurs clinically with distant hematogenous metastases. Of 36 cases from the Presbyterian Hospital in New York City one patient developed metastatic spread, while of the malignant cystosarcomas at the Memorial Hospital in New York City approximately 25 per cent were accompanied by proven distant metastases. Metastatic involvement of the axillary lymph nodes, however, is extremely rare. Before classifying these large tumors, the pathologist must examine multiple sections to determine the presence or absence of malignant tissue since the pattern may vary in different areas. It is well to recognize that prior to the publication of the above reviews, the term cystosarcoma was not applied so liberally. This view point has been summed up in a simple fashion by McDonald and Harrington,[12] who stated that "cystosarcoma phyllodes implies a huge tumor of the breast which is a benign fibroadenoma in approximately 90 per cent of instances and a fibrosarcoma in the remainder." All authors agree that there is a close relationship between fibroadenoma and cystosarcoma, and that their differentiation rests on a careful appraisal of the histological pictures.

This report deals with the problem of large tumors in the adolescent female, tumors of such size that they are clinically termed cystosarcoma phyllodes or excite

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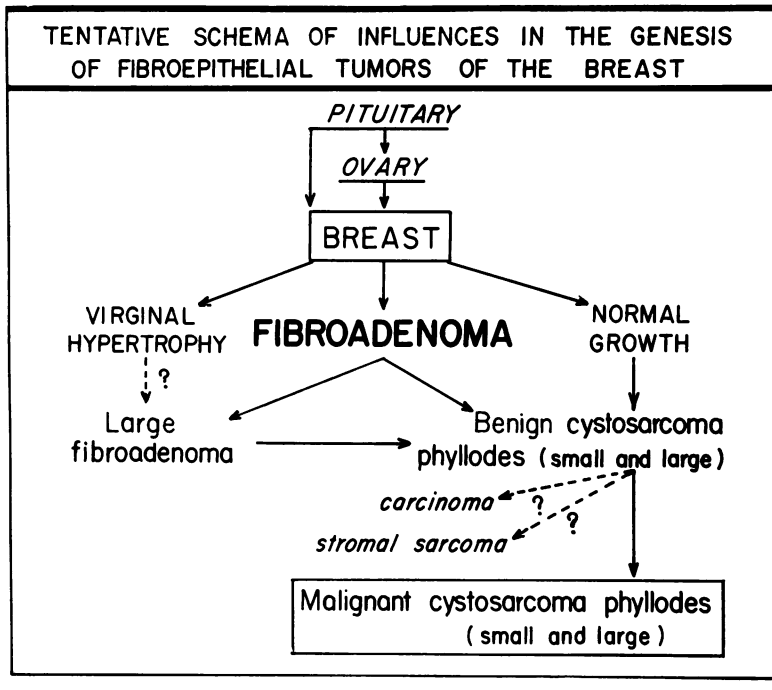


FIG. 1. Tentative schema of influences in the genesis of fibroepithelial tumors of the breast.

the suspicion of malignancy. At this age a third entity, virginal hypertrophy, must be distinguished from fibroadenoma and cystosarcoma. Under the strong hormonal stimulus of puberty, presumably largely estrogenic, both breasts become diffusely hypertrophied in this condition, sparing no normal glandular tissue. By this gross difference the process of hypertrophy may be differentiated from huge fibroepithelial tumors which are localized and demarcated from the normal breast tissue. The latter is often compressed to a mere thin rim about the tumor. Histologically, virginal hypertrophy resembles fibroadenoma so closely that the pathologist frequently cannot distinguish between the conditions.[1, 9]

When faced with massive breast enlargement at puberty, the clinician therefore must decide between large fibroadenoma, cystosarcoma, and virginal hypertrophy, while remembering that fibroadenoma often may be bilateral and hypertrophy unilateral. Although the gross clinical features should be characteristic in most cases, one wonders whether several of the reported instances of massive bilateral fibroadenoma in young girls [2, 12] did not indeed represent true diffuse hypertrophy. Possibly large fibroadenoma and virginal hypertrophy are variations of the same underlying process, the one diffuse and the other localized. In this regard it is well known that fibroadenoma frequently appears and grows at periods of estrogenic stimulation such as those associated with puberty and pregnancy, and both fibroadenoma and virginal hypertrophy have been linked clinically and experimentally with excessive production of estrogenic hormones.[3] A similar relationship between diffuse and nodular hyperplasia is seen in other organs particularly subject to hormonal control, such as the thyroid and adrenal cortex. Although comparison by analogy may be misleading, this observation conforms to the general pattern of response to endocrine stimulus which is observed in certain target organs.

The development and relationships of the family of fibroepithelial conditions of the breast are listed in Figure 1. At first

glance the chart may appear over-complicated, but an attempt has been made to assemble the various terms and stages which the clinician may encounter and connect them by histological evidence as well as endocrine influences. The schema must be considered as more suggestive than literal, for the latter stages are not necessarily preceded by the earlier ones. Thus a malignant cystosarcoma may on occasion arise *de novo* without passing through the phase of fibroadenoma, and where the relationship is particularly uncertain, such as the development of carcinoma from preceding cystosarcoma the linkage is designated by question marks. Furthermore, the reader should remember that the various entities may be indistinguishable except on histological grounds and that one condition may overlap or include another. The chart should also suggest that the diagnostic terminology of the pathologists, while valid for histological differentiation, may be unnecessarily precise and confusing for clinical purposes. Only malignant cystosarcoma with metastases stands clearly apart on clinical grounds from the rest of the family group.

Several authors have recorded the occurrence of cystosarcoma phyllodes in the adolescent female. In the review of Treves and Sunderland [15] three cases with that diagnosis were listed between the ages of 15 and 19, and none of these were the malignant variety. Lester and Stout described six cases from 12 to 18 years of age, all with benign cystosarcoma, one of which was also described by Haagenson.[5] This patient, following excision of a large tumor, developed multiple recurrent benign masses which histologically resembled a fibroadenoma and did not act in a malignant fashion. Table 1 represents a compilation of reported cases of large breast tumors in the adolescent age group as collected from the English literature, since 1927. Included in the table are instances of large fibroadenoma, a few of which are perhaps virginal hypertrophy, and finally the cases of cystosarcoma phyllodes. Those tumors which have been called cystosarcoma phyllodes have apparently earned that distinction by virtue of their vigorous growth and active cytological stroma. No case in this group has proved to be either clinically or histologically malignant, although the tumors were bilateral in more than one third of the patients.

Apparently, the cystosarcoma of the "teens" does not behave like the typical form seen in middle life. Those described in the adolescent grow rapidly to a large size in a period of several months, but almost never ulcerate. They may be bilateral; however, they apparently have not been known to become malignant. Menstruation may or may not be established at the time the tumor develops, but usually the menarche follows shortly. This lesion has not been described in the prepubertal child. On the other hand, the usual cystosarcoma appears in middle age, having grown slowly from a pre-existing fibroadenoma. Cyst formation within the huge bulk and cutaneous ulceration frequently follow. Approximately one quarter of the tumors looks malignant histologically, and a small percentage metastasizes.

The case reports of two young girls with large breast tumors treated at the Cincinnati General Hospital illustrate the problems posed by this entity. Under such circumstances the proper therapy of these lesions places a particular responsibility on the surgeon, who justifiably hesitates to sacrifice the breast of an adolescent female.

Case Reports

Case 1. L. N. (CGH #307059), a thin, white, 13-year-old girl began to menstruate regularly at the age of 12. About five months prior to admission the right breast started to enlarge painlessly, reaching an unsightly size in comparison with the normal small dimension of the pubertal left breast. Finally the marked asymmetry caused the patient and her parents to seek medical

TABLE 1. *Large Breast Tumors in Adolescent Females, Collected Cases*

Author and Date	Age	Location	Menses	Diagnosis	Treatment	Remarks
1) Sellers (1927)[14]	12	Unilat.	No	Fibroadenoma	Radical mastectomy	Fibroadenoma opposite breast
2) Turner (1929)[16]	15	Unilat.	Yes	Fibroadenoma	Simple mastectomy	Mult. fibroadenoma opposite breast
3) Turner (1929)[16]	14	Bilat.	No	Fibroadenoma	Simple mastectomy, bilateral	Well—2 years
4) Martin (1933)[11]	16	Unilat. (33 pounds)	Yes	Lipo-fibromyxoma	Simple mastectomy	Cured
5) Lewis and Geschickter (1934)[8]	12	Unilat.		Fibroadenoma	Local excision	
6) Markowitz and Howell (1936)[10]	14	Unilat.	Yes	Fibroadenoma	Local excision	
7) Crile (1938)[2]	13	Bilat.	No	Fibroadenoma	Simple mastectomy, bilateral	Cured
8) Fugita and Kishi (1939)[4]	14	Bilat.	Yes	Fibroadenoma	Radical excision, bilateral	
9) Reed and Hiebert (1942)[13]	18	Bilat.	Pregnant	Fibroadenoma lactating breast	Simple mastectomy, bilateral	
10) Fox et al. (1944)[4]	15	Unilat.	Yes	Fibroadenoma	Radical mastectomy	
11) McDonald and Harrington (1950)[12]	13	Bilat.	Yes	Fibroadenoma	Simple mastectomy, bilateral	
12) McDonald and Harrington (1950)[12]	13	Bilat.	No	Fibroadenoma	Simple mastectomy, bilateral	
13) McDonald and Harrington (1950)[12]	15	Bilat.	Yes	Fibroadenoma	Simple mastectomy, bilateral	
14) McDonald and Harrington (1950)[12]	Under 20	Unilat.		Fibroadenoma	Simple mastectomy	
15) Treves and 16) Sunderland 17) (1951)[15]	15–19	Unilat.		Cystosarcoma phyllodes	Simple mastectomy	Cured
18) M.G.H. case record (1952)[1]	13	Unilat.	No (inconsistent spotting)	Cystosarcoma phyllodes	Simple mastectomy	

TABLE 1 (*Continued*)

Author and Date	Age	Location	Menses	Diagnosis	Treatment	Remarks
19) Lester and Stout (1954)[7]	18	Bilat.	Yes	Cystosarcoma phyllodes benign	Simple mastectomy, bilateral	Recurrent fibro adenoma living and well 11 years
20) Lester and Stout (1954)[7]	15	Unilat.		Cystosarcoma phyllodes benign	Local excision	Well 1 year
21) Lester and Stout (1954)[7]	13	Unilat.		Cystosarcoma phyllodes benign	Local excision	Well 6 months
22) Lester and Stout (1954)[7]	16	Bilat.		Cystosarcoma phyllodes benign	Simple mastectomy, bilateral	
23) Lester and Stout (1954)[7]	12	Unilat.		Cystosarcoma phyllodes benign	Radical mastectomy	Well 4 years
24) Lester and Stout (1954)[7]	17	Unilat.		Cystosarcoma phyllodes benign	Simple mastectomy	Well 3 years

help. The right breast contained a firm, mobile, well delineated, 12-cm. mass which had replaced most of the normal substance. It had thinned out and rendered hyperemic the overlying skin and areola without fixation or ulceration, and had produced a striking distention of the superficial veins. One pea-sized node was felt in the right axilla (Fig. 2).

On 8/28/58 an encapsulated tumor was excised through a transverse curved incision, preserving the areola with the upper flap as a full thickness layer. The tumor, coated with areolar tissue superficially and a rim of normal breast on its superior margin, was removed with an ellipse of attached redundant skin. The remaining breast and areola were reconstructed into a small but cosmetically presentable structure. The specimen, weighing 365 Gm., was sharply encapsulated and when sectioned bulged uniformly without evidence of internal necrosis or cyst. The diagnosis was fibroadenoma, although histologically, the pathologist could not exclude virginal hypertrophy (Fig. 3). The patient is entirely well one year later.

Case 2. E. P. (CGH #361358), age 14, a well developed, colored girl passed through a normal menarche one year before admission, and both breasts had attained a normal adult size. About one month previously she discovered a lemon-sized, nontender mass in the outer half of the right breast which grew larger in the interval before admission. This extended medially beneath the areola as a discrete, rubbery, mobile tumor about 10 × 15 cm. in size, with a nodular contour. The axillae contained no palpably enlarged nodes (Fig. 5).

On 9/4/58, through a lateral incision, a well encapsulated tumor was removed, preserving the areola. The remaining breast appeared normal. The specimen, which measured 11 × 8 cm., presented a uniform, gray, bulging surface devoid of cyst or necrosis (Fig. 4). The histological diagnosis was mammary hypertrophy and hyperplasia with adenofibroma. Again the pathologist considered the picture to be indistinguishable from virginal hypertrophy. One year postoperatively the patient remained well.

Discussion

In both cases the tumor was excised locally with a capsule and a thin margin of normal breast. Frozen section is not very useful except to identify the fibroepithelial nature of the growth, for the abnormal tissue is so large that the surgeon is at a

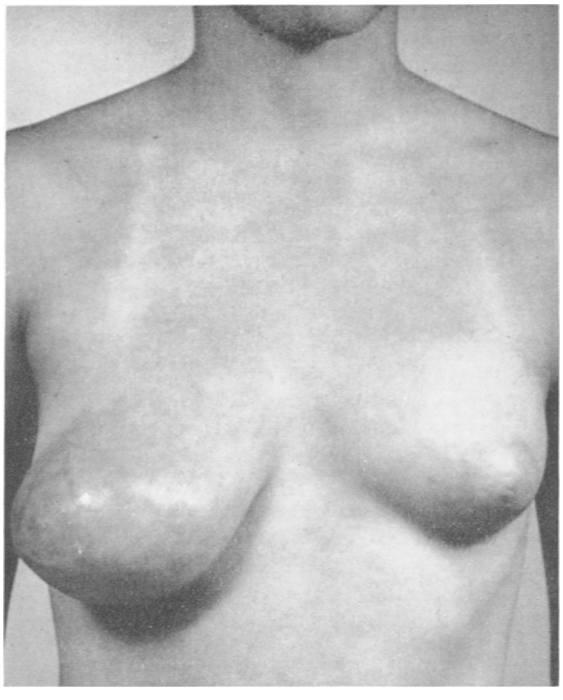


FIG. 2. Case 1: L. N., 13-year-old, pubertal girl with a mobile, unilateral mass. Thinned, hyperemic skin and distended superficial veins suggest rapid growth.

loss as to where to take his biopsy. Thus the proper surgical approach rests on careful preoperative considerations rather than histological help during the procedure.

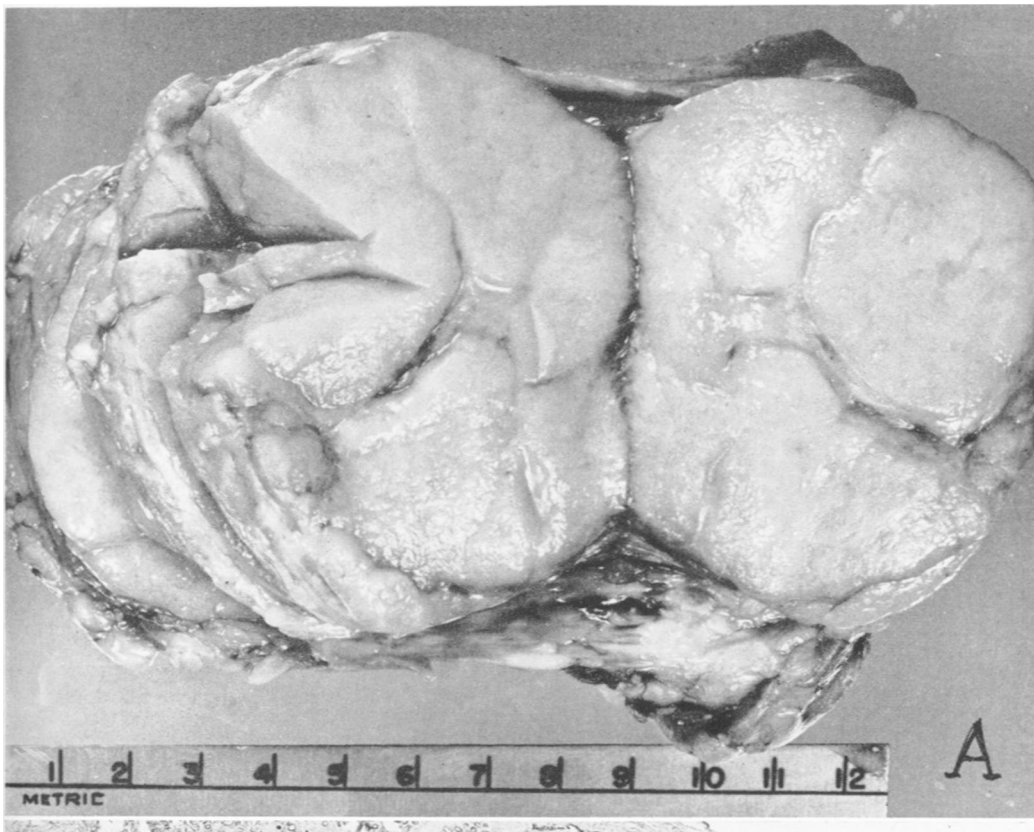
While committed to preserving the adolescent breast if at all possible, the surgeon does not wish to endanger life through inadequate excision of a malignant tumor. Virginal hypertrophy is ideally managed by resection of the excess breast tissue and reconstruction of the remainder. Fibroadenoma responds well to local excision. Cystosarcoma and giant fibroadenoma in the abolescent should, if possible, be treated by local excision. It appears to be safe and logical to treat the so-called cystosarcoma *of adolescence* as a fibroadenoma because the author has failed to find any instance in the English literature of the last 25 years in which the former acted as a malignant tumor. Of course the patient must be followed carefully for the development of a new fibroadenoma which may grow in the remaining breast tissue. If any appear, these may likewise be treated by local excision.

It is intriguing that in many of the collected cases the tumor grew rapidly during several months as though stimulated in some undetermined powerful manner, out of all proportion to normal pubertal development. Beyond indications that the ovarian hormones, estrogen and progesterone, in concert with the pituitary mammotrophic and somatotrophic hormones control the development of the human breast, little specific endocrinologic information is available concerning patients with cystosarcoma or adenofibroma or virginal hypertrophy. The earlier views [8] that hyperestrinism was responsible for juvenile adenofibroma and juvenile hypertrophy probably represent an oversimplified explanation, but one can hardly escape the feeling that in these massive tumors of the growing breast the local tissues have developed an unusual sensitivity to the effect of one or more of the above hormones or perhaps a unique ability to concentrate the hormone. From empirical experience to date we can only observe that while established menstruation is not a prerequisite to tumor growth, active breast development, however, has invariably started. With the modern chemical technics of steroid and protein analysis that are now available, we may safely anticipate that specific substances responsible for the growths will be isolated from the blood, urine, or tissues of these patients.

Conclusions

The diagnosis of large breast tumors in adolescent females rests primarily on three possibilities: giant fibroadenoma, cystosarcoma phyllodes, and virginal hypertrophy.

Giant fibroadenoma and cystosarcoma phyllodes are closely related variants of a similar pathological process. Virginal hypertrophy is often confused histologically with fibroadenoma, and each may be pos-



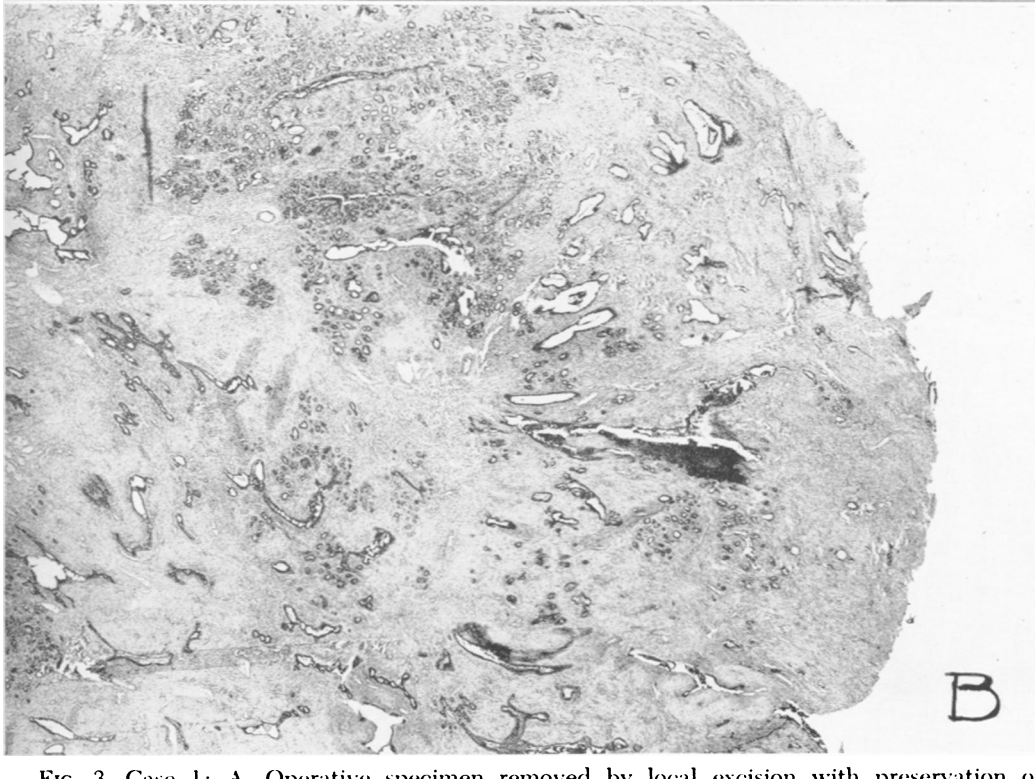


FIG. 3. Case 1: A. Operative specimen removed by local excision with preservation of areola and residual breast tissue. B. (from × 10) Histological appearance. Diagnosis: adenofibroma resembling mammary hypertrophy.

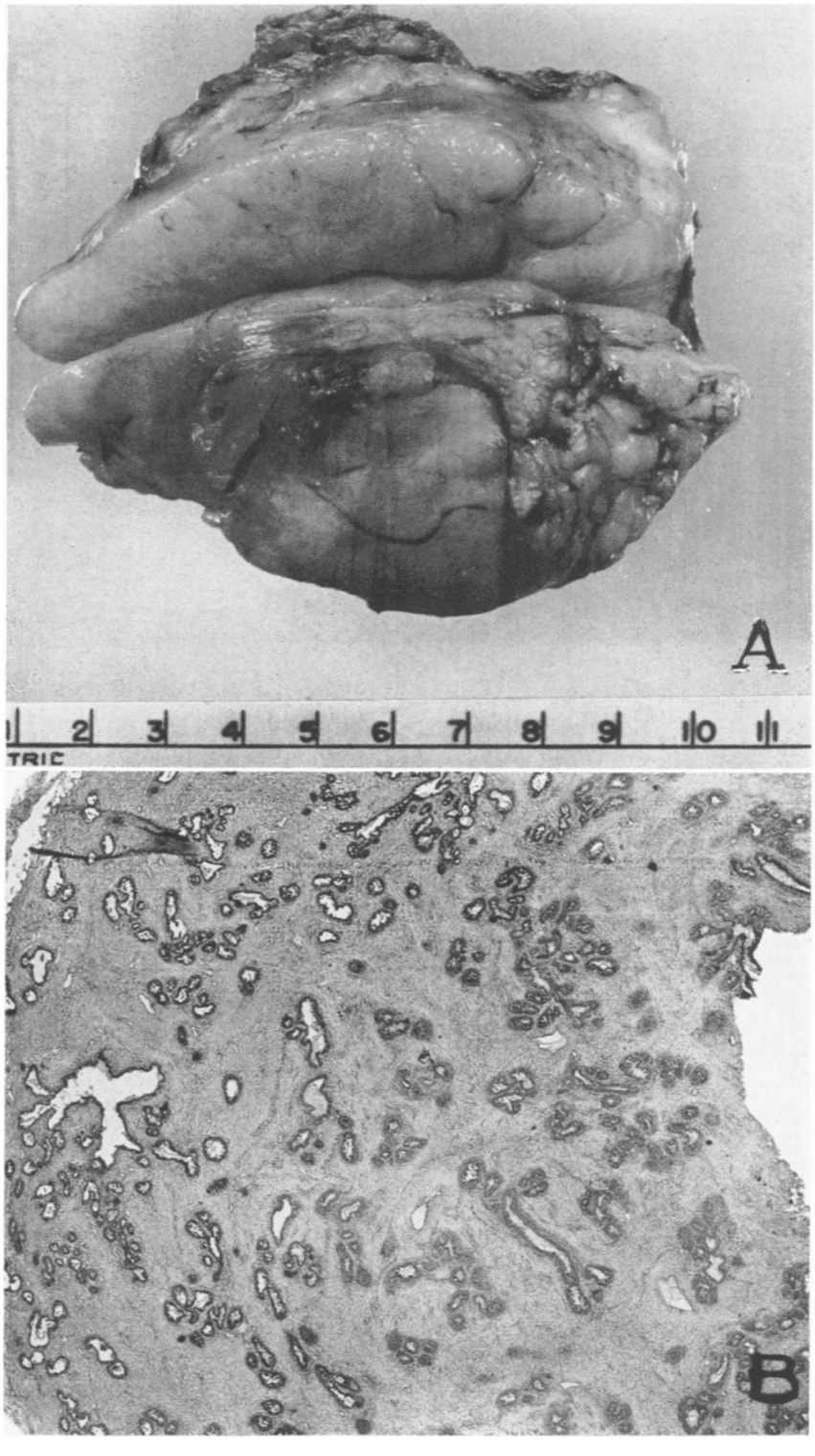


FIG. 4. Case 2: A. Encapsulated solid specimen removed by local excision. Rest of breast normal. B. (from · 10) Microscopic diagnosis: mammary hyperplasia and hypertrophy or adenofibroma.

bly a different manifestation of a common mulus. A brief discussion of the inter- tionship between these forms of mas- e breast enlargement is presented.

t is suggested that tumors diagnosed as tosarcoma phyllodes in the adolescent group behave differently than the ical lesion of middle age, and that the on is closely related to, and may be ted as a large fibroadenoma. While adult form of cystosarcoma metastasizes small, but definite, percentage of pa- ts, the juvenile variety apparently does

wo cases of large juvenile breast tumors reported in which local excision with rvation of remaining breast was per- ed.

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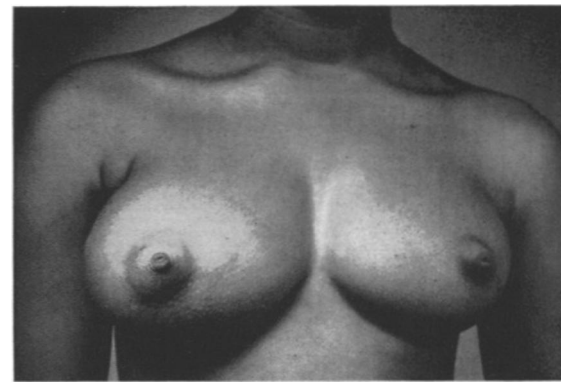

FIG. 5 Case 2: E. P., 14-year-old girl with a nodular mass, 10 × 15 cm., in outer half of right breast, extending medially to beneath the areola. The tumor had recently enlarged.

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