TE - 384

Benign Cystosarcoma Phyllodes of Breast in an Adolescent Female

Isaac Roisman, MD, Vivian Barak, PhD, Elimelech Okon, MD, Jonah Manny, MD, and Arie L. Durst, MD

KEY WORDS: cystosarcoma phyllodes, breast, adolescent female

Cystosarcoma phyllodes is an exceedingly rare breast lesion in adolescent females. This report describes a 14-year-old girl with this lesion. The clinical features, imaging, histopathology, and therapy are discussed.

Case Report

A 14-year-old girl was admitted to the hospital on November 29, 1978, with a growing mass in the right breast, initially noticed by the patient some 5 months earlier. There was neither retraction of the nipple nor discharge from it. On physical examination, a 5-cm mass in diameter was palpated in the outer quadrant of the right breast. No enlargement of the axillary nodes was detected. At operation, a well-capsulated mass was seen and excised, including the surrounding healthy tissue (up to 10 cm in diameter). The postoperative course was uneventful. The patient left the country and was lost for follow-up thereafter for a period of 11 years. In October 1989, she returned to the clinic. The patient had married and given birth to six children. On examination, there were no signs of recurrence.

Histological Examination

A biopsy from the breast showed typical picture of phyllodes tumor with leaflike projection. Higher magnification showed an increase of fibroblasts in the stroma. No mitotic figures were found. Cystosarcoma phyllodes was diagnosed (Figs. 1, 2).

Discussion

Müller (1) in 1838 gave the first full description of cystosarcoma phyllodes on morphologic appearance. However, this title is considered unsatisfactory. Since then, the

Received from the Departments of Surgery (I.R., J.M., A.L.D.), Oncology (V.B.), and Pathology (E.O.), Hadassah University Hospital, Jerusalem, Israel. Accepted for publication July 26, 1990.
Address correspondence to Dr. Isaac Roisman, P.O. Box 45470, Haifa—31454, Israel.

0888-6008/91/$3.50

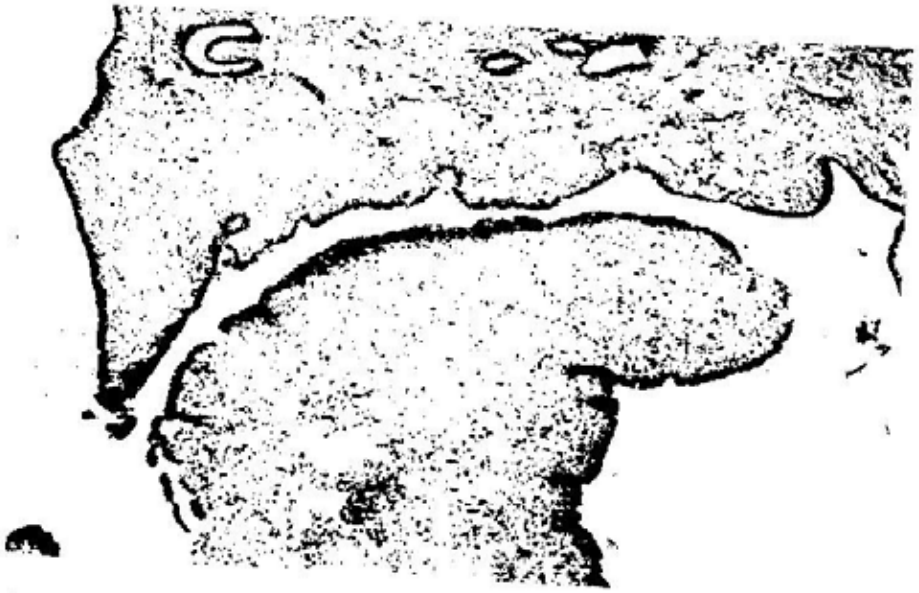

Figure 1. A biopsy from the breast showing typical picture of phyllodes tumor with leaflike projection (hematoxylin and eosin ×88).

term has come to include both benign and malignant variants of this fibroepithelial neoplasm. It accounts for 1% to 2% of breast lesions in adolescent females (2). It is seen in less than 0.5% of all breast tumors (3) and 2.5% of fibroepithelial tumors (4). According to McDaniel and Crichlow (5), no more than 700 cases had been reported in the literature when they published their article in 1986.

It is usually seen in females, but it was also described in the male breast (6,7). Chua and Thomas (8) write that the incidence in a multiracial Asian society is 3.83% of surgically removed breast tumors compared with 0.5% to 2.5% in Western series. The profile of the Asian phyllodes patient is that of a female aged 25–30 years, whereas her Western counterpart is in her fourth decade. As said, it is extremely rare below the age of 20, but in the Asian context as much as one-quarter to one-third may be in the adolescent group.

The name originates from the Greek words *phyllon* (leaf, i.e., the larger surface clefts resemble leaves in a book) and *eidosis* (form). The tumor on section shows a lobulated, leaflike appearance and contains large cysts. There were only three patients younger than 20 years among the 94 patients reviewed by Norris and Taylor (9). Three further patients were included in the series of McDivitt et al. (10). In Salvadori et al. (11) a series of 81 female patients with phyllodes tumors of the breast was examined. Ages ranged from 9 to 88 years, and only three patients below the age of 20 were reported. Other reports include the following: 10 (12), 11 (13,14), 12 (15), 13 (2), 14 (16), 15 (17), and 17 years old (18). Four patients between the ages of 10 and 14 and 23 patients between ages 15 and 18 were examined in the Chua et al. (19) series.

There is no classical history for cystosarcoma phyllodes. A lump may have been noted for several weeks or years; occasionally recent rapid growth may be reported

BREAST DIS
1991; 4:299–305

Figure 2. Higher magnification showing an increase of fibroblasts in the stroma. No mitotic figures were found (hematoxylin and eosin ×342).

(2). It is bilateral in 25% of patients. The size varies from 2 cm to 28 cm. It is a bulky, fleshy, mobile, firm tumor and has a typical "teardrop" appearance. It is painless, but mastalgia was also described (20). The skin is stretched over the mass with large distended veins, which may cause necrosis of the skin and secondary infection.

The differential diagnosis includes the following: large fibroadenoma, fibrocystic disease, mastitis, abscess, medullary carcinoma (21), virginal hypertrophy, lipoma, hemangioma, and lymphangioma (14).

X-ray mammography shows a well-defined and lobulated mass (22) with coarse calcifications. Sonomammographic appearances have been reported (23). They have good border definition with a homogeneous internal echo pattern. Sometimes, fluid-filled clefts could be imaged within a solid lesion (23). Various factors have been claimed to stimulate the growth of cystosarcoma phyllodes. Among these are trauma, lactation, pregnancy, and excessive estrogen stimulation in the absence of estrogen antagonists, such as progesterone (14).

Norris and Taylor (9) initiated the use histologic patterns in separating the benign from malignant lesions in this disorder. The distinction is based in tumor size, stromal counter, cellular atypia, degree of mitotic activity, focal calcification, and/or patterns of infiltration that bear little relationship to malignant behavior. The distinction can be very difficult, as many tumors show borderline appearances (11,18). Most of the borderline and malignant cystosarcomas were very cellular (24). Umpleby et al. (25) consider that mitotic activity in the stromal cells, more than three mitoses per 10 high-power fields, is considered the most important criterion in assessing the malignant potential of cystosarcoma phyllodes. Agnantis et al. (24) believed that the term *benign cystosarcoma phyllodes* was misleading, and they proposed instead the term *fibroadenoma phyllodes*.

Turalba et al. (26) summed up the observations on the entity of cystosarcoma phyllodes as they have appeared in the literature:

1. The size of the mass is not a good indicator of the metastatic potential of the tumor.
2. Lymph node metastasis is extremely rare.
3. Metastasis—through the blood. Sites of metastasis are lung and bone.
4. The surgical approach has uncertain influence upon the rate of local recurrence or distant metastasis, especially of malignant lesions.
5. The usefulness of radiation and chemotherapy has been downplayed, possibly contributing to the slow progress in the management of the disease.
6. The biologic behavior of the tumor is the same as sarcoma of the breast.
7. To support the grading system, the flow cytometric analysis of DNA aneuploidy and proliferative index may be used.

Azzopardi (27) used four microscopic criteria to distinguish between benign and malignant cystosarcoma phyllodes:

pushing margin
overgrowth of stromal tissue
three or more mitoses per 10 high-power fields
cellular atypia of stromal cells

Also, Ward and Evans (28) stress that stromal overgrowth is a significant histologic indicator of malignant behavior of this entity. Giani et al. (29) found that progesterone receptor (PR) in five benign phyllodes tumors were at a very high level, almost as high as in malignant tumors. Agnantis et al. (24) showed that 15 patients out of 16 has mucinous stromal degeneration, and hyalinosis was observed in about half of the patients.

Layfield et al. (30) study the DNA histograms obtained by flow cytometry from a series of 10 phyllodes tumors to determine if the analysis of DNA ploidy would help to predict clinical behavior. They were unable to report any relation between ploidy and histologic appearance, metastasis, or recurrence. In Murad et al. (31), study of 12 phyllodes tumors by flow cytometry reported a close correlation between DNA ploidy, histologic appearance, and clinical behavior. Since the histogenesis of the stromal cell in cystosarcoma phyllodes is controversial, Auger et al. (16) undertook an immunohistochemical and ultrastructural study of 11 cases to assess the histogenesis of the stromal component. Immunohistochemistry using antibodies to vimentin, desmin, actin, high and low molecular weight keratins and S 100 proteins were used for staining. In four benign cases, the stromal cells stained positively only for vimentin. They demonstrated that there is epithelial hyperplasia in benign cystosarcoma phyllodes and that their stromal cells are composed of fibroblasts and myofibroblasts. Approximately 20% of all cystosarcoma phyllodes are histologically malignant, although reports vary widely between 1% and 40% (10,32,33). A longer history, tumor size, and older patients have all been reported to be associated with malignancy. Histologic malignancy does not necessarily imply a malignant clinical course.

The preoperative diagnosis of cystosarcoma phyllodes is difficult, with small tumors being likely to be considered fibroadenomas and large tumors, carcinomas. The use of frozen section at operation does not obviate these problems because the differentiation between cystosarcoma phyllodes and carcinoma can be difficult.

BREAST DIS
1991; 4:299–305

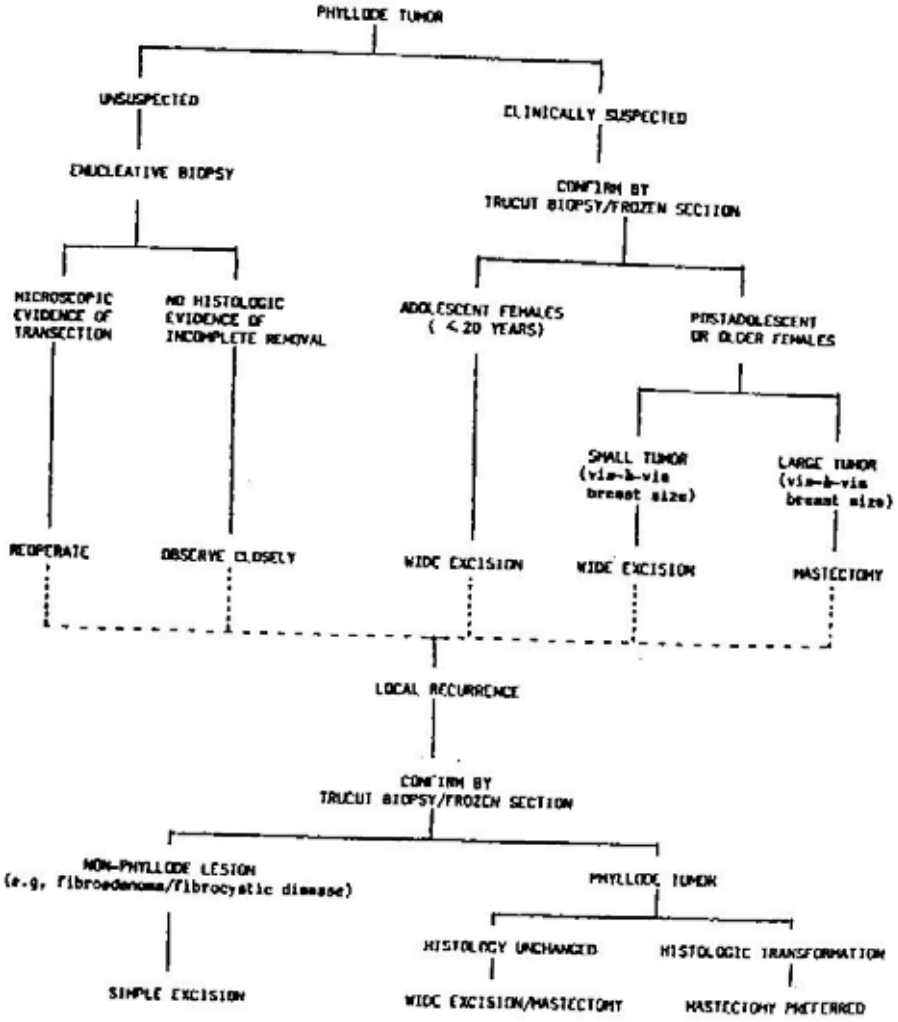

Figure 3. Algorithm for surgical management of phyllode tumor. Cited from Chua et al. (19).

Surgery has been the only method of treatment of phyllodes tumors. The surgical management has varied in the past, ranging from local excision to radical mastectomy, and depends in part on the dimensions of the tumor (20). Chua et al (19) describes an algorithm for surgical management of phyllode tumor (Fig. 3).

Cystosarcoma, whether benign or malignant, is almost never multifocal and rarely metastasizes to regional lymph nodes. Therefore, total removal of the breast or the axillary lymph nodes is usually unnecessary (34). However, an initial wide excision is recommended to remove the tumor completely in order to avoid local recurrence. This can be performed safely by wide local excision for small tumors with adequate rim of normal surrounding breast tissue (13,35,36). Palmer et al. (15) support a wide surgical excision rather than mastectomy as the initial treatment for cystosarcoma phyllodes. Even recurrent tumors can be treated with a repeat wide excision (15).

Local recurrence in the Inoshita (37) series of benign cases is extremely rare. The

exceptions are treated by wide excision or simple mastectomy. As in the Chua and Thomas (38) series, a higher incidence of recurrence among patients less than 20 years old was recorded and likewise where larger tumors exceeding 5 cm in diameter were evident. To allow for early detection of possible local recurrence, the patient should be periodically monitored.

References

1. Müller J: Uber den feinern bau und die formen der krankhoften geschwielste. Lfg 1. Berlin, Reimer, 1838, pp. 54–60.
2. Mollitt DL, Golladay ES, Gloster ES, et al.: Cystosarcoma phylloides in the adolescent female. J Pediatr Surg 1987;22:907–910.
3. Smith RJ: Cystosarcoma phyllodes: A review of the literature and report of two cases. J Natl Med Assoc 1971;63:436–440.
4. Rix DB, Tredwell SJ, Forward AD: Cellular intracanalicular fibroadenoma: clinicopathological relationships. Can J Surg 1971;14:31–37.
5. McDaniel MD, Crichlow RW: Cystosarcoma phyllodes. In: Strombek SO, Rosato FE (eds), Surgery of the Breast. New York, Thieme Inc., 1986, pp. 151–152.
6. Nielsen VT, Andreasen C: Phyllodes tumour of the male breast. Histopathology 1987;11:761–762.
7. Johansson L, Balldin G: Malignant cystosarcoma phyllodes in a man treated with polyestradiolphosphate. Case report. Acta Chir Scand 1986;152:781–785.
8. Chua CL, Thomas A, Ng BK: Cystosarcoma phyllodes—Asian variations. Aust N Z J Surg 1988;58:301–305.
9. Norris HJ, Taylor HB: Relationship of the histologic features to behavior of cystosarcoma phyllodes: Analysis of ninety-four cases. Cancer 1967;20:2090–2099.
10. McDivitt RW, Urban JA, Farrow JH: Cystosarcoma phyllodes. Johns Hopkins Med J 1967;120:33–45.
11. Salvadori B, Cusumano F, Del-Bo R, et al.: Surgical treatment of phyllodes tumors of the breast. Cancer 1989;63:2532–2536.
12. Serour F, Birkenfeld S, Amsterdam E, et al.: Cystosarcoma phyllodes of the breast in a 10 year old child. Chir Pediatr 1985;26:371–372.
13. Blanckaert D, Lecourt O, Loeuille GA, et al.: Phyllodes tumor of the breast in an 11-year-old child. Pediatrie 1988;43:405–408.
14. Orenstein A, Tsur H: Cystosarcoma phylloides treated by excision and immediate reconstruction with silicon implant. Ann Plast Surg 1987;18:520–523.
15. Palmer ML, De Risi OC, Pelikan A, et al.: Treatment, options and recurrence. Potential for cystosarcoma phyllodes. Surg Gynec Obstet 1990;170:193–196.
16. Ogun D, Gunhan O, Goze F: Cystosarcoma phyllodes. A malignant cystosarcoma phyllodes in a 14-year-old girl. Turk J Pediatr 1986;28:199–203.
17. Auger M, Hanna W, Kahn HJ: Cystosarcoma phylloides of the breast and its mimics. An immunohistochemical and ultrastructural study. Arch Pathol Lab Med 1989;113:1231–1235.
18. Jimenez JF, Gloster ES, Perrot LJ, et al.: Liposarcoma arising within a cystosarcoma phyllodes. J Surg Oncol 1986;31:294–298.
19. Chua CL, Thomas A, Ng BK: Cystosarcoma phyllodes: A review of surgical options. Surgery 1989;102:141–147.
20. Durante E, Altavilla G: Il tumore filloide della mammella. Chirurgia 1989;2:27–35.
21. Vorherr H, Vorherr UF, Kutvirt DM, et al.: Cystosarcoma phyllodes: epidemiology, pathohistology, pathobiology, diagnosis, therapy, and survival. Arch Gynecol 1985;236:173–181.
22. D'Orsi CJ, Feldhaus L, Sonnerfeld M: Unusual lesions of the breast. Radiol Clin North Am 1983;21:67–80.

23. Cole-Beuglet C, Soriano R, Kurtz B, et al.: Ultrasound, X-ray mammography and histopathology of Cystosarcoma phylloides. Radiology 1983;146:481–486.
24. Agnantis NJ, Apostolikas N: Histologic classification of cystosarcoma phyllodes: A study of 33 cases. Breast 1981;7:24–28.
25. Umpleby HC, Moore I, Royle GT, et al.: An evaluation of the preoperative diagnosis and management of cystosarcoma phyllodes. Ann R Coll Surg Engl 1989;71:285–288.
26. Turalba CIC, el-Mahdi AM, Ladaga L: Fatal metastatic cystosarcoma phyllodes in an adolescent female: Case report and review of treatment approaches. J Surg Oncol 1986;33:176–181.
27. Azzopardi JG: Problems in breast pathology. In Bennington JL (ed), Major Problems in Pathology, Vol. 11. Philadelphia, WB Saunders, 1987, pp. 346–365.
28. Ward RM, Evans HL: Cystosarcoma phyllodes. A clinicopathologic study of 26 cases. Cancer 1986;58:2282–2289.
29. Giani C, D'Amore E, Delarue JC, et al.: Estrogen and progesterone receptors in benign breast tumors and lesions: relationship with histological and cytological features. Int J Cancer 1986;37:7–10.
30. Layfield LJ, Hart J, Neuwirth H, et al.: Relation between DNA ploidy and clinical behavior of phyllodes tumors. Cancer 1989;64:1486–1489.
31. Murad TM, Hines JR, Beal J, et al.: Histopathological and clinical correlations of cystosarcoma phyllodes. Arch Pathol Lab Med 1988;112:752–756.
32. Kessinger A, Foley JF, Lemon HM, et al.: Metastatic cystosarcoma phyllodes: A case report and review of the literature. J Surg Oncol 1972;4:131–147.
33. Briggs RM, Walters M, Rosenthal D: Cystosarcoma phyllodes in adolescent female patients. Am J Surg 1983;143:712–714.
34. Mesez S: Cystosarcoma phyllodes of the lacteal glands. Zentralbl Chir 1987;112:616–621.
35. Senocak ME, Gogus S, Hicsonmez A, et al.: Cystosarcoma phylloides in an adolescent female. Z Kinderchir 1989;44:253–254.
36. Hart J, Layfield LJ, Trumbull WE, et al.: Practical aspects in the diagnosis and management of cystosarcoma phyllodes. Arch Surg 1988;123:1079–1083.
37. Inoshita S: Phyllodes tumor (cystosarcoma phyllodes) of the breast. A clinicopathologic study of 45 cases. Acta Pathol Jpn 1988;38:21–33.
38. Chua CL, Thomas A: Cystosarcoma phyllodes tumors. Surg Gynecol Obstet 1988;166:302–306.