MALIGNANT VARIANT OF CYSTOSARCOMA PHYLLODES

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Although Cumin (2), Chelius (1), and others (see 5) had previously written upon the subject, Johannes Müller (6), in 1838, described cystosarcoma phyllodes in detail:

"The tumor forms a large mass, with a more or less uneven surface. The fibrous substance which constitutes the greater part of it is of a greyish white color, extremely hard, and as firm as fibro-cartilage. Large portions of the tumor are made up entirely of this tissue, but in some parts are cavities or clefts not lined with a distinct membrane. These cavities contain but little fluid; for either their parietes, which are hard like fibro-cartilage, and smooth, lie in close apposition with each other, or a number of firm irregular laminae sprout from the mass and form the wall of the fissures; or excrescences of a foliated or wart-like form sprout from the bottom of the cavities and fill up their interior. These excrescences are perfectly smooth on the surface, and never contain cysts. The laminae lie very irregularly and project into the cavities and fissures like the folds of the psalterium in the interior of the third stomach of ruminant animals. In one instance the author saw these laminae here and there regularly notched and crenated like a cock's comb. Sometimes the laminae are but small and the warty excrescences from the cysts very large, while in other instances both are greatly developed. Occasionally these warty excrescences are broad, sessile, and much indented; others have a more slender base, and somewhat resemble cauliflower conglobata.

"Tumors of this kind attain an enormous size; hitherto the author has seen them only in the female breast, nor are they even there of frequent occurrence. They are decidedly innocent, occur earlier than is usual for cancer in the mamma to develop, and sometimes they appear even in youth. They have but little tendency to grow to the skin or to the subjacent muscles, and are not attended with retraction of the nipple. They are not disposed to soften internally but continue to grow slowly until they have attained an enormous size, when they at length burst, and a very ill-looking suppurating fungus forms upon their surface. Even in this state, however, operation has been performed with a successful result.

"Swelling of the axillary glands is not a common occurrence and, when it is met with, is the consequence of simple irritation, and subsides after operation. The extraordinary forms which cystosarcoma phyllodes assumes at once suggest the notion of its cancerous nature; and yet the disease is perfectly innocent, and as far removed from carcinoma as are those non-suppurating cauliflower conglobata of the penis, and of the female genitals, which have so often been mistaken for cancerous structures."

Up to 1931 reports of 101 cases of cystosarcoma phyllodes had accumulated in the literature, which was at that time summarized by Lee and Pack (5), who submitted six additional cases. In one of these both breasts were affected by neoplasms but the lesions were not histologically identical. The tumor of the left breast was adenocarcinomatous, while that of the right was a giant intracanalicular fibro-adenomyxoma, characteristically phyllode in nature.

On the basis of the published material it has been concluded that cystosarcoma phyllodes arises from a pre-existent fibro-adenoma, probably of the intracanalicular type (4, 5). It is not denied that fibro-adenomata may undergo a malignant change but that they progress from a neoplasm of phyllode character to one with malignant tendencies is not, indeed, sufficiently emphasized. A few writers suggest such a possibility. Friend (3), Westermark (11),
and Silvan (10) have each reported a case in which a sarcomatous transition was observed. Pearce (7) followed the course of an intracanalicular fibroma through a phyllode stage to a fungating sinus with lancinating pain and cachexia. Prym (9) emphasized the presence of metastases. Poulsen (8) concludes that about 25 per cent are malignant.

Despite the fact that local recurrences are common and that occasionally, at least, death results from lung involvement, it is an accepted belief that in general cystosarcoma phyllodes is a purely benign process. Practically every author who has written on the subject stresses the innocence of these tumors. Pathologists, however, no longer adhere to the conception that benign tumors metastasize but that a certain number recur locally after incomplete removal is well known.

Although individual experience is limited by the paucity of these tumors, there is ample evidence, corroborated in the following case report, that a malignant form of cystosarcoma phyllodes actually exists.

**Case Report**

H. K., a single white female, aged thirty-four years, was referred by Dr. J. J. O'C. with a tumor in the left breast on Sept. 28, 1939. The family history was negative for cancer and the patient's health had been unusually good. Two years previously a tumor about the size of a hen's egg was accidentally discovered in the outer lower quadrant of the left breast. There was no history of local injury, pain, or discharge from the nipple. The menses had always been regular, painless, and normal. There was no history of pregnancy and, therefore, none of lactation. During the six months prior to admission the tumor had grown to eight or ten times the size of the normal breast. There was no weight loss, the strength was well maintained and the patient had continued at her employment.

Physical examination was entirely negative except for the left breast. The latter projected almost perpendicularly from the chest wall and extended from 1 cm. lateral to the right border of the ensiform to the left mid axillary line, and from the third interspace above to the level of the umbilicus (Fig. 1). The tumor was smooth in contour but irregular in

![Fig. 1. Tumor of Left Breast before Operation](image-url)
outline, consisting of firm nodular and cystic masses which projected beyond the surrounding breast surface. The vertical and transverse measurements were 21 and 19 cm. with the greatest diameters 9 cm. from the chest wall. The nipple was not retracted but, together with the surrounding areola, was flattened, broadened, and deeply pigmented. No discharge could be expressed. Above and medial to the laterally displaced areola and nipple was a cystic area, about 5 cm. in diameter, over which the skin was atrophic, scaly, blanched, and about to separate. The surrounding skin was edematous, as shown by increased thickness, pitting on pressure and enlarged pores of the peau d'orange type. Over the nodular mass numerous dilated superficial capillary and venous radicals were visible within the skin substance. The skin was generally fixed to the underlying tumor, apparently because of its being taut. The tumor was likewise immovable beyond narrow limits and seemed somewhat fixed to the underlying structures.

Roentgen examination of the thorax, lungs, and bones showed no evidence of metastasis. The blood Wassermann test was negative. The blood count and urine were normal. The skin patch test was moderately positive for tuberculosis.

The clinical diagnosis was considered to be either sarcoma or papillary cystic carcinoma. Because of the undesirability of leaving an extensive skin defect, 5250 r of roentgen therapy were given by Dr. W. J. Corcoran over a period of ten days, in the hope of reducing the size of the growth, but without appreciable effect.

Accordingly, on Nov. 15, 1939, a simple mastectomy was performed by the writer through transversely elliptical incisions made sufficiently wide apart to permit of immediate closure of the wound under slight skin tension. The posterior surface of the fibrous capsule was attached to the anterior fascia of the corresponding pectoralis major muscle for a distance of 9 × 5 cm. The involved fascia was edematous and thicker than normal, but was not nodular. The neoplasm and the fascia to which it was attached were removed en masse by sharp dissection. Bleeding from surrounding enlarged veins was unusually profuse.

The specimen consisted of an oval, irregular, partially encapsulated tumor, on the anterior surface of which was an elliptical area of greatly thickened and edematous skin.
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measuring 22 × 12 cm. Included in the skin flap was the flattened pigmented nipple and expanded areola. The intact specimen weighed 3781 grams.

The tissue cut with smooth but firm resistance, and a large quantity of pale serous and mucoid fluid escaped. The skin was edematous, being a full centimeter in thickness. The cut surface of the tumor was heterogeneous in appearance, uneven, grayish white in most areas, and a glistening, pale pink in others. In one section there were several cysts measuring 0.5 to 2 cm. in diameter. These did not have a lining membrane. One of them contained a pedunculated polypoid outgrowth. The tumor in general was irregularly lobulated, the lobules being encapsulated, firm, oval, and grayish white in color. Between adjacent lobules narrow clefts were observed. Breast tissue could not be identified grossly.

Microscopic examination of the tumor shows two lesions; one a simple fibroadenoma, and the other the characteristic intracanalicular jelly-like growth to which the name cystosarcoma phyllodes is due. Reports on the microscopic diagnosis from a number of well known pathologists were somewhat divergent. They were carcinosarcoma, myxoadenoma, adenocarcinoma, degenerating fibroadenoma, fibroadenoma with early carcinomatous changes, and finally, from four pathologists of large experience, cystosarcoma phyllodes. The structure does not differ greatly from other specimens of cystosarcoma as seen in large collections of tumor slides, or photomicrographs reproduced in various papers and textbooks. There is a jelly-like stroma containing large branching cells (Fig. 2) and cells with large irregular nuclei; numerous degenerated nuclei are also seen. Some of these cells have very large cell bodies and unless one were familiar with the picture, the diagnosis of sarcoma would be suggested. In the original material there was no definite sarcomatous structure. Obviously there are groups of spindle-cells scattered about, but these are seen also in the tumors of patients who have been followed a sufficient length of time to say that no malignant change has occurred, or at least, after a simple mastectomy, that recurrence has not taken place.

It is easy to see why one pathologist of somewhat limited experience made a diagnosis of early carcinomatous change. He was looking at the hyperplastic epithelium which lines...
certain of the ducts and cystic cavities in the tumor (Figs. 3 and 6). These are reminiscent of the lesions produced by the administration of a large amount of female sex hormone to the smaller rodents. Undoubtedly some disturbance of the secretion of theelin was present in this patient, and it may be that the underlying cause of the sudden and astounding growth is connected with some hormonal excess or abnormality. A considerable part of the growth, however, is unquestionably due to edema (Figs. 4 and 5), for these patients are apt to give a history of a small lump in the breast for a considerable period, followed by a sudden increase in size, so that the tumor may reach remarkable dimensions in the course of a few weeks. A certain number of mitotic figures are present in the connective-tissue cells, but this is frequent enough in the hyperplasias produced in animals with sex hormones. Abnormal mitoses are also seen, especially of the multipolar forms and irregular degenerating types of nuclei which are common in the lesion under discussion (Fig. 5).

Immediate recovery was uneventful following operation and the patient was discharged from the hospital on Nov. 23, 1939, eight days postoperatively.

On March 27, 1940, re-examination disclosed the presence of a recurrent tumor underlying the medial fifth of the firmly healed scar and extending equally above and below the former line of incision. It was round and measured $6 \times 6 \times 3$ cm. Laterally and below this principal mass were three subcutaneous nodules, each about 1 cm. in diameter. At this time, also, all other physical and laboratory examinations were negative.

On April 5, 1940, a second operation was performed. Bleeding was again excessive, a circumstance that resulted in a temporary anemia. Thirteen days later, however, the patient was again discharged from the hospital.

The second specimen removed resembled the first grossly except for the fact that there were four distinct tumors and the pectoral muscles were included. There was neither muscle nor lymph node involvement.

Subsequent examinations may be summarized as follows:

**Aug. 21, 1940**: General condition excellent. Weight 135 lb. Two recurrent subcutaneous nodules, one above and one below the line of incision, 2 cm. in diameter.

**Oct. 17, 1940**: General health good. Weight 136 lb. Diffusely outlined tumor $5.5 \times 4$ cm. in left infraclavicular region. Subcutaneous nodule 2 cm. in diameter medial to center of scar.

**Nov. 21, 1940**: General health good. Weight 136 lb. Diffusely outlined, firm tumor, $7 \times 5$ cm., in outer middle third of right breast. Infraclavicular tumor slightly reduced.
The glands are hyperplastic, but there are no mitotic figures either in the epithelium of the glands or in any of the connective-tissue cells in the field.

Jan. 4, 1941: General condition good. Weight 139 lb. Tumor in right breast practically imperceptible. Diminution in size of tumor in infraclavicular region. Two newly recurrent subcutaneous nodules, \(3 \times 2\) cm. and \(3.5 \times 2\) cm. respectively, above and medial to scar. Two similar tumors, \(4 \times 3\) cm. and \(3 \times 2.5\) cm. respectively, inferior and lateral to the scar.

Dr. William J. Corcoran gave about 10,400 r measured in air to the left thorax during 1940, and 1700 to the right breast.

The patient died April 20, 1941, nineteen months after she was first seen. Autopsy showed extensive growth on the chest at the site of removal of the left breast, metastases in the right breast, in the anterior mediastinum, and the lung. The liver, spleen, omentum, and peritoneal cavity were free of tumor. The uterus and ovaries were not involved. X-ray studies of the skeleton revealed no resorption of bone. A photomicrograph of a lung metastasis is reproduced in Fig. 7.

**DISCUSSION**

An analysis of this and other cases discloses that cystosarcoma phyllodes arises on the basis of a pre-existent fibroadenoma; it grows to excessive proportions in a comparatively brief interval; it does not have a tendency to infiltrate, but it does invade and replace breast structures; it recurs locally, and it may on occasion metastasize to a distance. It likewise is subject to fatty changes in the cells of the growth, to myxomatous alterations which produce cavities filled with gelatinous fluid, and may eventually show necrosis (4).

In this case a small tumor, probably a fibro-adenoma, was discovered eighteen months before the onset of rapid growth. Within six months it
progressed to a weight of approximately 8 lb. The gross aspect, as well as the histopathologic picture, was typically that of cystosarcoma phyllodes. There was evidence of fatty infiltration and cavity and cyst formation, with mucoid fluid. The skin was actually invaded, as was evident in a section of the original specimen. Recurrences appeared rather promptly after two operations. The recurrences were of moderately wide distribution and were radio-resistant. The clinical manifestations were those of sarcoma. The histopathologic diagnoses, made by competent pathologists from these recurrences, establish the malignancy of this particular neoplasm and suggest that it is a malignant variant of cystosarcoma phyllodes.

References