

# Estradiol Binding Protein in Cystosarcoma Phyllodes of the Breast

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**Abstract**—In two cases of cystosarcoma phyllodes significant amounts of estradiol receptor protein were demonstrated.

Determination of steroid hormone receptors may in the future serve as a prognostic indicator and provide a rational basis for endocrine therapy.

## INTRODUCTION

CYSTOSARCOMA phyllodes is a rare fibro-epithelial breast tumor [1-3]. In recent years concepts about this tumor have undergone radical changes. It is important to recognize that contrary to former views the tumor may turn out to be malignant [4-10]. It is generally accepted that the malignant component is of stromal origin and that in most major series the incidence of malignancy varies from 20 to 30%. The management of cystosarcoma phyllodes shows discouraging results irrespective of therapeutic efforts and histological characteristics [6, 8, 10]. Poor correlation between the histological appearance and the biological behaviour of the tumor has recently been emphasized [10]. The recurrence rate is high with figures of up to 30% in benign series, and the majority of malignant tumors run a fatal course.

The detection of estrogen binding protein in tissue from cystosarcoma phyllodes is therefore of considerable importance. The finding may give rise to a new approach to rational therapy. Estradiol hormone receptor studies in 2 patients with cystosarcoma phyllodes are presented here.

## MATERIAL AND METHODS

### Case 1

An otherwise healthy 57-yr-old postmenopausal woman presented with a painless lump in her left breast. The tumor was lo-

cated centrally and after removal by simple mastectomy measured 7 × 6 cm on section.

The tumor was solid and lobulated with plump finger-like projections into the surrounding tissue. Histological examination showed marked proliferation of the connective tissue component. No normal breast lobules were seen, but there were a number of ducts covered with regular epithelium with areas of proliferation. The mesenchymal element consisted mainly of fibrous connective tissue, but there were also large areas of adipose tissue. There was no distinct demarcation between the connective and fatty tissue. In addition there were areas of fat necrosis. The connective tissue component was generally cellular and contained spindle-shaped to ovoid nuclei with moderate, but nowhere marked, pleomorphism. A relatively large number of mitoses with some atypical forms were seen.

Histologically this tumor was classified as a cystosarcoma phyllodes of malignant type, though the degree of malignancy was considered low. There was no evidence of co-existent carcinoma.

### Case 2

An otherwise healthy 59-yr-old postmenopausal woman presented with a painless lump in the upper lateral quadrant of the left breast. The tumor was treated by wide resection and measured 2 × 3 cm on section.

On gross examination, the tumor was solid and well demarcated with a protruding lobulated cut surface. Microscopically, a fibroadenoma with both peri- and intracanalicular

features was found. A richly proliferating fibrous stroma dominated the picture. The stromal fibroblast-like cells were uniform and arranged in interdigitating fascicles and whorls. Very few mitoses were present. The stroma compressed the relatively few ducts creating an irregular branching pattern. However, cystic dilated lumina were also seen. The epithelium was well differentiated with slight to moderate intraductal proliferation. No papillomatosis or squamous metaplasia was found.

Histologically, the tumor was classified as a benign form of cystosarcoma phyllodes, also called fibroadenoma phyllodes.

## RESULTS

### *Demonstration of estradiol binding protein*

Tissue from both tumors was treated according to the standards suggested by the EORTC study group [11]. The resulting supernatant was assayed for  $^3\text{H}$  estradiol binding capacity.

As suggested by Korenman [12] and modified by Daehnfeld [13] 5 different  $^3\text{H}$  estradiol concentrations were used. By this method only free receptors sites are determined, while filled sites under the study conditions of short time and low temperature do not dissociate.

The results of the estradiol binding protein determination demonstrated significant amounts of estradiol binding protein in both tumors. In the tumor from case 1, 150 fmole/mg estradiol receptor protein was demonstrated, while in the tumor from case 2, 43 fmole/mg estradiol receptor protein was found.

In comparison it should be added that estradiol receptor level in 25 random selected fibroadenoma and other benign tumors and 18 random selected samples of hyperplastic human mammary tumor all were below 10 fmole/mg protein.

Because of the histological appearance and results of estradiol receptor protein determination adjuvant endocrine therapy with tamoxifen, 10 mg 3 times daily was initiated in

case 1 [16]. The patient continued to be seen at outpatients every 3 months, and after more than 1 year shows no evidence of local recurrence or distant metastases.

In case 2 there was no histological indication for mastectomy and adjuvant therapy was not indicated. However, the patient has been followed in outpatients for 6 months.

## DISCUSSION

The correlation between the content of steroid hormone receptor protein in breast carcinoma and the therapeutic effect of endocrine manipulation in advanced disease has been well established. Whether or not a similar relationship exists between receptor protein content and endocrine therapy in breast sarcoma remains to be elucidated.

Review of the literature reveals no previous report of estradiol binding protein having been demonstrated in cystosarcoma phyllodes, but significant amounts of progesterone binding protein have been recently in a single case [17].

Significant amounts of estradiol binding protein were found in the two cases of cystosarcoma phyllodes presented here. Demonstration of steroid hormone receptor may indicate that cystosarcoma phyllodes is a hormone dependent tumor and therefore may respond to endocrine therapy.

The origin of receptor protein in carcinoma of the breast is epithelial component. Demonstration of significant amounts of estradiol receptor protein in benign cystosarcoma phyllodes may indicate a potential for malignant transformation. From a theoretical point of view estradiol binding protein may originate in co-existent carcinomatous elements in the sarcoma. However, meticulous histological examination revealed no malignant epithelial component in these tumors.

It is therefore probable that the estradiol binding protein was located in the stromal component in both tumors irrespective of their histological appearance.

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