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Letter to the Editor

Estrogen Receptors in Cystosarcoma Phyllodes of the Breast

W. M. PORTON* and J. POORTMAN†‡

**Department of Pathology, Diakonessenhuis, Oudenrijn Hospital and Military Hospital in Utrecht and †Department of Endocrinology, University Hospital, Utrecht, The Netherlands*

VERY RECENTLY Palshof *et al.* described in this journal [1] two cases of cystosarcoma phyllodes in which they demonstrated significant amounts of estradiol receptor proteins: 150 and 43 fmol/mg protein respectively.

It is well-documented that in advanced mammary cancer the presence of this estradiol binding protein correlates with the therapeutic effect of endocrine manipulations.

In analogy of this well-established relationship, Palshof *et al.* suggested that the presence of estradiol binding protein in cystosarcoma phyllodes may indicate that this breast tumor is a hormone-dependent tumor.

During the last two years we had the opportunity to measure the estradiol receptor concentration in eight cases of cystosarcoma phyllodes. We found that 4 out of the 8 tumors had significant amounts of estradiol receptors present, while 4 others had no estradiol receptors. This finding suggests that this breast tumor should not be considered as a hormone-dependent tumor *per se*. Receptor studies in these eight patients with cystosarcoma phyllodes of the breast are presented here.

Some clinical data and the pathological findings in the eight patients studied are given in Table 1.

The method used in our laboratory for the measurement of estradiol receptor concentration is a multiple dextran-coated charcoal assay analyzed by Scatchard-plot, as recommended by the N.I.H. concensus development panel [2]. Our method is a modification of the method proposed by the E.O.R.T.C. study group [3].

The modification implies that we use an eight-point assay: four concentrations of ^{3}[H]–E_2 ($3\times10^{-10}-2\times10^{-9}$ M) for total binding and the same concentrations of ^3H–E_2 plus 10^{-6} MDES to assess non-specific binding.

The technique has been published in detail by van Paassen *et al.* [4] and by Poortman *et al.* [5].

Although there is as yet no international quality control program for the receptor determinations, we suggest that our method and that used by Palshof *et al.* should give identical results.

The results of the estradiol receptor determinations are included in Table 1.

Of the tumors investigated, four showed significant amounts of estradiol receptors while four did not show any specific binding for estradiol. The concentration range we found was between 15 and 90 fmol/mg protein. The value of the dissociation constant calculated for the positive cases was less than 1 nM (0.2–0.9 nM).

The quality of the receptor-assay in our laboratory is checked by participation in the National Quality Control Program on lyophilized calf uterus and human mammary cancer tissue [6]. Fibro-adenoma, benign tumors and "normal" hyperplastic human mammary tissues always have less than 3 fmol/mg protein.

Our findings show that some cases of cystosarcoma phyllodes have significant amounts of specific estrogen receptors, whereas in other cases estrogen receptors are absent.

If the correlation between the presence of estrogens receptors and the therapeutic effect of endocrine treatment also exists for this type of breast tumor, our data suggest that this type of tumor may be either hormone-dependent or hormone-independent.

Cystosarcoma phyllodes has received a variety of names, such as: cellular intracanilicular fibro-adenoma; Brodie's tumor; and giant fibro-adenoma (fibro-adenoma gigantosum). It may attain a very large size, especially during pregnancy, but can also be small.

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†To whom all correspondence should be sent.

Table 1. Pathological findings

No.	Age	Pathological findings	Amount of tissue processed (g)	Receptor concentration (fmole/mg protein)	K_d (nM)
1	69	B-cell type	1.0	90	0.6
2	47	B-cell type	0.50	42	0.2
3	32	A-cell type	0.30	—	—
4	22	B-cell type	0.45	37	0.8
5	39	A-cell type	1.0	—	—
6	40	A-cell type	0.20	—	—
7	30	A-cell type	0.75	—	—
8	21	B-cell type	0.80	15	0.9

Mostly, there is a mass of loose connective tissue stroma separated by two layers of proliferating duct epithelium, but occasionally the stroma shows secondary changes and there may even be cartilage or bone formation in it. The epithelial component can even show papillomatosis and/or apocrine metaplasia.

By meticulous and careful examination, the histological appearance of the cystosarcoma phyllodes-type tumor can be subdivided in two types: the "A-cell" type, in which the epithelial components are more striking; and the "B-cell" type, in which the stromal components are more dominating and expressive Figs. 1 and 2 respectively.

Despite the considerable variation in the microscopical appearance of these tumors, it is almost always possible to distinguish more or less between these two types.

The names "A-cell" type and "B-cell" type are considered to distinguish the epithelial (c.q.) and the stromal predominating components. Much to our surprise, we found that the four cases of the A-cell tumor were receptor negative, while the four cases of the B-cell type were receptor positive. This finding supports the suggestion of Palshof *et al.* [1] that the estradiol-binding protein in their two cases was located in the stromal components.

Besides this observation, there were no further histo-pathological characteristics which were associated with the presence or absence of the receptor proteins.

It is generally accepted that this type of breast neoplasm can change to malignancy [7] Whether the histological appearance (A-cell type vs. B-cell type) or the presence or absence of estrogen receptors is of predictive value in this respect remains to be elucidated.

The follow-up of our patients after the biopsy or operation is too short to give any suggestive evidence in this direction. The further development of correlation of estrogen receptors (and possible progesterone receptors) with the clinical course of this disease require critical analysis of large number of patients. As this cystosarcoma phyllodes is not so frequently diagnosed, we should encourage others to investigate their cases in this respect.

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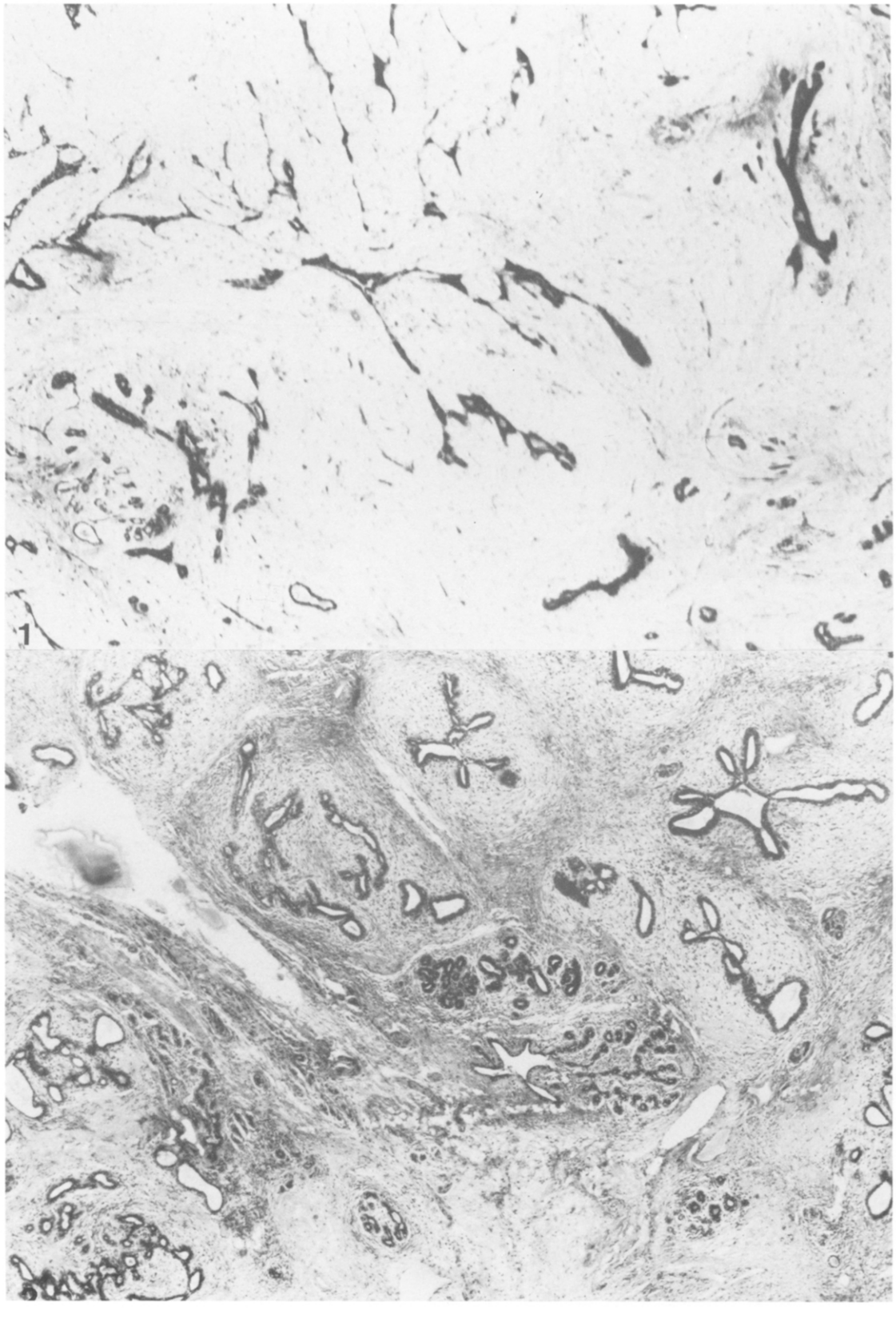

Fig. 1. Histological appearance of cystocarinoma phyllodes-type tumor (A-cell type), in which the epithelial components are more striking (×12).

Fig. 2. Histological appearance of cystocarcinoma phyllodes-type tumor (B-cell type), in which the stomal components are more dominating and expressive (×12).