

Histopathological Characteristics and Oestrogen Receptor Content in Primary Breast Carcinoma

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Summary. 159 primary breast carcinomas were examined histologically with regard to grade of anaplasia, cellularity, amount of elastic tissue, and whether they were of ductal or lobular origin. Possible correlations between these variables and the oestrogen receptor (OR)-content were investigated. There was a marked tendency toward a greater number of OR-positive tumors in the group rich in elastosis. A significant correlation between the OR-content and the histological grade was found, whereas there was no correlation between either the OR-content or the grade of anaplasia and the cellularity. Furthermore, the group of tumors that were lobular in derivation had a significantly greater number of OER-positive tumors than the group ductally derived.

Key words: Breast carcinoma – Oestrogen receptor – Histology – Cellularity – Elastosis.

Introduction

Since the demonstration of correlations between the presence of oestrogen receptor (OR) protein in breast carcinoma and response to both endocrine therapy and prognosis (McGuire et al. 1975; Knight et al. 1977), possible relationships between other variables and OR-content have been investigated. The majority of investigations of a relationship between histological grade of the tumor and OR-content have failed to reveal any correlation (Sander 1968; Johansson et al. 1970; Feherty et al. 1971; Aspegren et al. 1974; McGuire et al. 1975; Rosen et al. 1975). However, in recent years a correlation has been demonstrated between the grade of anaplasia of the tumor and the OR-content (Masters et al. 1978; Maynard et al. 1978; Martin et al. 1978; Martin et al. 1979; Antoniadis and Spector 1979). It has also recently been found that many breast

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carcinomas often contain large amounts of elastic tissue (Lundmark 1972; Shivas and Douglas 1972; Azzopardi and Laurini 1974), and a relationship between the OR-content and degree of elastosis has been reported (Masters et al. 1975; Masters et al. 1978; Fisher et al. 1980).

In the present work the histological grade, the cellularity and the degree of elastosis in primary carcinoma of breast and the relationship to the OR-content has been investigated.

Material and Methods

159 primary carcinomas of the breast were examined. All tumors were surgically removed in 1975–1977 and at the time of operation a portion of tumor tissue was removed for OR analysis. From this same portion a section was taken for histological examination while the remainder was used for the radio-receptor assay. The tissue used for histological examination was embedded in paraffin and stained using a routine Haematoxylin-Eosin stain for histological grading and a Victoria-blue staining method for elastic tissue. The tumors were examined histologically and classified without prior knowledge of the OR-content. The classification was based upon the criteria given by Bloom and Richardson (1957), where the tumors are graded depending on the tendency to tubular formation, nuclear pleomorphism and the amount of mitoses and hyperchromasia. There are three grades, I: highly differentiated, II: intermediately differentiated, and III: poorly differentiated. The tumors were further classified as lobular or ductal derived carcinomas. Cellularity was evaluated by means of a semi-quantitative method and divided into three groups: with less than 1/3 (+), between 1/3 and 2/3 (++), and more than 2/3 (+++) of the tumor consisting of tumor cells compared with stroma. Tumors were graded for occurrence of elastic tissue into grade 0, 1, and 2, where grade 0 contained no elastic tissue grade 1 had small to moderate amounts, and grade 2 was rich in elastic tissue. Deposits in relation to neoplastic tissue only were taken into account, for example tumors with deposits around blood vessels and normal ducts were considered negative.

The OR-content was determined by a dextran-coated-charcoal method described by Daehnfeldt and Briand (1977). Tumors with OR-values < 10 fmol/mg cytosol protein were considered to be OR-negative whereas those with OR-content ≥ 10 fmol/mg cytosol protein were classified as being positive.

The data was examined independently of menopausal status and occurrence of lymphoid metastases.

For the statistical analysis a χ^2 -test was performed, with a P -value of 0.05. To examine the relationship between elastosis and the OR-content, an analysis for linear trend has been applied (Armitage 1971).

Results

Among the 159 tumors 57 were classified as being grade I, 79 as grade II, and 23 as grade III. 33 of the tumors had low cellularity, 50 were intermediate, and 76 were rich in cells. Of the 159 tumors, 16 were lobular carcinomas and the remaining tumors were of ductal origin.

The degree of elastosis was estimated in 123 of the 159 tumors. 28 of the tumors did not contain elastic tissue, 64 had small to moderate amounts, and 31 were rich in elastic tissue.

In Table 1 the relationship between the histological grade and the OR-content is illustrated. A statistically significant higher number of OR-positive tumors occur among the highly differentiated group ($P < 0.005$). This difference is especially marked in the grade III tumors where only 30% of the tumors are OR-positive compared to 70% of the grade I tumors and 67% of the grade II tumors.

Table 1. Relationship between OR-content and histological grade

	Grade I	Grade II	Grade III	Total
OR —	17	26	16	59
OR +	40	53	7	100
Total	57	79	23	159

Table 2. Relationship between OR-content and tumor cellularity

	+	++	+++	Total
OR —	15	19	25	59
OR +	18	31	51	100
Total	33	50	76	159

Table 3. Relationship between histological grade and cellularity

	+	++	+++	Total
1	17	16	24	57
2	13	26	40	79
3	3	8	12	23
Total	33	50	76	159

Table 4. Relationship between OR-content and elastosis

	0	1	2	Total
OR —	17	29	10	56
OR +	11	35	21	67
Total	28	64	31	123

Table 5. Relationship of OR-content and lobular and ductal carcinomas

	Ductal	Lobular	Total
OR —	56	3	59
OR +	87	13	100
Total	143	16	159

The relationship between the OR-content and the cellularity of the tumors is shown in Table 2. No significant difference is found between the cellularity of the OR-positive and the OR-negative tumors. The grade of anaplasia in relation to the cellularity is shown in Table 3 and here, too, no correlation is found. Although the OR-content appears to be independent of the degree of elastosis (Table 4), a very strong tendency toward the occurrence of a greater number of OR-positive tumors in the group rich in elastosis is found when the data is analyzed for a linear trend ($P < 0.05$). 68% of the tumors in this group are OR-positive compared to 39% in the group of tumors with

no elastic tissue. Lobular carcinomas are more frequently OR-positive ($P < 0.05$) than ductal carcinomas (Table 5). 82% of all lobular carcinomas were positive whereas the incidence in the material on the whole is 63%.

Discussion and Conclusion

In accordance with previous reports, a correlation has been found between the OR-content and the grade of anaplasia in primary mammary tumors. Highly differentiated tumors contained a significantly higher proportion of OR-positive tumors than the dedifferentiated tumors. The histological grade of the tumor in itself has previously been proven to be a prognostic factor in breast cancer (Bloom and Richardson 1957; Schiødt 1966). Knowledge of the OR-status of the tumor together with the histological grade provides an even better possible basis for a prognostic factor. No correlation has been found between the cellularity of the tumors and either the OR-content or the histological grade of anaplasia. However, others have found a tendency toward higher OR-values in tumors with high cellularity (Terenius et al 1974; Masters et al. 1978; Antoniades and Spector 1979). The fact that the cellularity of the tumor is not related to either grade of anaplasia or receptor status, while the dedifferentiated tumors are shown to be preferentially OR-negative, indicates that the absence of OR-receptors in the latter group is actually due to a loss of the ability of the tumor cells to synthesize this specific protein rather than a property of the number of tumor cells in the tissue.

Previous reports on the presence of elastosis in mammary tumor tissue have indicated that a high degree of elastosis may be correlated with the presence of oestrogen receptor (Masters et al. 1978; Maynard et al. 1978) and to a higher response rate for endocrine therapy (Masters et al. 1979). Although no significant correlation between the degree of elastosis and the OR-content is found in the present data, there is a strong tendency toward the occurrence of a greater number of OR-positive tumors among tumors rich in elastic tissue. These results resemble those of Fischer et al. (1980).

A preponderance of OR-positive tumors among lobular derived carcinomas has been found in this material, as has been the case in other studies (Rosen et al. 1975; Antoniades and Spector 1979). This relationship may be explained by the fact that it is the lobular structures in the normally functioning breast that are especially sensitive to hormonal influence.

In conclusion, correlations have been demonstrated between the OR-content and the histological grade of anaplasia and the degree of elastosis. No correlation was apparent between the degree of anaplasia and the cellularity of the tumors.

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