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ER in normal and pre-cancerous breast

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Keywords

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Introduction

Oestrogen is thought very likely to influence the pathogenesis of breast cancer and its role may relate to exposure of breast cells to oestrogen or oestrogenic compounds. Alternatively, tumours may respond abnormally to oestrogen as a consequence of changes in number, distribution or function of cells expressing the oestrogen receptor (ER).

In normal lobules, ER positive (ER+) cells account for 4-15% of the epithelium and localise as single, scattered cells surrounded by ER negative cells (ER-). In ER+ breast cancers, however, most cells are receptor-positive and ER expression appears contiguous. It is, therefore, conceivable that an increase in ER+ cells in the non-neoplastic breast, particularly when contiguous, could represent a pre-cancerous change.

Aims

To investigate the above hypothesis by comparing the number and distribution of ER+ cells in:

1) intra-luminal proliferations associated with different levels of risk of developing cancer as determined from prospective studies

2) cancerous and non-cancerous breasts

Comments

Recently there has been some controversy over the significance of ER+ cells in normal breast tissue and whether they represent a pre-cancerous state. This study found that there was no associated increased risk when ER+ cells are present and that age of the patient is clearly important when comparing risk populations. The role of increasing levels of ER in pre-cancerous in situ proliferations

remains unclear. The loss of the age-related control of ER between HUT and ADH lesions is an important observation indicating a step in the pathogenesis of breast cancer that warrants further investigation. This paper may also have important implications regarding the role of anti-oestrogens in the prevention of breast cancer.

Methods

The study population comprised 48 consecutive cancer bearing breast specimens age matched to within 1 year with 48 benign breast specimens. In addition 151 archival breast samples exhibiting the following changes were obtained: hyperplasia of usual type (HUT)(n = 38); atypical ductal hyperplasia (ADH)(n = 23); lobular in situ neoplasia (LIN)(n = 32); ductal carcinoma in situ (DCIS) of low nuclear grade (n = 26), of intermediate nuclear grade (n = 17) and gynaecomastia (n = 15).

The controls were autopsy breast tissue from 29 females. Also included were 13 reduction mammoplasty and nine autopsy male breast tissue specimens. The ER status was detected with a mouse monoclonal anti-ER antibody (clone 1D5). Immunohistochemistry was performed using a standard streptavidin-biotin method with prior microwave antigen retrieval. Contiguous ER expression was defined as 10 or more ER+ cells in contact with each other. The intraluminal proliferations were assessed for both contiguous ER expression and the percentage of ER+ cells within the lesion and the surrounding breast.

Results

In the normal pre-menopausal breast, ER+ cells comprised the minority and were distributed singly, being surrounded by ER- cells. ER+ cells showed a statistically significant increase with age reaching a plateau after the menopause and the increase was associated with a tendency for positive cells to become contiguous in patches of variable size. A small proportion of lobules showing involutional change comprised over 90% ER+ cells. The percentage of ER+ cells was slightly increased in HUT and the relationship to age was maintained. The staining pattern was variable; in some lesions ER+ cells were surrounded by ER- cells whereas in others there were contiguous groups of positive cells sometimes accounting for more than 90% of cells in the lesion. In contrast, all cases of ADH, LIN and DCIS exhibited positivity of contiguous cells accounting for the majority in the lesions. Furthermore, the relationship between the proportion of ER+ cells and age was lost in these lesions.

Discussion

An increase in the proportion and contiguity of ER+ cells in the female breast were clearly associated with age and involution. The significance of this feature is not clear but there was no evidence that it represented a pre-cancerous change. The significance of the different patterns of ER staining in HUT require further investigation. The clonal and molecular genetic status of HUTs showing contiguous and non-contiguous ER+ cells may be important in understanding their clinical significance.

As with normal breast, the proportion of ER+ cells in HUT correlated with age. In ADH and DCIS, however, the percentage of ER+ cells was very high even in younger women and the age relationship was lost. The transition from HUT to ADH seems therefore to be an escape by ER+ cells from the age-related factors which normally control receptor expression. This autonomy of ER-expressing cells may be a precursor of other molecular events which eventually lead to loss of control of cell division and cell function which characterise in situ and invasive breast carcinomas.

References

1. Shoker BS, Jarvis C, Sibson DR, Walker C, Sloane JP: Oestrogen receptor expression in the normal and pre-cancerous breast. J Pathol. 1999, 188: 237-244.