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HER2 expression during the menstrual cycle

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Keywords

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Introduction

There has been much controversy over the timing of breast cancer surgery with respect to the menstrual cycle. It has been reported that surgery performed during the follicular phase of the cycle is unfavourable when compared with surgery performed during the luteal phase. This difference may possibly be due to biological markers that fluctuate during the menstrual cycle.

Aims

To investigate whether tumour cells respond to cyclical hormone fluctuations with corresponding changes in marker expression.

Comments

This is an interesting paper that suggests that the HER2 receptor fluctuates in progesterone-receptor-positive cancers during the menstrual cycle. If true, this may be of particular importance to the introduction of the new anti-HER2 antibody therapy. However, the findings only just reached statistical significance ($P = 0.05$) and, although a similar trend was seen in oestrogen-receptor-positive cases, it is not stated whether these results were significant. This paper does raise some interesting questions; however, much larger studies will be required to answer them.

Methods

Samples from 198 consecutive premenopausal women with breast cancer, for whom the phase of the menstrual cycle was known, were obtained. These were stained using a peroxidase-streptavidin method

on Bouin-fixed, paraffin-embedded material. The antibodies used were anti-c-erbB-2 mAb cB11, anti-p53 mAb D07, anti-bcl2 mAb 100, anti-progesterone receptor mAb 1A6 and polyclonal anti-cathepsin D. The sections were considered positive when more than 5-10% of the tumour cells were labelled.

Immunostaining was also performed on a further eight hormone-receptor-positive cases that had undergone previous core or needle biopsies during the luteal phase and surgery during the follicular phase or *vice versa*.

Southern blot analysis was carried out on 23 frozen primary breast carcinomas using a [^{32}P] c-erbB-2 coding region probe. All tumours were from premenopausal women and were known to be HER2-positive by immunohistochemistry.

Results

There was no fluctuation of hormone receptor expression within tumour cells during the menstrual cycle (biochemical analysis of oestrogen receptor [ER] and immunohistochemical analysis of progesterone receptor [PR]). HER2, p53, and Bcl2 but not cathepsin D were more commonly expressed in hormone-receptor-negative cases.

In patients with PR-positive cases, HER2 overexpression was seen in 20% (10/50) of tumour samples obtained from patients operated on in the follicular phase of the menstrual cycle and in only 8% (7/84) obtained during the luteal phase (P= 0.05). A similar difference in the frequency of HER2-positivity was seen for ER-positive tumours (20% vs 11%). However, no such change was seen in the PR-negative tumours or for the markers p53, Bcl2 and cathepsin D.

Of the eight cases that had previous needle cores, two cases scored HER2-positive on the specimen removed during the follicular phase and were negative on the specimens removed during the luteal phase. The remaining six cases were either positive or negative on both samples.

Southern blot analysis showed that *HER2* gene amplification was present in 9 of 12 hormone-receptor-negative cases and in only 2 of 11 hormone-receptor-positive cases (P = 0.02).

Discussion

The frequency of expression of p53, Bcl2 and cathepsin D was found to be independent of menstrual phase during which the tumour was excised. However, an increase in the expression of HER2 was observed in hormone-receptor-positive tumours resected during the follicular phase as compared to those excised during the luteal phase of the cycle. The increase in HER2-positivity was not due to gene amplification in most cases.This finding may be important for the timing of treatment with the new anti-HER2 antibody and may also explain the increased survival of patients operated during the luteal phase.

References

1. Balsari A, Casalini P, Tagliabue E, Greco M, Pilotti S, Agresti R, Giovanazzi R, Alasio L, Rumio C, Cascinelli N, Colnaghi MI, Menard S: Fluctuation of HER2 expression in breast carcinomas during the menstrual cycle. Am J Pathol. 1999, 155: 1543-1547.