Effects of Mammary Surgery on Prolactin Secretion in Common and in Triple Negative Breast Cancer Patients

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Abstract

Despite the well documented potential stimulatory activity of prolactin (PRL) on mammary tumors, hyperprolactinemia following breast surgery has proven to be able to predict a more favourable prognosis in breast cancer. This apparent controversial result is probably due to mammary stimulation that induces PRL secretion in normal conditions, therefore the failure of PRL increase after breast surgery could reflect an alteration in the neuroendocrine control of mammary tissue growth and differentiation. On this basis, a study was planned in order to investigate the effects of breast surgery on PRL secretion in Triple Negative Breast Cancer (TNBC), which represents the most malignant subtype of mammary tumors. The study included 100 breast cancer patients treated by quadrantectomy, evaluating PRL serum levels before and 7 days after surgery. The diagnosis of TNBC occurred in 16/100 investigated patients. Postsurgical hyperprolactinemia was observed in 53/84 (63%) patients with common breast cancer and in only 2/16 (13%) TNBC patients. This difference was statistically significant. The present preliminary study, demonstrates a lower frequency of surgery-induced hyperprolactinemia in TNBC compared to the other mammary tumorhistotypes and furthermore it suggests that the more aggressive behavior of TNBC could depend to some extent on a more pronounced alteration in the neuroendocrine control of mammary tissue.

Keywords

Breast cancer, Breast surgery, Hyperprolactinemia, Prolactin, Triple negative breast cancer

Introduction

Several experimental studies have shown that prolactin (PRL) may be a growth factor for breast cancer [1-3]. Despite the well demonstrated stimulatory activity of PRL on breast cancer growth, either on its development or progression, the evaluation of PRL secretion in patients with mammary tumors is not generally taken into consideration by oncologists. The only available data concerning the relation between PRL blood concentrations and prognosis of human breast cancer refer to many years ago, and suggest that the evidence of high PRL levels is associated with a poor prognosis in all conditions [4-6]. While the occurrence of mammary surgery-induced hyperprolactinemia appear to predict a lower percentage of relapse and a longer survival [7]. This finding is not surprising, since PRL secretion has to respond to each mammary stimulation, including breast surgery. Therefore, the lack of PRL increase after mammary surgery would be a biological sign of the presence of altered neuroendocrine control of mammary tissue growth. Moreover, it is known that the most aggressive type of mammary tumor is represented by triple negative breastcancer (TNBC) [8,9], which constitutes about 15-20% of the overall mammary tumors and is characterized by the lack of expression of the three main receptors involved in the pathogenesis of breast cancer, including ER, PgR and HER-2. Furthermore, it has recently been shown that the expression of PRL receptor (PRL-R) tends to be reduced in TNBC, and the lack of PRL-R expression has appeared to predict a more aggressive disease [10]. Hence, within the group of TNBC, it would be possible to identify a more malignant sub-type of cancer characterized by negative PRL-R, thereby indicating a quadruple negative breast cancer. So far, it is known that tumor malignancy depends not only on its...
genetic characteristics, but also on the regulation of its growth by the immune and the neuroendocrine system. Therefore, it could be interesting to investigate PRL response to breast surgery in TNBC. This preliminary study was performed in an attempt to analyze PRL blood levels before and after mammary surgery in TNBC patients, by comparing the results with those observed in common breast cancer.

Patients and Methods

This study included 100 breast cancer women, who underwent breast surgery. The clinical protocol was explained to each patient, and written consent was obtained. Eligibility criteria were, as follows: Histologically proven breast cancer, breast surgery consisting in quadrantectomy, no chronic therapy with drugs stimulating PRL secretion, and no administration of anti-dopaminergic drugs for at least 1 day prior to study. PRL detection was performed on venous blood samples drawn in the morning of surgery after an overnight fast and 7 days after surgery. Serum levels of PRL were measured in duplicate with an immunoradiometric method (IRMA) using commercially available kits. Normal values of PRL for women observed in our laboratory (95% confidence limits) were less than 23 ng/ml. Data were reported as mean +/- SE, and statistically analyzed by the chi-square test and the Student’s t test, as appropriate.

Results

TNBC occurred in 16/100 (16%) patients, while the remaining 84 patients had tumor histotypes other than the TNBC. As shown in Table 1, the characteristics of the two groups of patients were well comparable for the main clinical variables, including age, performance status and menopausal status. No significant difference was seen in presurgical PRL serum levels between TNBC and common breast cancer patients post surgical hyperprolactinemia with values higher than 23 ng/ml occurred in 53/84 (63%) patients with mammary tumors other than TNBC and in only 2/16 (13%) TNBC patients. Therefore, the percentage of surgery-induced hyperprolactinemia observed in TNBC was significantly lower compared to that found in patients with less malignant histotypes (P < 0.001). PRL mean levels observed before and after surgery are illustrated in Figure 1.

Discussion

This preliminary study, carried out on a considerable number of patients, shows a reduced occurrence of surgery-induced hyperprolactinemia in TNBC patients compared to the other histotypes. Since previous studies, when the existence of the TNBC subtype was still unknown, had already shown that the lack of surgery-induced PRL increase was associated with a negative prognosis in breast cancer [7], the low frequency of surgery-induced hyperprolactinemia in TNBC could now constitute a biological sign of its greater malignancy, reflecting an altered neuroendocrine control of mammary tissue. PRL has proved to either stimulate cell

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>COMMON BREAST CANCER</th>
<th>TNBC</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>84</td>
<td>16</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>52 (29-75)</td>
<td>54 (28-73)</td>
</tr>
<tr>
<td>Median performance status (ECOG)</td>
<td>0 (0-1)</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>Postmenopausal status</td>
<td>48 (57%)</td>
<td>7 (44%)</td>
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Table 1: Clinical characteristics of patients with common or Triple Negative Breast Cancer (TNBC)

Figure 1: PRL mean levels before and after breast surgery in common and TNBC patients
proliferation in TNBC, or promote its biological differentiation [10]. Hence the post surgical levels of PRL could modulate the growth and the differentiation of potential micrometastases in TNBC. Therefore, longitudinal studies are required in order to establish whether the occurrence of post surgical hyperprolactinemia may predict a more favourable prognosis in TNBC patients.

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References