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Relationship between expression of ER, PR, Her-2, Ki-67 and neoadjuvant chemotherapy effect in breast cancer

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Abstract ***Objective:*** The purpose of the study was to investigate the relationship between the expression of estrogen receptor (ER), progestogen receptor (PR), human epidermal growth factor receptor (Her-2), Ki-67 and the effect of neoadjuvant chemotherapy in breast cancer. ***Methods:*** The expression of ER, PR, Her-2 and Ki-67 in 45 breast cancers which received neoadjuvant chemotherapy was detected by immunohistochemistry. ***Results:*** The effective rates in ER negative and PR negative groups were higher than those in ER positive and PR positive groups (83.3% vs 59. 4%, 82.4% vs 60.6%). There was no significant difference of the effective rate between Her-2 overexpressed group and Her-2 non-overexpressed group (81.8% vs 64.1%), and the same thing happened between Ki-67 negative group and Ki-67 positive group (67.7% vs 63.2%). ***Conclusion:*** In the patients with breast cancer, ER, PR negative ones were more sensitive to neoadjuvant chemotherapy. These patients may get more benefits from chemotherapy. ER, PR could be feasible markers for predicting the effective rate of neoadjuvant chemotherapy.

Key words breast cancer; neoadjuvant chemotherapy; estrogen receptor (ER); progestogen receptor (PR); human epidermal growth factor receptor (Her-2); Ki-67

The incidence of breast cancer increased dramatically these years In china. Neoadjuvant chemotherapy is extensively applicated in the treatment of breast cancer. Taxotere, epirubicin, cyclophosphamide (TAC) is one of the most commonly used regimens in neoadjuvant chemotherapy of breast cancer. The expression of estrogen receptor (ER) and progesterone receptor (PR) and human epidermal growth factor receptor 2 (Her-2) and Ki-67 for determining the prognosis of patients with breast cancer has play an important guiding role. The correlation between the expression of ER, PR, Her-2, and Ki-67 and the effection of preoperative application of TAC has been reported abroad. We studied the correlation of ER, PR, Her-2 and Ki-67 and the affection of preoperative use of TAC of 45 breast cancer patients from June 2011 to May 2013 in our hospital (The Affiliated Hospital of Qingdao University, China).

Materials and methods

We studied 45 breast cancer patients from June 2011 to May 2013 in our hospital (The Affiliated Hospital of Qingdao University, China), 22 patients were of phase II, 23 were of phase III. Median age was 49 years. Premenopausal and perimenopausal cases were 32, postmenopausal cases were 13. There were no distant metastases examined by Chest X-ray, ultrasound, ECT, and other auxiliary examination. These patients had not received endocrine therapy, radiation or chemotherapy previously.

The patients before treatment were diagnosed by tubular needle biopsy, for 2–4 cycles of TAC chemotherapy, 21 d for a cycle, the surgery performed after chemotherapy 10–15 days . Preoperative chemotherapy was expected to four cycles, evaluated by ultrasound and mammography every 2 cycles. When disease progressed, we changed chemotherapy scheme or surgery. We reduced 10% dosage the second cycle when granulocyte less with fever after 1 cycle, and to give the prophylactic use of granulocyte colony stimulating factor. Chemotherapy after surgery, 10–20 days after 2–3 weeks postoperative adjuvant chemotherapy (a total of 6–8 cycles). We performed before and after chemotherapy of breast ultrasound examination and check with mammography.

Ejection type tubular needle biopsy in patients with normal in the supine position, according to the result of breast ultrasound and mammography in breast skin

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surface marking the puncture point, regular disinfection, local infiltration anesthesia, 2% lidocaine application specifications for 14 g tubular needle, operator skill fixed punctured the skin, hand to tubular needle into the tumor, start the ejection device, instantaneous cutting, for 3–5 elongated specimen. Specimens for histological detection. Hollow needle biopsy and surgical excision specimens were both conventional paraffin embedding, sectioning, conventional HE staining and immunohistochemical S-P method, ER, PR, Ki-67 and Her-2. Rat anti human ER, Ki-67 single resistance, rabbit anti-human Her-2 and immunohistochemical kit buy from Zhongshan Reagent Company (China).

Curative effect evaluation

Clinical evaluation according to curative effect evaluation standard of solid tumor (RECIST 1.0) was divided into: complete remission (CR): clinical examination within tumor; partial response (PR): maximum length to diameter combined tumor shrink by more than 30%; Progressive diseases (PD): with the minimum value compared with the maximum length to diameter combined tumor increased by more than 20%; stability (stable disease, SD): couldn't met the partial response and couldn't met the PD was defined as the SD; (CR + PR) / total × 100% efficient (response rate, RR). Pathological complete response (PCR) was defined as no invasive residual tumor in primary breast tumors and no lymph node lesions residue. If there was any lymph node metastasis, invasion of primary tumor without STD stove for primary focal complete remission (tumor-pCR).

Results

Forty-five cases were treated by neoadjuvant chemotherapy, after complete remission in 7 cases (15.5%) and partial in 23 cases (51.1%), 11 cases (24.4%) in a stable condition, illness development 4 cases (8.8%), PCR in 3 patients (6.6%), adopting the new adjuvant chemotherapy after treatment, the ER (–), a total of 18 cases, of which 15 cases clinical effectiveness, the effective rate was 83.3%; ER (+) was 27 cases, including 16 cases of clinical effectiveness, the effective rate was 59.2% (–) PR, a total of 19 cases including 16 cases of clinical effectiveness, the effective rate was 84.2%; PR (+), a total of 26 cases, including 15 cases clinical effectiveness, the effective rate of 57.6%, its Her-2 was a express, a total of 29 cases, including 20 cases clinical effective and effective rate was 68.9%; its Her-2 overexpression of 16 cases, including 11 cases of clinical effectiveness, the effective rate of 68.7%, Ki-67 (-), a total of 29 cases, 21 cases of clinical effectiveness, effective rate was 72.41%; Ki-67 (–), a total of 16 cases, among which, 10 cases were clinically effective, effective rate of 68.7% above, all tests negative patients compared with patients with positive, in addition to its Her-2 did not appear significant differences ($P < 0.05$) other negative patients significantly increased efficiency, compared with the positive difference had statistical significance ($P < 0.05$; Fig. 1–8).

Discussion

Neoadjuvant chemotherapy in the treatment of breast cancer can reduce tumor classification, increase operation chance, reduce primary lesions. To eliminate small metastases, reduce transfer opportunities. We can also through the new adjuvant chemotherapy tumor sensitivity to chemotherapy regimens, tumor of the curative effect of chemotherapy, judged whether by reflecting the efficacy of cancer chemotherapy sensitivity index to provide more accurate basis for postoperative adjuvant chemotherapy. ER, PR, Her-2 and Ki-67 is closely related to the occurrence, recurrence and metastasis of breast cancer as immunohistochemistry markers. In patients with hormone-dependent breast cancer, ER and PR in tumor growth, differentiation and proliferation has obvious control effect, while the PR protein synthesis and is regulated by the ER. A lot of research has confirmed that good breast cancer cell differentiation and development slower for ER positive patients, application of endocrine therapy effect is better, and ER negative patients with cancer cell differentiation is poorer, progress faster, endocrine therapy is poor, high risk of recurrence patients have more chance to benefit from chemotherapy. Therefore, ER and PR can be used as more reliable indicators of hormone therapy [1], our results showed that, the total effective rate was 66.6%, RR of ER and PR negative group was higher than the positive group, there was statistically significant difference ($P < 0.05$) consistent with the above conclusion basic. Therefore, we believe that the new adjuvant chemotherapy can kill receptor negative breast cancer cells, increase hormone receptor expression after neoadjuvant chemotherapy.

Research has shown that Her-2 gene amplification can block certain cells apoptosis induced by chemotherapy, and Her-2 expression of patients are more sensitive to anthracycline-based drugs. Penault-Liorea F [2] think that Her-2 is an endogenous tyrosine kinase activity of transmembrane receptor glycoprotein, belongs to the epidermal growth factor receptor family. Most studies suggest that its Her-2 expression and amplification tumor cell proliferation activity to strengthen the malignant degree of increase, is breast cancer especially with regional lymph node positive breast cancer prognosis evaluation and hormone receptor expression is more valuable than the clinical stages of independent index [3]. In this study, it was clinical effective in 20 cases (68.9%) in Her-2 none over expresser, it's clinical effective in 11 cases (68.7%) in

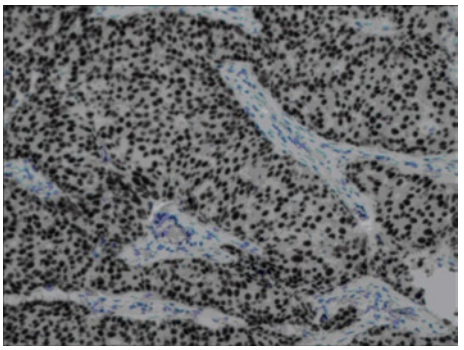

Fig. 1 ER expression before neoadjuvant chemotherapy

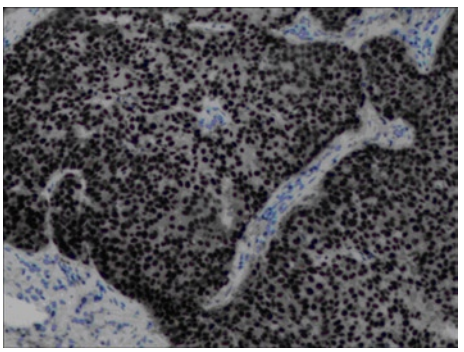

Fig. 2 ER expression after neoadjuvant chemotherapy

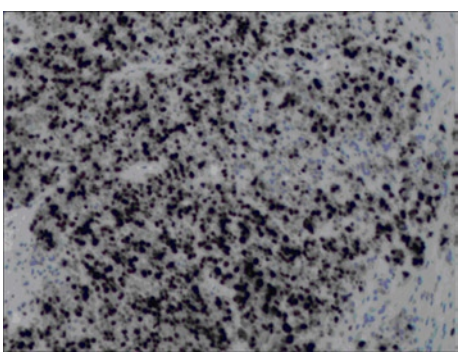

Fig. 3 PR expression before neoadjuvant chemotherapy

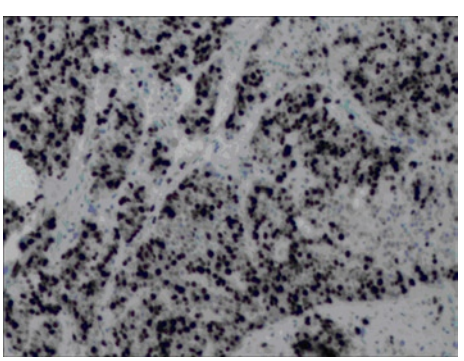

Fig. 4 PR expression after neoadjuvant chemotherapy

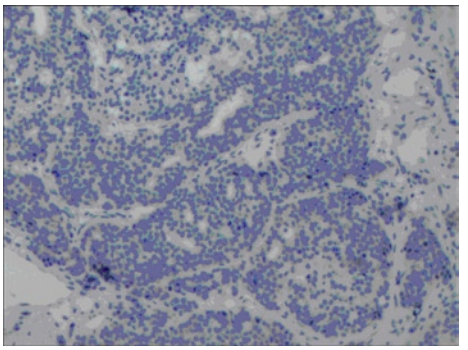

Fig. 5 Her-2 expression before Neoadjuvant chemotherapy

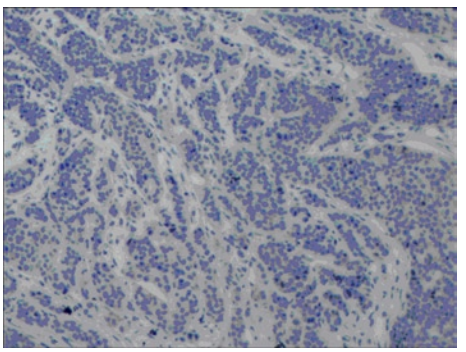

Fig. 6 Her-2 expression after neoadjuvant chemotherapy

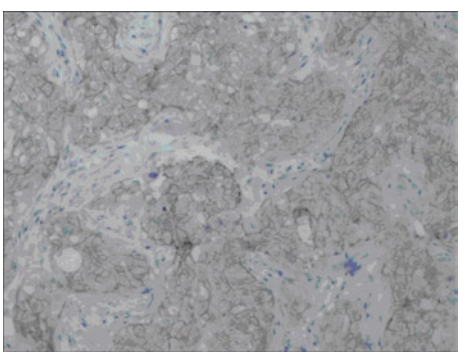

Fig. 7 Ki67 expression before neoadjuvant chemotherapy

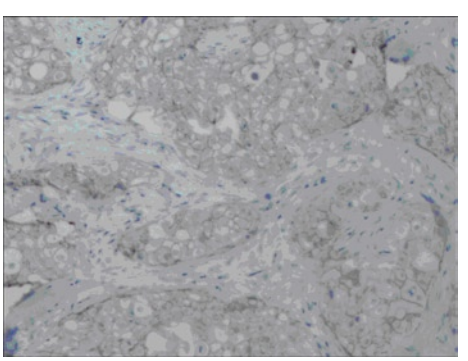

Fig. 8 Ki67 expression after neoadjuvant chemotherapy

Her-2 expresser, and there was no statistically significant difference between the two groups ($P > 0.05$), indicating that Her-2 expression was no relevant with the treatment effect.

Ki-67 is a cell mitosis period increased significantly, the late falling fast reaction cell proliferation of antigen, Ki-67 dyeing ratio increases, tip cell proliferation activity. There are a lot of clinical trials in the neoadjuvant chemotherapy is discussed Ki-67 level and curative effect, the relationship between the positive node is not the same (1%–40%), elevated level of Ki-67, clinical CR and higher proportion of pCR [4]. Ki-67 neoadjuvant chemotherapy is the best clinical response index (20%) [5]. High Ki-67 express is relatively easy to achieve CR [6], our study shows that after neoadjuvant chemotherapy, effectively improve Ki-67 negative patients with chemotherapy, and the expression of Ki-67 before and after neoadjuvant chemotherapy changed dramatically, prompt high Ki-67 expression can be used as chemotherapy sensitivity index. Therefore, breast tumor tissue estrogen and progesterone receptor and Ki-67 expression can be used as a prediction index, the efficacy of neoadjuvant chemotherapy of breast cancer make chemotherapy individualized treatment, patients will benefit from chemotherapy [7].

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