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Analysis of HER2 Gene Amplification and Certain Prognostic Factors in Breast Cancer

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Abstract: Objective: The HER2 gene amplification and certain prognostic factors in breast cancer were analyzed. Method: The gene amplification and protein expression of human epidermal growth factor receptor in 100 breast cancer tissues detected by FISH and IHC detection method in the hospital from January 2020 to December 2021 were analyzed. To analyze some breast cancer prognostic factors. Result: 0 is 8 cases of HER-2 protein breast cancer, (1+) is 11 cases, (2+) is 49 cases, (3+) is 32 cases. The HER2 gene was amplified in 49 cases, of which 23 cases showed red signals in clusters, and 26 cases showed red signals in dots. 51 cases of HER-2 gene were not amplified. There are differences in the detection results of FISH and IHC detection methods (P＞0.05). ER, PR and polysomy of chromosome 17 are prognostic factors associated with HER2 gene amplification in certain breast cancers. (P＜0.05) Conclusion: To analyze the HER2 gene amplification in breast cancer and targeted select FISH and IHC detection methods can improve the therapeutic effect and prognostic factor, which deserves clinical attention.

Keywords: Breast Cancer; HER2; Gene Amplification; Prognostic Factors

Introduction

Breast cancer is an uncontrolled proliferation of mammary epithelial cells under the action of various carcinogenic factors. Breast cancer has become the number one killer of women's health. The HER2 gene is an epidermal growth factor, and HER2 gene amplification indicates that the tumor has a higher degree of malignancy than non-amplified tumors. HER2 gene amplification is a gene infiltration of breast cancer and is a key gene marker for the diagnosis of breast cancer. Some scholars found that breast cancer patients with HER2 gene amplification are resistant to certain chemotherapy drugs. The prognosis of patients is poor, and recurrence and metastasis occur earlier, which directly affects the overall survival of patients.[1] At present, HER2 gene amplification has been used as an important reference for judging the prognosis of breast cancer. Therefore, by taking effective methods to detect the HER2 gene amplification in breast cancer, it can directly provide the best treatment and prognosis for patients. The details are as follows:

1. Data and Method

1.1 General Data

The gene amplification and protein expression of human epidermal growth factor receptor in 100 breast cancer tissues detected by FISH and IHC detection method in the hospital from January 2020 to December 2021 were analyzed. To analyze some breast cancer prognostic factors. The 100 patients were all female, with an age range of 28 to 72, and an average age of 44.32±3.33. Inclusion criteria: ① All patients were aware of the study and agreed. ② All patients had breast cancer. ③ The patients were all female. Exclusion criteria: ① The medical history data is incomplete.

1.2 Method

FISH Detection Method: All patients were detected by Fluorescence in Situ Hybridization. First, fix the sample, do

sample preparation, pre-treatment and pre-hybridization. We do a good job of denaturing probes and samples, and use different probes to hybridize to detect different target sequences. Unbound probes are removed by washing, the hybridization signal is detected, and the results are analyzed.

IHC Detection Method: They were fixed in 4% central formaldehyde, embedded in conventional paraffin, sectioned at 4um, and stained with HE. Immunohistochemical staining was performed by MaxVision method, and primary antibodies were ER, PR and HER-2.

1.3 Observation Target

Analysis of HER-2 protein and HER-2 gene.

The HER-2 gene was analyzed by FISH and IHC detection methods.

The relationship between some prognostic factors of breast cancer HER2 gene amplification was analyzed from the aspects of age, histological grade, lymph node metastasis, ER, PR and polysomy of chromosome 17.

1.4 Statistical Method

The data were included in SPSS 20.0 software for analysis, measurement data were compared using t test, and represented by ($\bar{x} \pm s$), and rate count data were examined by $\chi 2$ test, which was represented by rate (%), ($P<0.05$) was considered to be significantly different, with statistical significance.

2. Result

2.1 Analysis of HER-2 protein and HER-2 gene

HER-2 protein: In breast cancer, 0 is 8 cases, accounting for 8%; (1+) is 11 cases, accounting for 11%; (2+) is 49 cases, accounting for 49%; (3+) is 32 cases, accounting for 32%.

HER-2 gene：The HER-2 gene was amplified in 49 cases, of which 23 cases showed red signals in clusters, and 26 cases showed red signals in dots. 51 cases of HER-2 gene were not amplified.

2.2 Analysis of FISH and IHC test results

IHC detection: (0~1+) 18 cases, (2+) 34 cases, (3+) 6 cases. FISH detection: (0~1+) 4 cases, (2+) 20 cases, (3+) 18 cases. Two groups (0~1+) ($X^2=10.010$, P=0.002), (2+)（$X^2=4.972$，P=0.026), (3+) ($X^2=6.818$, P=0.009). The data show that there are differences in the detection results of the FISH detection method and the IHC detection method. (P>0.05)

2.3 Analysis of the relationship between some prognostic factors of HER2 gene amplification in breast cancer

The data showed that age, histological grade, and lymph node metastasis were not significant($P>0.05$), ER、 PR and polysomy of chromosome are prognostic factors associated with HER2 gene amplification in some breast cancers. ($P<0.05$) .Table 1 shows that.

Table 1 **Analysis of the relationship between some prognostic factors of HER2 gene amplification in breast cancer [n,(%)]**

Groups	cases	-	+	χ^2	P
Age（years）					
<50	49	26	23	0.243	0.622
≥50	51	27	24		
Histilogical grade					
I					
II	9	5	4	0.116	0.733
III	77	45	32		
ER	14	9	5		
-					
+	33	11	22	4.391	0.036
	45	30	15		
PR					
-	35	11	24	5.853	0.016
+	43	31	12		
polysomy of chromosome 17					
-					
+	76	45	31	4.160	0.041
	24	7	17		
lymph node metastasis					
exist	55	26	29	0.226	0.635
absent	45	22	23		

3. Discussion

Human epidermal growth factor receptor 2 over-expression is closely related to the degree of cancer progression in more epithelial cells. Tumors with high HER2 expression show strong metastatic ability and infiltration ability, are less sensitive to chemotherapy, and are extremely prone to recurrence. When the normal HER2 expression level is low, the expression level is high during embryonic development, which plays an important role in cytoplasmic proliferation, differentiation and migration during development. Abnormalities of the HER2 gene have been found in breast, ovarian, and gastrointestinal cancers. In HER2 breast cancer, over-expression is generally detected by immunohistochemistry.[2] Gene mutations are detected by gene sequencing.Gene amplification was detected by in situ fluorescence hybridization. Generally, the HER2 gene is amplified at the DNA level, which is almost manifested in protein over-expression, which can be confirmed in breast cancer. Breast cancer HER2 gene amplification rate will reach 15% to 20%, overexpression will reach 15% to 20%.[3]

FISH detection is an in situ fluorescence detection technology, that is, a specific labeled nucleic acid with a known sequence is a process in which the probe hybridizes with the nucleic acid in the cell or tissue section, so as to accurately quantitatively locate the specific nucleic acid sequence. In situ fluorescence detection technology does not require radioisotope labeling, and can simultaneously detect multiple sequences in the same sample through different labeled probes.[4]In situ fluorescence detection techniques take direct and indirect labeling methods. The direct labeling method means that fluorescein is directly covalently bound to the probe nucleotide or pentose phosphate backbone, or that fluorescein

nucleoside triphosphate is incorporated when the probe is labeled by the nick translation method. The indirect labeling method means that the DNA probes are labeled with biotin and detected with fluorescein or streptavidin after hybridization. At the same time, the avidin-biotin-fluorescein complex can also be used to amplify the fluorescent signal. FISH testing is used to examine chromosome 17 centromere and HER-2 gene amplification in breast cancer. FISH detection has high sensitivity and specificity, and is an effective clinical detection method.[5] IHC is an immunohistochemical assay. Since the 1970s, immunohistochemistry has been used in pathological diagnosis, which has a great impact on tumor diagnosis and prognosis. At the same time, it also expands people's understanding of various diseases and tumor formation processes, and improves the level of pathological diagnosis and research. The samples for immunohistochemistry are mainly frozen or paraffin-embedded tissues. The tissue was sliced into slices about 4μm thick and sealed before processing. Pathological diagnosis means performing histological examination under the microscope after the tumor specimens removed by surgery or autopsy are fixed and stained to facilitate the diagnosis of the disease. [6] IHC immunohistochemistry is a common clinical detection method for HER-2 receptor protein. IHC is simple to operate and has low cost. However, in the detection process, protein fixation specimens and processing are very easy to be damaged, resulting in lower detection accuracy. FISH detection has good stability and repeatability, and can be clearly displayed by microscope, which can make up for the shortcomings of IHC detection. This study analyzed the HER2 gene amplification in breast cancer and some prognostic factors of breast cancer. The result shows that, in the protein breast cancer, 0 is 8 cases of HER-2，(1+) is 11 cases of HER-2, (2+) is 49 cases of HER-2, (3+) is 32 cases of HER-2. The HER-2 gene was amplified in 49 cases, of which 23 cases showed red signals in clusters, and 26 cases showed red signals in dots. 51 cases of HER-2 gene were not amplified. There are differences in the detection results of the FISH detection method and the IHC detection method. ($P > 0.05$). ER 、 PR and polysomy of chromosome are prognostic factors associated with HER2 gene amplification in some breast cancers. ($P < 0.05$) . For the prognostic factors of HER-2 gene amplification in breast cancer, it is believed that there is no relationship with age, histological grade, and lymph node metastasis, but there is a certain relationship with EP, PR and polysomy of chromosome 17. Therefore, in order to ensure the outcome of patients, targeted measures should be taken according to the actual influencing factors.

All in all, analysis of the HER2 gene amplification in breast cancer and targeted select FISH and IHC detection methods can improve the detection accuracy and indirectly improve the treatment effect, which is worthy of clinical attention.

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