

The Expression of PS2 Protein in Breast Cancer and its Clinical Significance

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Abstract Objective To study the expression of PS2 protein in breast cancer and the relationship with patient's clinical character. **Methods** PS2 protein was examined by immunohistochemistry in 50 patients with breast cancer. **Results** The intensity of PS2 expression was directly related with histological types, tumor size, lymph nodes metastasis, distant metastasis, pathological grade and ER expression. **Conclusion** PS2 can be used as one of the prognostic factors of breast cancer.

Key words PS2; breast cancer; prognostic factor

The incidence of breast cancer tends to increase year by year and it has been known that some oncogene and suppressive oncogene had relatively special association with breast cancer. We studied the expression of PS2 protein in breast cancer using immunohistochemical method in order to probe the relation between cancer. PS2 protein and biological behavior of breast cancer.

MATERIAL AND METHODS

Specimens collection

The specimens of breast cancer were obtained from archived tissue specimens of surgically resected tumors from 50 patients treated in Changhai Hospital. The study population completely consisted of females. The mean age of patients was 47. All the patients had never undergone chemotherapy and radiotherapy before operation. Histological classification is adopted according to WHO standard of histological classification in breast cancer.

Reagents and immunohistochemical staining

We adopted immunohistochemical method. A mouse monoclonal anti-human PS2 protein antibody was bought from Beijing Zhongshan Biotechnological Limited Corporation. 4 μ m thick tissue sections were placed on positively charged slides, heat in a 60°C oven for 30 minutes and underwent microwave according to the condition of first antibody. Slides were incubated in a 3% hydrogenperoxide-methanol solution to reduce endogenous peroxidase activity, followed by incubation in 40°C refrigerator with anti-human PS2 protein antibody

(1:50) overnight. Then the slides were incubated with biotin-labelled antimouse IgG for 30 minutes each, followed by DAB staining, haematoxylin staining nucleus, dehydrating, clearing and mounting. PBS substituting for first antibody were used as negative controls and positive controls were breast cancer tissue sections known as positive.

Judgement of results

Positive cells: Positive signals were shown in cytoplasm. If there are more than 20 percent positive cells in breast cancer sections, the results are regarded as positive, or else negative.

Statistical analysis

Chi-square test was used to analyze the comparison of rate.

RESULTS

PS2 expression in breast cancer

We found PS2 immunoreactivity in 52 percent (n=26) of all breast cancer sections tested.

Relations between PS2 expression and clinicopathologic features of breast cancer

Patients of carcinoma in situ expressed more PS2 than those of infiltrating lobular carcinoma and infiltrating ductal carcinoma ($P < 0.05$). Pathological grade I + II showed significant differences with grade III ($p < 0.05$). And the diameters of tumor were statistically significantly associated with PS2 expression ($P < 0.05$). The dif-

Table 1 Relations between PS2 expression and clinicopathologic features of breast cancer

	N	Rate of PS2 Positive	Chi-sprare value	P
Histological type				
Carcinoma in situ	3	3(100%)*		
Infiltrating lobular carcinoma	15	11(73.33%)*	8.201	<0.05
Infiltrating ductal carcinoma	32	12(39.79%)		
Pathological grade				
I + II	26	18(69.23%)*		
III	24	8(33.33%)	6.443	<0.05
Tumor diameter				
<2cm	8	7(87.5%)*		
2-5cm	25	13(52%)*	5.949	<0.05
>5cm	17	6(35.29%)		
Axillary nodes				
-	25	19(76%)**		
+	25	7(28%)	11.538	<0.01
Distant metastasis				
-	31	21(67.74%)**		
+	19	5(26.32%)	8.099	<0.01
Estrogen receptor				
-	26	18(75%)**		
+	26	8(30.77)	9.782	<0.01

* $P < 0.05$ ** $P < 0.01$

ferences between the status of axillary nodes in breast cancer and PS2 expression reached statistical significance ($P < 0.01$). And the same relation was also seen in the status of distant metastases and ($p < 0.01$) ER seeing in table 1

DISCUSSION

PS2 protein as a member of the family of trefoil proteins, was discovered in the MCF-7 oestrogen-dependent breast cancer cell lines. PS2 gene located on chromosome 21q, comprises 3 exons and 2 introns. PS2 protein is composed of 84 amino acid residues and its structure is similar to insulin-like growth factors and the spasmodic polypeptide extracted from the porcine insulin. The latter has growth-stimulating effects on MCF-7 breast cancer cell lines^[1]. Some studies have shown PS2's functions such as gathering mucus, stimulating cellular motility, cellular proliferation/differentiation^[2] and neuropeptide.

PS2 protein in normal tissues is mostly expressed in epithelia of gastric mucosa, few in breast, endometrium and conjunctivas^[4]. PS2 protein in malignant tissues is expressed in carcinomas of stomach, pancreas, colorectum, ovary with mucus differentiated, bladder and prostate. Wang^[5] analyzed the expression of PS2 protein in a series of 236 human neuro-endocrine tumors and

PS2 immunoreactivity was detected in 42% of small cell lung carcinomas, 36% of lung carcinoids, 33% of pheochromocytomas, 38% of carotid-body tumors, 31% of pancreatic neuro-endocrine tumors, 60% of stomach carcinoids. No pituitary tumors displayed PS2 protein expression. Most research indicated that there were significant association between PS2 expression and ER/PR status. Statistical analysis showed significant correlation between PS2 expression and the response to endocrine therapy. Patients with PS2-positive carcinomas had a better total survival time and disease-free survival than those with PS2-negative carcinomas. Consecutive expression of PS2 protein indicated improved prognosis and can be regarded as an indicator to receive hormonal therapy in breast cancer^[6,7].

In the study, the rate of PS2-positive is 52 percent, similar to the literatures documented. The intensity of PS2 protein was directly related with histological type, tumor size, lymphnodes metastasis, distant metastasis, pathological grade and ER expression. PS2 expression were significantly different between lobular carcinomas and ductal carcinomas. The prognosis of PS2-positive patients were better than that of PS2 negative. In summary, PS2 can be used as a prognostic factor in breast cancer.

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