Correlation analysis on serum tumor markers of breast cancer patients with brain metastases and the clinicopathological factors

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Abstract: Objective: To analyze the correlation between serum tumor markers of breast cancer patients with brain metastases(CEA, CA125 and CA153) and the clinicopathological factors. **Method:** In Jiang Su Cancer Hospital, 166 cases of breast cancer patients with brain metastases were chosen from August, 2007 to August, 2013. Analyze the level of CEA, CA125 and CA153 in serum, and evaluate their correlation with the clinicopathological factors. **Result:** The survival time of the patients was 0.3-32.7 months (mean 9.5 months), one-year survival rate was 41.6%, and two-year survival rate was 7.2%. In serum, the positive express rate of CEA was 43.4% (72/166), CA125 was 44.6% (74/166), and CA153 was 51.8% (86/166). The multiple brain metastases were related to high serum CA153; PS score, multiple brain metastases and concomitant extracranial metastasis were all relate to CA125; the prognosis effect of patients whose serum CEA less than 5ng/ml was better than those CEA over 5ng/ml, the median survival time of the former was 13.1 months, and the later was 6.0 months; taken 35U/ml as boundary, the prognosis effect of patients whose CA125 less than this value was better than those patients whose CA125 over this value, and the median survival time of the former was 16.8 months, the later was 6.9 months, which was statistical significance ($P<0.05$). The multifactor analysis showed that the independent factors which influence the prognosis effect of breast cancer patients with brain metastases were therapeutic method of brain metastases, PS score, and the express level of CEA. The discrepancies of the three were statistical significance ($P<0.05$). **Conclusion:** Breast cancer patients with brain metastases' CA125 and CA153 express levels are correlate to its clinicopathologic feature; the express levels of CEA, CA125 are closely relate to the prognosis; the independent factors which influence the prognosis effect of breast cancer patients with brain metastases are CEA that whose high express level has bad effect to patient.
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1. Introduction

There is report that 10% -16% breast cancer patients have symptomatic brain metastases, and 18-30% breast cancer patients have brain metastases based on the autopsy [1]. The home and abroad studies point out that some scholars ever analyzed and described the prognostic factors and clinicopathologic features of breast cancer patients with brain metastases, but only limit to primary tumor condition, age, the express condition of hormone receptor (estrogen receptor, human epidermal growth factor receptor 2 and progesterone receptor) and extracranial metastasis condition [2-3]. However, the prognosis evaluation studies about tumor marker carcino-embryonic antigen CEA, carbohydrate antigen 125 (CA125) and carbohydrate antigen 153 (CA153) in serum of breast cancer patients with brain metastases were not much[4]. From August, 2007 to August, 2013, 166 cases of breast cancer patients with brain metastases were chosen from our hospital, and were analyzed the level of CEA、CA125 and CA153 in their serum. The report is as follow.

2. Material and Method

2.1 Material

All the 166 cases of breast cancer patients with brain metastases were female, aged 26-79 years old (mean 49.2 ±3.6 years old), the pathological tissue biopsy diagnosed with breast cancer, cranial CT or MR inspection diagnosed with brain metastases.

2.2 Method

Excluded 14 cases patients have developed to Ⅳ stage, the rest patients in I~III stages were received modified radical mastectomy or radical surgery, and 2 cases received breast conserving therapy. Among 166 patients, 120 cases implemented adjuvant chemotherapy or neoadjuvant chemotherapy, and 104 cases implemented radiotherapy. When discovered the appearance of brain metastases, 94 cases implemented whole brain radiotherapy, 118 cases implemented systemic chemotherapy, 12 cases implemented targeted drug-herceptin treatment, and 16 cases implemented resection of brain metastases. Collected all the patients' medical records, brain metastases time, ER, PR, HER-2 express situation, PS score of brain metastases,

numbers of brain metastases, levels of serum CEA, CA125 and CA153 when brain metastases happens, and lactate dehydrogenase level, etc, as table 1. Follow-up visit was implemented when diagnosed with breast cancer. Every patient may be followed by telephone or clinic ways, and the follow-up time was 6.2-170.0 months (mean 41.0 months). Calculated the survival rate and the lifetime when patients were diagnosed with brain metastases.

Table 1. Clinicopathologic features and single factor survival analysis of 166 cases of breast cancer patients with brain metastases

Items	Constituent ratio (%)value	Median survival time (month)	95% CI	P
Age (year)				
<40	24.1	13.1	7.1~19.0	
40~60	63.9	8.1	6.2~9.9	0.775
≥60	12.0	7.4	0.0~18.1	
Pathological type				
Invasive ductal carcinoma	86.7	9.3	6.3~12.3	
Invasive lobular carcinoma	4.8	3.0	0.0~12.3	0.294
Else	8.5	13.1	12.8~13.3	
Numbers of brain metastases				
Solitary	33.7	20.0	16.5~23.5	0.000
Multiple	66.3	6.9	4.3~9.5	
PS score				
≤1	42.2	20.0	16.5~23.6	0.000
>1	57.8	5.5	3.0~ 8.0	
Extracranial metastasis				
Without	34.9	16.8	10.8~22.9	
Bone or lymph node	15.7	6.9	1.5~12.2	0.117
Multiple metastases with viscera	49.4	8.1	5.2~10.9	
Treatment				
Symptomatic	18.1	0.9	0.7~1.2	
Chemotherapy or radiotherapy	22.9	8.0	5.5~10.5	0.000
Chemotherapy and radiotherapy	49.4	12.5	9.3~15.7	
Operation	9.6	18.8	10.9~26.6	
ER				
Negative	52.4	8.0	5.9~13.4	0.870
Positive	47.6	12.0	8.2~15.9	
PR				
Negative	68.3	9.3	5.1~13.5	0.579
Positive	31.7	9.6	4.0~15.2	
HER-2				
Negative	60.5	11.7	7.3~16.1	0.082
Positive	39.5	8.0	3.5~12.6	
SerumCEA (ng/mL)				
≤5	56.6	13.1	7.5~18.6	0.000
>5	43.4	6.0	3.2~8.9	
SerumCE125 (U/mL)				
≤35	55.4	16.8	11.2~22.4	0.001
>35	44.6	6.9	4.3~9.4	
SerumCE153 (U/mL)				
≤25	48.2	12.0	5.4~18.6	0.060
>25	51.8	8.1	5.8~10.4	
SerumLDH (U/L)				
≤300	60.2	14.5	7.7~21.3	0.006
>300	39.8	7.2	2.4~12.0	

2.3 Statistical Method

Using SPSS14.0 system software; and using percentage to describe clinicopathologic feature; correlation study between the express levels of serum CEA, CA125 and CA153 and clinicopathologic feature of breast cancer patients when brain metastases happens using X^2 test; multiple-factor analysis using proportional hazard model; and $P<0.05$ is considered statistical significance.

3. Result

The survival time of the selected patients was 0.3~32.7 months (mean 9.5 months), the one-year

survival rate was 41.0 % and two-year survival rate was 7.2 %. The positive express rate of serum CEA was 43.4% (72/166), CA125 was 44.6% (74/166), and CA153 was 51.8% (86/166). Multiple brain metastases was relate to serum CA153, P<0.05; PS score, multiple brain metastases, and associated extracranial metastasis were all relate to CA125, P<0.05; the prognosis effect of patients whose serum CEA less than 5ng/ml was better than those whose CEA over 5ng/ml, the median survival time of the former was 13.1 months, and the later was 6.0 months, p=0.000; taken 35U/ml as boundary, the prognosis effect of patients whose CA125 less than this value was better than those patients whose CA125 over this value, and the median survival time of the former was 16.8 months, the later was 6.9 months, p=0.001.The multifactor analysis showed that independent factors influence the prognosis effect of breast cancer patients with brain metastases were therapeutic method to brain metastases, PS score, and the express level of CEA; and the differences among the three were statistical significance (P<0.05), as table 2.

Table 2. Multi-factorsurvival analysis of 166 case breast cancer patients with brain metastases

Items	Assignment	B	SE	P value	Exp (B)	95%CI
Treatment method						
Symptomatic/ Chemotherapyorradiotherapy/ Chemotherapy and Radiotherapy/operation	1/2/3/4	-0.686	0.171	0.000	0.503	0.359~0.703
CEA (ng/mL)						
≤5/>5	0/1	0.601	0.262	0.022	0.824	1.091~3.050
PS score						
≤1/>1	0/1	2.722	0.438	0.000	15.217	6.454~35.87

4. Discussion

Yerushalmi, etc scholars analyzed 1656 cases metastatic breast cancer patients, and came to the conclusion that the higher of the level of CEA, CA125, and CA153 in serum, the worse of the prognosis, the correlation between the high-level of molecular subtypes of CEA, CA125, and CA153 and metastatic sites was not obvious[5]. For the amount of patients with brain metastases were less, Yerushalmi, etc's study could not strongly prove the relation between tumor markers and prognosis, and between tumor markers and clinicopathologic features. Arrieta, etc scholars considered that high express of CEA in serum was the independent prognosis factor and risk factor of lung cancer patient had brain metastases; CEA express on the surface of tumor cell may be the physiological and pathological mechanism leading to brain metastases[6]. Currently, the Japanese studies showed that CEA level in serum was independent factor that influences the associated death of colon cancer patient with brain metastases, but for those patients whose CEA were less than 50ng/ml, the prognosis effect were better [7-8]. This research results showed the prognosis effect of patients whose serum CEA level less than 5ng/ml was better than those CEA over 5ng/ml, the median survival time of the former was 13.1 months, and the later was 6.0 months, p=0.000.

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In conclusion, treatment method to breast cancer patients with brain metastases, PS score and level of CEA in serum when brain metastases happens are important factors influence the prognosis effect. In recent years, there are significant progresses in the study of breast cancer, but about the prognosis effect of patients had brain metastases is still not good. To study the prognosis factors of brain metastases patients is still a hot issue in clinic, especially for those can indicate better prognosis effect for brain metastases patients, which need active treatment. The DEA level in serum tumor marker is clinical significant for the brain metastases patients' prognosis effect evaluation.

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