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The application value of the detection of the level of tissue polypeptide antigen, ovarian cancer antigen X1, cathepsin L and CA125 on the diagnosis of epithelial ovarian cancer

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Abstract. – OBJECTIVE: We investigated the value of the joint detection of tissue polypeptide antigen (TPA), ovarian cancer antigen X1 (OVX1), cathepsin L (CTSL) and CA125 on the early diagnosis of epithelial ovarian carcinoma (EOC).

PATIENTS AND METHODS: From October 2011 to February 2015, 84 cases of patients under surgical treatment of epithelial ovarian cancer, 98 cases of patients with benign epithelial ovarian tumor and 51 subjects in healthy control group were selected to detect the level of TPA, OVX1 and CTSL in serum from the Obstetrics and Gynecology Department of the First Affiliated Hospital of Liaoning Medical University. The clinical data of patients with ovarian tumor were collected and analyzed, and the levels of CA12 were measured.

RESULTS: 3 indicators in the malignant group were significantly higher than those in the benign group and healthy control group ($p < 0.05$). The total positive rate and the positive rate of early detection of TPA on EOC were the highest, and the total positive rate of OVX1 was lower than that of CA125. The total positive rate and the positive rate of early detection of CA125+TPA on EOC were the highest. The positive rate of early detection and the total positive rate of the pairwise combined detection of the other index and CA125 on EOC were significantly higher than those of the single detection of CA125 ($p < 0.05$). The joint detection of CA125+ OVX1 and the single detection of CA125 were not statistically significant. However, the remaining differences were statistically significant ($p < 0.05$).

CONCLUSIONS: The level of TPA, OVX1 and CTSL in serum was potential detection index, the joint detection of TPA and CA125 was the ideal combination, which took into account the total positive rate, the positive rate of early detection on EOC and the improved diagnostic rate of EOC.

Key Words:

Carbohydrate antigen 125, Epithelial ovarian cancer, Tissue polypeptide antigen, Ovarian cancer antigen X1, Cathepsin L.

Introduction

The malignant ovarian tumor is one of the most malignant tumors and can seriously threaten a woman's life. Ovarian epithelial carcinoma accounts for 90% of malignant ovarian tumors because it does not exhibit typical early symptoms and there is a lack of early diagnosis method that is both sensitive and specific. Patients are often in late stage when they see a doctor; the 5-year survival rate for the late stage is 30%[1] while the survival rate of patients with early epithelial ovarian cancer is 90%[2]. Therefore, early discovery and early treatment of epithelial ovarian cancer have important significance for prolonging the survival time of the patients. Currently, the detection of cancer antigen 125 (CA125) is widely used internationally as a test as this protein is highly expressed in 80% of ovarian cancer patients. While this test has high sensitivity, CA125 can also increase significantly in some patients with benign tumors, in women with peritonitis disease[3] and in 30% of patients with digestive tract tumors. Therefore, its low specificity has limited its accuracy in the diagnosis of epithelial ovarian cancer[4]. This study found that there was a close relationship between tissue polypeptide antigen (TPA), ovarian cancer antigen X1 (OVX1), cathepsin L (CTSL) and the presence of ovarian cancer. The clinic found that the sensitivity and specificity of single tumor markers were limited, and the combined detection of multiple tumor markers in the diagnosis of ovar-

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ian tumors has attracted wide attention[5]. In the study, the value of combined detection of TPA, OVX1, CTSL and CA125 in serum on the diagnosis of ovarian epithelial cancer were discussed.

Patients and Methods

Patients

From October 2011 to February 2015, 182 cases of patients in the Obstetrics and Gynecology Department of the First Affiliated Hospital of Liaoning Medical University were enrolled in our study. This cohort included 84 cases of patients with EOC (48 cases of patients with serious cystadenocarcinoma, 27 cases of patients with mucinous cystadenocarcinoma and 9 cases of patients with ovarian endometrioid carcinoma). The age range of the subjects was between 31-73 years old. Also, 98 cases of patients with benign epithelial ovarian tumor (the range of age was 14-69 years old) were selected. At the same time, 51 cases were adopted as the healthy control group; the range of age was 22-69 years old. All patients were treated by the International Federation of Obstetrics and Gynecology (FIGO) in 2010 according to different clinical stages. Histological type relied on postoperative pathological results. All patients were under primary and initial operation without other malignant disease preoperatively, other treatments and without any endocrine disease.

Methods

4 ml fasting venous blood was collected in the morning from all the subjects preoperatively and incubated for 1h at room temperature. The blood sample was centrifuged at 3000 r/min for 5 min; then, the supernatant was obtained and stored in the refrigerator at -40°C. TPA, OVX1 and CTSL in serum were detected by enzyme-linked immunosorbent assay (ELISA). The clinical data of subjects was collected and the CA125 level in serum was analyzed.

Normal Reference Value

CA125 ≤ 35kU/L means negative, CA125 > 35kU/L means positive. The detection value of the healthy control group was regarded as the upper and lower critical values, and the upper critical values of TPA, OVX1 and CTSL were calculated as 51 U/L, 16 Ku/L and 3 mg/L. The positive decision method of combined detection: pairwise markers were combined and detected, one was positive defined positive, two were negative defined negative. According to TNM stage classification criteria suggested by Union for International Cancer Control (UICC), 29 cases were at stage I or II (early stage), and 55 cases at stage III or IV (late stage).

Statistical Analysis

SPSS19.0 software (SPSS Inc., Chicago, IL, USA) was used to perform the statistical analysis of results. Data of each groups are shown by $x \pm s$. The t-test was applied in the comparison of measurement data; the x^2-test was applied in the comparison of count data.

Results

The Detection Results of Three Kinds of Tumor Markers in Serum in Every Group

The levels of TPA, OVX1 and CTSL in the malignant group were significantly higher than those in the benign group and the healthy control group; the differences were statistically significant ($p < 0.05$). There were no statistically significant differences between the two groups ($p > 0.05$) (Table I).

The Positive Results of 4 Indexes Separately and Unitedly on the Detection of EOC in Different Clinical Stages

Separately, the positive rate of TPA on the early detection of EOC was the highest while CA125 was the lowest. The total positive rate

Table I. The detection results of three kinds of tumor markers in serum in every group.

	CA125 (kU/L)	TPA (U/L)	OVX1 (kU/L)	CTSL (3 μg/L)
The malignant group (84 cases)	1072.0 ± 1003.52	79.68 ± 44.73	27.94 ± 35.16	9.12 ± 5.78
The benign group (98 cases)	18.01 ± 8.19	45.31 ± 21.73	8.57 ± 4.71	2.21 ± 1.05
The healthy control group (51 cases)		29.94 ± 13.68	7.72 ± 1.74	2.08 ± 0.29

Note: There were statistical significance on the comparison between the malignant group and the benign group, the healthy control group ($p < 0.05$).

and the positive rate of early detection of TPA on EOC were the highest. The total positive rate of OVX1 on EOC was lower than that of CA125. The total positive rate of CTSL on EOC was higher than that of CA125 and the positive rate of early detection of CTSL on EOC was higher than that of CA125 alone. These results were statistically significant ($p < 0.05$). The late positive rate of CA125 on EOC was the highest and CTSL and TPA were located in the second. The total positive rate and the positive rate of early detection of CA125+TPA on EOC were the highest. The positive rate of early detection and the total positive rate of the pairwise combined detection of the other index and CA125 on EOC were significantly higher than those of the single detection of CA125 ($p < 0.05$). These results were statistically significant (Table II) ($p < 0.05$).

Discussion

CA125 is the most widely used and most studied tumor marker; it is also one of the most common tumor markers used in the diagnosis of ovarian cancer[6,7]. However, a lot of clinical gynecological diseases could also cause an increase in levels of CA125 such as breast cancer, pelvic inflammatory disease, endometriosis, etc. Due to further research, in recent years, the amount of markers in serum in the diagnosis of ovarian cancer gradually increased. However, due to a lack of sensitivity and specificity in many tumor markers, there are many limitations that exist in the diagnosis of this tumor. Therefore, many scholars suggest a joint detection of tumor markers in serum in order to improve the early diagnosis rate of malignant ovarian tumors and the accuracy of detection.

TPA is a sediment of decomposition fragments of organization keratin, which is composed of three subunits (B1, B2, and C). The activity of TPA mainly relies on B1 subunit. The decomposition and destruction of normal epithelial cells cause a release of contents into adjacent exocrine gland ducts. Due to the inhibition of abnormal genes on malignant cells, corresponding cells easily died and were destroyed in the process of cell division. The contents that were released into neighboring tissues were digested by trypsin, went into the blood system, and caused an increase in TPA. Therefore, the higher the degree of malignancy, the faster cells split and the greater the possibility of disruption in the division which can lead to a continuous release of contents. Some studies reported that TPA in serum had a higher positive rate in the diagnosis of liver cancer, pancreatic cancer, ovarian cancer and lung cancer, and it could lead to differential diagnosis in adenocarcinoma, squamous carcinoma, metastatic carcinoma and non-metastatic carcinoma. It had important reference value in the selection of therapeutic regimens for patients with these clinical tumors.

OVX1 is a type of modified Lewis antigen obtained from different human ovarian cancer cell lines. Some studies report that the combination of CA125 and OVX1 is the best complementary combination in the diagnosis of ovarian cancer by the joint detection of CA125 and various markers in serum. CTSL is a type of cysteine protease which was expressed in all the cells and was involved in the invasion and metastasis of the tumor. Some researchers[8] have observed that the level of CTSL in serum in ovarian cancer group was significantly higher than that in benign ovarian tumor group and normal healthy group. The same study also showed that the positive rate of the early detection of CA125 on EOC was the lowest at only 41.37%, indicating that the detection of CA125 had prodigious limitations in the early diagnosis of EOC. When the combination of CA125 and TPA, OVX1 and CTSL were pairwise detected, the early detection positive rate of EOC improved.

In our work, the early positive rate of the joint detection of CA125 and TPA was the

Table II. The positive results of 4 indexes separately and unitedly on the detection of EOC in different clinical stages [cases (%)].

Stage	CA125	TPA	OVX1	CTSL	CA125+TPA	CA125+OVX1	CA125+ CTSL
Early (29)	12 (41.37%)	18 (65.51%)	13 (44.82%)	17 (58.62%)	25 (86.20%)	19 (65.51%)	23 (79.31%)
Late (55)	55 (100.0%)	51 (92.72%)	38 (69.09%)	51 (92.72%)	55 (100.0%)	55 (100.0%)	55 (100.0%)
Total (84)	67 (79.76%)	69 (82.14%)	51 (60.71%)	68 (80.95%)	80 (95.23%)	74 (88.09%)	78 (92.85%)

highest at 86.20%, the joint detection of CA125+ OVX1 was 65.51% and the joint detection of CA125+CTSL was 79.31%; there were significant differences on the comparison between the joint detection and the single detection of CA125 ($p < 0.05$). On the other hand, the diagnosis rate of EOC also improved. In addition, the diagnosis rate of the joint detection of CA125 and TPA was the highest at 86.20%, CA125+ OVX1 was 88.09%, and CA125+CTSL was 92.85%; these results were significant ($p < 0.05$).

Conclusions

The joint detection of CA125 and TPA had the most diagnostic value among TPA, OVX1 and CTSL, which greatly improved the early positive rate and diagnosis rate on the detection of EOC. However, the joint detection of OVX1, CTSL and CA125 could increase the early positive rate and diagnosis rate of EOC. It also had an important significance in improving the diagnostic ability of EOC.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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