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DIAGNOSTIC USEFULNESS OF SERUM CA 125 IN PATIENTS WITH OVARIAN CANCER

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(tumor marker/CA 125/ovarian cancer)

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Serum CA 125 (an antigen common to most nonmucinous epithelial ovarian carcinoma) were measured in patients with gynecologic disease. CA 125 levels were elevated (34 U/ml or higher) in 77.8% (7/9) of ovarian cancer patients. As the CA 125 levels correlated well with the clinical course, we conclude that the measurement of serum CA 125 is useful for the diagnosis and follow up of patients with ovarian cancer.

Ovarian cancers are difficult to detect in the early stages. Thus, development of a specific antigen has long been awaited. A monoclonal immunoglobulin (OC 125) has recently been developed by somatic hybridization of spleen cells from mice immunized with an epithelial ovarian carcinoma cell line (1). The monoclonal antibody (OC 125) reacts with an antigen (CA 125) common to most nonmutinous epithelial ovarian carcinoma. Since then, CA 125, as a tumor marker has been used to diagnose ovarian cancer and for follow up treatment (2-4).

Serum CA 125 in Japanese patients with gynecologic diseases were measured by radioimmunoassay and the usefulness of CA 125 as a tumor marker is reported herein.

MATERIALS AND METHODS

Serum samples from 39 patients with myoma uteri, 21 with

endometriosis, 15 with benign ovarian tumor, 9 with malignant ovarian tumor, 36 with cervical cancer, 3 with endometrial cancer, one with Schnitzler metastasis, one with mammary cancer, one with vaginal cancer and one with tubal cancer were cryopreserved in the clinic of Obstetrics and Gynecology, Shimane Medical University Hospital. A pathohistological diagnosis was made postoperatively, in cases.

Measurement of levels of CA 125 in serum was made in Special Reference Laboratory, Tokyo, using CA 125 in Radioimmunoassay kit manufactured by Centocor, Inc., Malvern, PA, USA. The least detectable levels of CA 125 was 8 U/ml, therefore, the serum CA 125 level under 8 U/ml was calculated as 8 U/ml statistically.

14.7 ± 9.3 U/ml of the mean CA 125 levels (± S.D.) and 34 U/ml of the cut off value described previously (5) were used as a control.

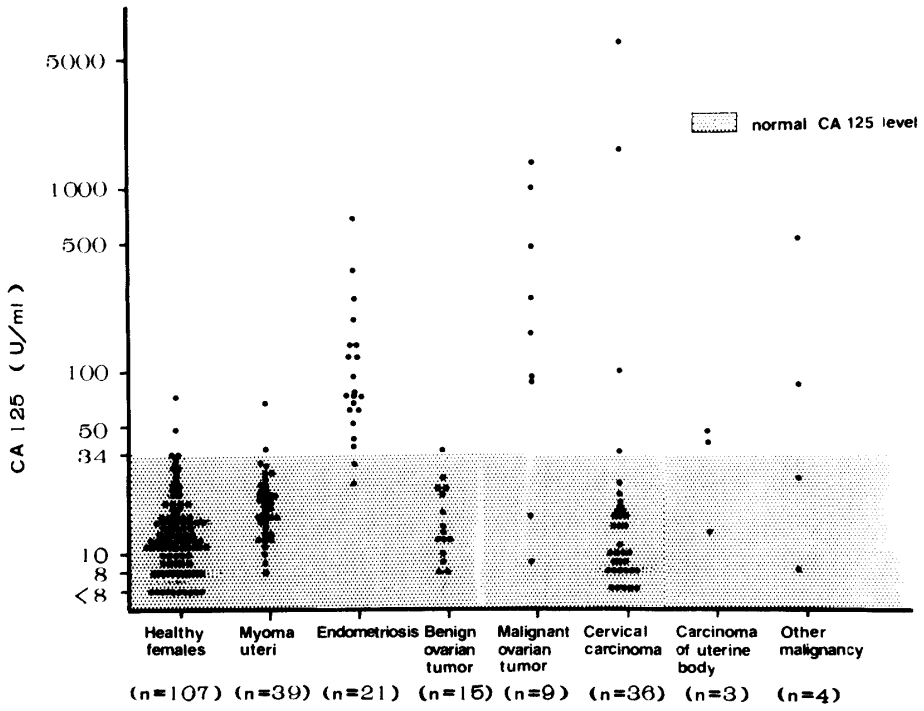

Fig.1. Serum levels of CA 125.

RESULTS

The serum CA 125 levels for patients with gynecological disease

Distribution of CA 125 in serum of healthy non-pregnant females and patients with gynecological disease and the mean CA 125 levels (± S.D.) and positive ratio are shown in Fig.1 and

Table I. CA 125 LEVELS IN SERUM OF PATIENTS WITH VARIOUS CLINICAL DISORDERS

Subjects	Total No.	CA 125 levels		
		Mean ± SD	No. > 34U/ml	Positive(%)
Healthy females	107	14.7 ± 9.3	4	3.7
Myoma uteri	39	20.3 ± 10.3	2	5.1
Endometriosis	21	132.7 ± 147.1	19	90.5
Adenomyosis	17	151.2 ± 157.3	16	94.1
External endometriosis	4	54.0 ± 26.8	3	75.0
Benign ovarian tumor	15	16.2 ± 7.6	1	6.7
Serous cystadenoma	6	12.2 ± 5.1	0	0
Mucinous cystadenoma	6	20.3 ± 7.6	1	16.7
Dermoid cyst	3	16.0 ± 7.3	0	0
Malignant ovarian tumor	9	388.4 ± 463.9	7	77.8
Serous cystadenocarcinoma	6	498.5 ± 512.1	6	100
Mucinous cystadenocarcinoma	1		0	0
Mixed mesodermal tumor	1		1	100
Dermoid cyst with malignant transformation	1		0	0
Cervical carcinoma	36	86.6 ± 303.1	4	11.1
Squamous cell carcinoma	31	14.8 ± 16.7	2	6.5
Recurrence of squamous cell carcinoma	4	16.3 ± 5.9	0	0
Adenocarcinoma	5	349.8 ± 625.9	2	40.0
Recurrence of adenocarcinoma	2	3900.0 ± 2300.0	2	100
Carcinoma of uterine body	3	33.0 ± 14.4	2	66.7
Other malignancy	4	156.3 ± 206.1	2	50.0
Schnitzler metastasis	1		0	0
Mammary carcinoma	1		1	100
Vaginal carcinoma	1		0	0
Tubal carcinoma	1		1	100

Table I, respectively. Two (5.1%) of 39 patients with myoma uteri had CA 125 levels in excess of 34 U/ml. The mean CA 125 levels (± S.D.) for 39 patients with myoma uteri was 20.3 ± 10.3 U/ml. Nineteen (90.5%) of 21 patients with endometriosis had CA 125 levels in excess of 34 U/ml. The mean CA 125 levels (± S.D.) for them was 132.7 ± 147.1 U/ml. The mean CA 125 levels for 17 patients with adenomyosis was higher than that for 4 patients with external endometriosis. The mean CA 125 levels (± S.D.) for 15 patients with benign ovarian tumor was 16.2 ± 7.6 U/ml, its positive ratio was 6.7% (1/15). Only one patient with mucinous cystadenoma of the ovary had CA 125 levels in excess of 34 U/ml, but the CA 125 level was 35 U/ml. On the contrary, the mean CA 125 levels for 9 patients with malignant ovarian tumor was 388.4

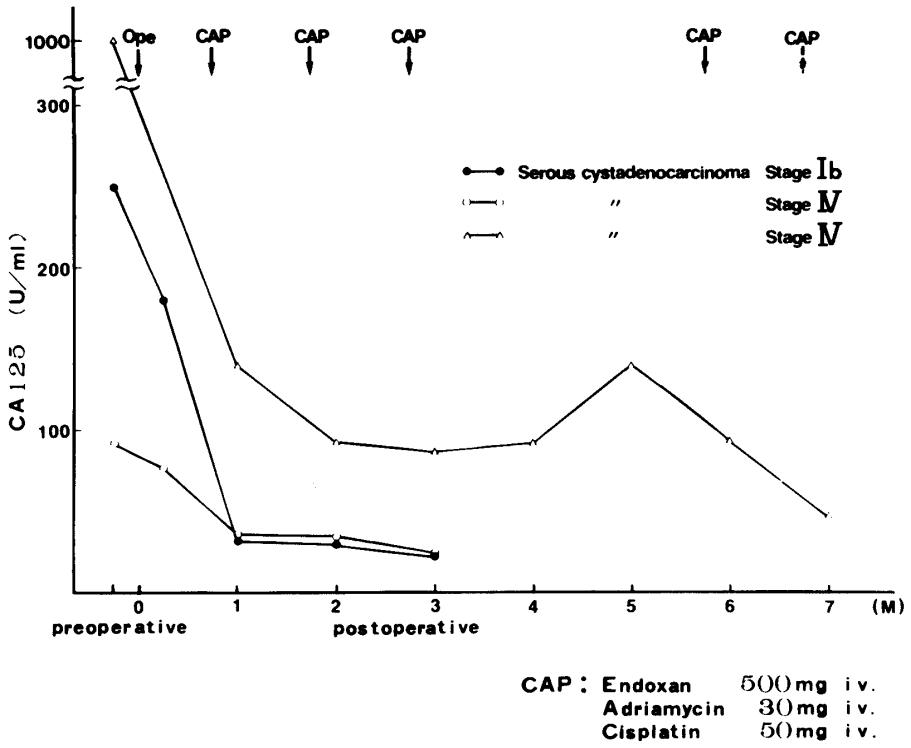

Fig.2. Changes in serum CA 125 after operation and chemotherapy.

± 463.9 U/ml. The serum CA 125 levels of patients with serous cystadenocarcinoma ranged from 89 to 1,400 U/ml. All had CA 125 levels in excess of 34 U/ml. But in two women (mucinous cystadenocarcinoma and dermoid cyst with malignant transformation), CA 125 levels were below 34 U/ml pre-operatively. Four (11.1%) of 36 patients with cervical cancer had CA 125 levels in excess of 34 U/ml. Serum CA 125 levels for two patients with squamous cell carcinoma of the cervix were pre-operatively 36 U/ml and 100 U/ml, respectively. In two of five patients with cervical adenocarcinoma, the CA 125 levels were in excess of 34 U/ml, the values being 1,600 U/ml and 6,200 U/ml, respectively. Both patients had a recurrence of the cervical adenocarcinoma. The mean CA 125 levels for 3 patients with carcinoma of uterine body was 33.0 ± 14.4 U/ml. In patients with other malignancies, one with mammary carcinoma and one with tubal carcinoma, the CA 125 levels were in excess of 34 U/ml.

Changes of serum CA 125 levels for 3 patients with serous cystadenocarcinoma of the ovary

Changes in serum CA 125 levels in patients with serous cystadenocarcinoma, one of stage Ib and two of stage IV, pre- and postoperatively are shown in Fig.2. Serum CA 125 levels (>34 U/ml) pre-operatively were reduced postoperatively and were reduced from about one third to about one seventh at one month after tumor resection. Serum CA 125 levels for two were below 34 U/ml within one month after operation. All patients had been prescribed CAP (Endoxan, Adriamycin and Cisplatin) therapy. One patient with stage IV of the disease had 7 courses of CAP therapy. After 3 courses of CAP therapy, the chemotherapy was discontinued as diabetes mellitus was evident. After interruption of chemotherapy, serum CA 125 levels tended toward an increase. Two months later, CAP therapy was resumed and the serum CA 125 levels were gradually reduced. After 7 courses of CAP therapy, the serum CA 125 levels were less than 34 U/ml.

DISCUSSION

Since a monoclonal antibody was prepared by Köhler and Milstein (6) in 1975, this technique has been used as a marker. CA 125 was detected on the surface epithelial cells of ovarian epithelial tumors (7). We measured serum levels of the CA 125 in patients with gynecologic tumors.

Positive ratio (>34 U/ml) of serum CA 125 for patients with ovarian cancer was high (77.8%), particularly in patients with serous cystadenocarcinoma of ovary (100%). This results corresponds with other reports (2,3). A positive ratio of serum CA 125 for patients with a benign ovarian tumor was low. Thus, for a pre-operative differentiation between benigh and malignant ovarian tumor, CA 125 proved to be useful. However, because almost all of cases in this study were advanced ovarian cancer, we don't know whether early ovarian cancer will be able to detect by measuring serum CA 125 or not. Further, because the positive ratio of serum CA 125 for patients with other diseases (endometriosis, recurrence of cervical adenocarcinoma and carcinoma of uterine body) was also high, the usefulness and limitation of CA 125 for clinical utilization requires further study.

In cases of ovarian cancer measured serum CA 125 continuous-

ly, serum CA 125 levels were reduced after tumor resection and chemotherapy gradually. Thus, CA 125 was useful for the montitoring of ovarian cancer after treatment.

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