

## Tumor markers in mature cystic teratomas of the ovary

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### Abstract

**Objective** The objective of this study was to evaluate the serum levels of tumor markers in patients with ovarian mature cystic teratomas.

**Method** Retrospective study of 215 patients operated at Zekai Tahir Burak Women Health Education and Research Hospital between January 2001 and October 2006 was performed.

**Results** The median age was 36 years (range 13–80). The mean tumor diameter was  $7.7 \pm 4.6$  cm (range 2–25). The mean serum CA 125 level was  $26.2 \pm 29.9$  U/mL (range 1.4–225, normal value <35), and the mean serum CA 19-9 level was  $83.5 \pm 179.2$  IU/mL (range 0.6–1,000; normal value <37). The elevated rate of CA 19-9, CA 125 was 39.6% (74/187) and 23.3% (50/215), respectively. The mean age of patients and the rate of bilaterality of tumors were similar in both patients with elevated CA19-9 and with normal CA 19-9 level ( $P > 0.05$ ). The mean tumor size of patients with elevated CA 19-9 was greater than those with normal CA19-9 level ( $P = 0.01$ ).

**Conclusion** Serum CA 19-9 has the highest positivity rate among other tumor markers in ovarian mature cystic teratomas. Elevated serum CA 19-9 levels are correlated with larger tumor size. But the diagnostic value of elevated CA 19-9 in patients with MCT would be poor if the test was used alone.

**Keywords** CA 19-9 · CA 125 · Mature cystic teratoma · Ovary · Tumor markers

### Introduction

Mature cystic teratoma (MCT) is a common benign neoplasm accounting for 10–20% of all ovarian tumors [1]. Most cases present as an asymptomatic adnexal mass incidentally detected on routine pelvic examination or with fat component and calcifications detected by pelvic imaging studies. Complications of mature cystic teratomas occur at about 20% of the cases which are torsion, rupture and infection and malignant transformation [2].

Serum tumor markers have been used in the management of pelvic masses and ovarian cancer. The CA 125 antigen is expressed in coelomic epithelia such as müllerian epithelium, peritoneum, pleura and pericardium [3]. Clinical application of Ca 125 in ovarian cancer includes monitoring disease response to treatment, detecting disease recurrence and estimating prognosis. Serum CA 125 also has a role in distinguishing benign pelvic masses from malignant ones [4]. CA 19-9, a side branch of the Lewis blood group system, is a sialylated Lewis A antigen that is highly expressed by many adenocarcinomas of the digestive tract. The müllerian duct-derived mucosa of the uterus and fallopian tubes also synthesizes Lewis blood group antigens [5]. Ovarian MCT contains various kinds of tissues since it originates in parthenogenesis of the oocyte. Some tumor markers, therefore, are expected to be positive. Although sonographic diagnosis of ovarian MCT can accurately be made, use of serum tumor markers have been shown to provide additional information and may aid in making a differential diagnosis which is very important for patients with ovarian tumors, because the surgery

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**Table 1** Serum tumor markers of patients

Tumor marker	<i>n</i>	Cutoff value	Serum level (mean ± SD)	Range	Elevated rate ( <i>n</i> /total)
CA 19-9 (U/mL)	187	37	83.5 ± 179.2	0.6–1000	39.6% (74/187)
CA 125 (U/mL)	215	35	26.2 ± 29.9	1.4–225	23.3% (50/215)
AFP (ng/mL)	165	11.3	1.8 ± 1.6	0.5–18.1	0.6% (1/165)
CEA (ng/mL)	178	3.4	2.3 ± 2.2	0.1–15.2	16.3% (29/178)
CA 15-3 (U/mL)	193	25	18.2 ± 8.2	3.8–58.2	18.7% (36/193)

performed is quite different for benign and malignant tumors [6, 7].

However, clinical usefulness of tumor markers in patients with MCT of the ovary has been evaluated only in few studies. In this study, we aimed to evaluate the serum levels of tumor markers in patients with ovarian mature cystic teratomas.

## Methods

Clinical features of 215 pathologically-confirmed MCT's at Zekai Tahir Burak Women Health Education and Research Hospital between January 2001 and October 2006 were reviewed, especially concerning tumor markers. Data were obtained from hospital charts and the pathology registry. Formaldehyde was used for specimen fixation. Average tumor size (greatest diameter) was determined by the review of both the operative records and the gross pathologic descriptions. All three germ cell layers were examined histopathologically. The cases with malignant transformation were excluded from the study.

All the blood samples were obtained preoperatively. The determination methods were radioimmunoassay for AFP, CA 19-9, CA 15-3 and CA 125 and enzyme immunoassay for CEA. Analyses are performed on the Modular Analytics E170 module (Roche Laboratory Systems, Mannheim, Germany). The cutoff values for AFP, CEA, CA 19-9, CA 15-3 and CA 125 are 11.3 ng/ml, 3.4 ng/ml, 37 U/mL, 25 U/mL and 35 U/mL, respectively. As a part of gynecologic examination, all patients underwent transvaginal or transabdominal sonography. Other imaging and endoscopic procedures were performed in patients with highly elevated serum tumor markers to rule out any gastrointestinal disease.

Oophorectomy, cystectomy, or hysterectomy with unilateral or bilateral salpingo-oophorectomy was performed as treatment modality according to, age, fertility desire, and presence of other pathology.

Statistical analysis was performed with the SPSS/PC 11.0 package (SPSS: Chicago, IL). Statistical evaluation of the data was performed by Chi-square test, Student's *t* test. A *P* value <0.05 was considered statistically significant.

## Results

The mean age of all patients was 37.3 ± 12.9 years (range 13–80). Thirty-six patients (16.7%) were postmenopausal. Tumor size ranged from 2 to 25 cm in diameter with a mean (±SD) of 7.7 ± 4.6 cm. The bilaterality rate was 9.8% (21/215).

The serum levels of tumor markers are shown in Table 1. The mean serum CA 19-9 level was 83.5 ± 179.2 IU/mL, mean serum CA 125 level 26.2 ± 29.9 U/mL, mean serum alpha-fetoprotein level (AFP) 1.8 ± 1.6 ng/mL, mean serum carcino-embryogenic antigen (CEA) level 2.3 ± 2.2 ng/mL, and mean serum CA 15-3 level 18.2 ± 8.2 U/mL. Among the five tumor markers, CA 19-9 revealed the highest elevated rate (39.6%), whereas AFP revealed the lowest (0.6%).

The comparison of patients with and without an elevated CA 19-9 level is presented in Table 2. The mean tumor size of patients with elevated CA 19-9 level was significantly greater than those with normal CA 19-9 level (8.8 ± 4.5 vs. 7.1 ± 4.5 cm, respectively, *P* = 0.01). Likewise, the mean serum CA 125 level and the rate of elevated CA 125 were significantly higher in patients with elevated serum CA 19-9 level. There was no statistically significant difference in terms of mean age, rate of bilaterality between the two groups.

Patients having normal CA 19-9 and CA 125 level constituted 53.5% of the study population. Elevated CA 19-9 and normal CA 125 levels were detected in 41 patients (21.9%). Whereas 13 patients (7%) had elevated CA 125 levels but normal CA 19-9 levels. Elevation of both CA 19-9 and CA 125 levels were detected in 33 patients (17.6%). CA 19-9 levels were greater than 100 IU/mL in 32 patients (17.1%) and greater than 500 IU/mL in 9 patients (4.8%).

## Discussion

Mature cystic teratoma is the most commonly encountered germ cell neoplasm of the ovary. Although frequently asymptomatic and detected incidentally, some of the cases may come to clinical attention with complications which are seen approximately in 20% of cases.

**Table 2** Comparison of patients with or without an elevated CA 19-9 level

	Patients with elevated CA19.9 (N = 74)	Patients with normal CA19.9 (N = 113)	P value
Age (mean ± SD)	36.9 ± 13.4	37.5 ± 12.6	0.768
Menopause n (%)	14 (18.9)	21 (18.6)	0.954
Tumor size	8.8 ± 4.5	7.1 ± 4.5	0.01
Bilaterality	9 (12.2)	9 (8.0)	0.341
Elevated CA 125 n (%)	33(44.6)	13 (11.5)	<0.001
Serum CA 125 level (mean ± SD)	33.8 ± 26.9	21.0 ± 28.4	0.003
Serum CA 19.9 level (mean ± SD)	193.6 ± 247.7	11.5 ± 8.9	<0.001

Results of this study have showed that CA 19-9 is more frequently elevated than CA 125 and hence a more useful marker in MCT. CA 19-9 was reported to be elevated in as many as 59% of cases [8]. CA 19-9 was elevated in 39.6% of patients with mature cystic teratoma in our study. The diagnostic value of elevated CA 19-9 in patients with MCT would therefore be poor if the test was used alone. But elevated serum CA 19-9 may be suggestive of MCT in patients with a pelvic mass the nature of which could not be determined by sonography alone.

CA 19-9 has been immunohistochemically demonstrated in the bronchial mucosa and glands of MCT and it has been shown to be secreted into the cystic cavity of the lesion. The mechanism of an elevated CA 19-9 in MCT is principally the leakage from cystic cavity into the blood stream [9]. Elevation of CA 19-9 therefore might be anticipated with larger or bilateral MCT since leakage into the blood-stream is more probable in both conditions. In the literature, data regarding association between serum CA 19-9 levels and certain clinical features other than malignant transformation are very limited and few studies have addressed this issue. Our results indicate that tumor size was the only clinical finding that correlated with elevated CA 19-9 levels, however, bilaterality is not associated with elevated serum CA 19-9 levels. This is in contrast to the study of Dede et al. in which elevated CA 19-9 was associated with a high rate of bilaterality with a likelihood ratio of 2.8 [7]. This was the only study that has stated such an association. Menopausal status was also not correlated with serum CA 19-9 levels.

An important finding of our study is that 32 (17.1%) patients had highly elevated levels of CA 19-9 (>100 IU/mL) and 9 (4.8%) having greater than 500 IU/mL. During the preoperative period imaging and endoscopic procedures revealed no extra ovarian disease in those patients. Abnormally high elevations of CA 19-9 in MCT have also been previously reported in the literature [10]. Consistently Ito [9] have reported that 31 out of 250 patients with MCT had CA 19-9 levels greater than 101 IU/mL. Preliminary evaluation of gastrointestinal tract for malignancies is therefore

unnecessary if clinical findings and sonography suggest MCT, since highly elevated CA 19-9 levels were encountered in our patients who do not have concomitant gastrointestinal pathology.

Two conclusions can be derived from this study. First, among other tumor markers, CA 19-9 has the highest positivity rate in MCT which correlates well with tumor size but not with bilaterality or menopausal status. However, it has a limited diagnostic value when used alone. Second, a highly elevated level of CA 19-9 is not an uncommon finding in patients with MCT, therefore does not necessitate immediate evaluation of gastrointestinal tract.

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