Preoperative diagnosis of malignant transformation in mature cystic teratoma of the ovary

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Summary

Objective: Malignant transformation of mature cystic teratomas (MCT) of the ovary is extremely rare. There are no established criteria of diagnosis before surgery for carcinoma arising from MCT of the ovary. Thus, we analyzed retrospectively tumor size and preoperative values of tumor markers in patients with MCT and investigated the possibility of preoperative diagnosis.

Methods: This was a retrospective case series of 278 patients with MCT of the ovary. Data were obtained from hospital charts and the pathology registry. Average tumor size (greatest diameter) was determined by the preoperative findings of both MRI and ultrasound examination.

Results: Malignant transformation was seen in five patients (11%) among those whose tumor was ≥ 10 cm in diameter, four patients (23%) among those whose pretreatment serum SCC level was ≥ 2.0 ng/ml, two patients (13%) among those over 60 years of age and five patients (2%) with a tumor on one side. Mean tumor size and serum SCC level were significantly higher than those of benign MCT.

Conclusions: We conclude that patients over 60 years old who have unilateral MCT with SCC value of ≤ 2.0 ng/ml and ≥ 10 cm tumors may be a high-risk group for malignant transformation.

Key words: Mature cystic teratomas; Malignant transformation; Tumor markers.

Introduction

Mature cystic teratoma (MCT) is the most common germ cell tumor of the ovary, accounting for 10% to 20% of all ovarian tumors [1]. Malignant transformation of MCT of the ovary is extremely rare, accounting for only 1.9% of all MCTs [2]. Malignant transformation of MCT of the ovary arises in any of all three germ layers; however, the ectoderm seems to be the layer most likely to undergo this change. Of the malignant transformations reported, squamous cell carcinomas make up over 80% [2]. Other rare malignancies include adenocarcinoma, malignant melanoma, thyroid adenocarcinoma, and sarcomatous changes [3]. There are no established criteria for diagnosis before surgery for carcinoma arising from MCT of the ovary. Thus, we analyzed retrospectively tumor size and preoperative values of tumor markers in patients with MCT operated on at our hospital between 1994 and 2003 and investigated the possibility of preoperative diagnosis.

Materials and Methods

This was a retrospective case series of 278 patients with MCT of the ovary, diagnosed and treated at Nishi-Kobe Medical Center. All cases were operated on during a 9-year period, from 1 July, 1994 to 31 December, 2003. Data were obtained from hospital charts and the pathology registry. All specimens of consecutive patients were evaluated histologically by the co-author pathologist. Average tumor size (greatest diameter) was determined by the preoperative findings of both MRI and ultrasound examination.

The preoperative serum CA125 and CA19-9 levels were categorized into three groups - less than 35 U/ml, 35-199 U/ml, and 200 U/ml or greater. For 29 patients (10%) and 13 patients (5%), preoperative serum CA 125 and CA19-9 were unavailable, respectively, and thus categorized as unknown. The preoperative serum SCC level was categorized into three groups - less than 1.5 U/ml, 1.5-1.9 U/ml, and 2.0 U/ml or greater. For 142 patients (51%), preoperative serum SCC was unavailable, and thus categorized as unknown.

Statistical analysis was carried out by use of the Student's *t*-test. The significance level was $p < 0.01$. Data are represented as mean ± SD.

Results

The distribution of predicted malignant risk factors is displayed in Table 1. The mean age of the patients was 35.0 ± 13.0 years (7-79). Two patients (13%) among those over 60 years of age had squamous cell carcinoma arising from MCT, whereas none among those under 20 years of age, two (1%) among those from 20 to 39 years of age and one (1%) among those from 40 to 59 years of age were diagnosed with malignant transformations arising from MCT.

The tumors were seen on the right side in 110 patients (39%), left side in 127 patients (46%), and both sides in 41 patients (15%), respectively. Malignant transformation was seen to five patients (2%) with a tumor on one side, but there was no malignant transformation in patients with tumors on both sides.

Tumor size ranged from 2 cm to 25 cm in diameter with a mean (± SD) of 7.0 ± 3.0. Malignant transformation was seen in five patients (11%) among those whose tumor was ≥ 10 cm in diameter, but there was no malignant transformation in patients whose tumor was < 10 cm.

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Table 1. — *Predicted risk factors for malignancy.*

Risk factors	Total no. of cases	Malignancy [n (%)]	Benign [n (%)]
Age (yrs)			
< 20	17	0 (0)	17 (100)
20-39	173	2 (1)	171 (99)
40-59	72	1 (1)	71 (99)
≥ 60	16	2 (13)	14 (87)
Tumor size (cm)			
< 10.0	231	0 (0)	231 (100)
≥ 10.0	47	5 (11)	42 (89)
SCC (ng/ml)			
< 1.5	106	0 (0)	106 (100)
1.5-1.9	13	0 (0)	13 (100)
≥ 2.0	17	4 (23)	13 (77)
unknown	142	1 (1)	141 (99)
CA 125 (U/ml)			
< 35.0	205	3 (1)	202 (99)
35.0-199.9	41	2 (5)	3 (95)
≥ 200.0	2	0 (0)	2 (100)
unknown	30	0 (0)	30 (100)
CA 19-9 (IU/ml)			
< 35.0	147	1 (1)	146 (99)
35.0-199.9	70	2 (3)	68 (97)
≥ 200.0	31	2 (7)	28 (93)
unknown	30	0 (0)	8 (100)
Total	278	5 (2)	274 (98)

Table 2. — *Characteristics of all participants before treatments.*

	Malignancy (n)	Benign (n)
Age (yrs)	48.6 ± 20.0 (5)	34.8 ± 12.8 (273)
Tumor size (cm)	11.2 ± 1.6 (5)*	7.0 ± 2.9 (273)
SCC (ng/ml)	19.1 ± 31.8 (4)*	1.2 ± 1.2 (132)
CA 125 (IU/ml)	24.8 ± 16.1 (5)	25.7 ± 32.7 (243)
CA 19-9 (IU/ml)	8344.8 ± 16439.0 (5)*	98.7 ± 239.6 (243)

Data are represented as mean ± SD; *p < 0.01 vs benign patients.

Malignant transformation was seen in four patients (23%) among those whose pretreatment serum SCC level was ≥ 2.0 ng/ml and two patients (7%) among those whose pretreatment serum CA19-9 level was ≥ 200 U/ml. However pretreatment serum CA125 level had no tendency in relation to the malignant transformation of MCT.

Totally five patients (2%) were found to have malignant transformation of MCT and the mean tumor size, serum SCC level and serum CA19-9 levels were significantly higher than those of benign MCTs (11.2 ± 1.6 vs 7.0 ± 2.9 cm, 19.1 ± 31.8 vs 1.2 ± 1.2 ng/ml and 8344.8 ± 16439.0 vs 98.7 ± 239.6 U/ml, $p < 0.01$, respectively). Mean age of the patients with malignant transformation was comparable to that of patients with benign MCT (48.6 ± 20.0 vs 34.8 ± 12.8). The pathological examination revealed squamous cell carcinomas in four cases and an adenocarcinoma with squamous cell carcinoma in one case.

Discussion

This study has investigated the possibility of preoperative diagnosis in malignant transformation of MCT. The malignant transformation rate of MCT of 2% in our study did not differ from that of a previous report [2]. Preoperative diagnosis of MCT of the ovary is relatively easy if bony tissues including teeth, bones, and cartilage are detected. However, preoperative diagnosis of malignant transformations in these tumors is very difficult. Definitive diagnosis in such cases is most often rendered postoperatively. Suzuki *et al.* reported that the combined use of serum macrophage colony stimulating factor (M-CSF) and SCC seemed to be useful in the diagnosis of malignant squamous cell carcinoma arising from MCT of the ovary [4]. On the other hand, it has also been reported that CA125 and CA19-9 are not useful for discriminating MCT of the ovary harboring transformed SCC from those without malignant transformation [4]. In our study 23% of patients with a pretreatment serum SCC value of ≥ 2.0 ng/ml were diagnosed with malignant transformations. These findings suggest that those who have MCT with SCC values of ≥ 2.0 ng/ml may be a high-risk group for malignant transformation.

Although malignant transformation could occur in any age, patients with this condition are often detected a decade later than those with benign MCT [3]. Peak incidence for this malignancy occurs between 40-60 years of age [5], with most cases being menopausal. In our study, 13% of patients over 60 years of age have squamous cell carcinoma arising from MCT.

MCT are bilateral in 10-17% of all cases [2]; however, malignant change in a bilateral cyst is relatively uncommon. In fact, all our 5 cases with malignant transformation arise in unilateral MCT.

Several authors have also suggested that larger MCT are at the risk for malignant degeneration [6]. This study also showed that 11% of patients with ≥ 10 cm tumors were diagnosed with malignant, whereas all of patients with < 10 cm tumors were diagnosed with benign MCT.

In conclusion, we conclude that patients over 60 years old who have unilateral MCT with SCC value of ≧ 2.0 ng/ml and ≧ 10 cm tumors may be high risk group of malignant transformation.

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