Can malignant transformation in mature cystic teratoma be preoperatively predicted?

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Summary

Purpose of investigation: The study aimed to determine whether malignant transformation of mature cystic teratoma (MCT) can be preoperatively predicted by presenting two cases of MCT with malignant transformation and comparing their clinical factors with those of benign MCT encountered at around the same time. *Materials and Methods:* Age, maximum tumor diameter, tumor marker levels (serum squamous cell carcinoma (SCC) and carbohydrate antigen (CA) 19-9, the presence of solid tumor masses, and the presence or absence of contrast enhancement in pelvic magnetic resonance imaging (MRI) were investigated in two cases of MCT with malignant transformation and 76 cases of benign MCT in which surgery was performed and a pathological diagnosis given by the department from 2004 to 2010. *Results:* The mean ages of the two cases with malignant transformation and the cases of benign MCT were 42.5 years and 34.2 years, respectively. The mean maximum diameter of the two tumors with malignant transformation and the cases of benign MCT were 130 mm and 73.6 mm, respectively. The mean serum levels of SCC in the two cases with malignant transformation and the cases of benign MCT were 31.5 ng/ml and 0.92 ng/ml, respectively. Contrast enhancement and the presence of solid masses in images of MCT with malignant transformation were apparent. *Conclusion:* In order to accurately detect malignant transformation of MCT, the authors found it to be important to determine whether tumors larger than 100 mm in diameter were present and to check for the presence of solid masses enhanced in pelvic MRI examination, as well as to measure at least serum SCC and CA19-9 even in relatively young patients.

Key words: Mature cystic teratoma; Malignant transformation; Solid mass enhancement; Serum SCC level.

Introduction

Mature cystic teratoma (MCT) that transforms to malignancy is rare. The authors investigated whether malignant transformation of mature cystic teratoma can be predicted prior to surgery by clinically comparing two cases of MCT that transformed to malignancy with other MCT cases. The authors report the results of this investigation along with a discussion of the literature.

Case Report

Case 1

A 49-year-old patient, gravida 2 and para 2, with no relevant family or medical history, was diagnosed with an ovarian tumor and referred to the department in 2007. Pelvic magnetic resonance imaging (MRI) identified a tumor 14 cm in diameter in the pelvis. MCT accompanied by malignant transformation was suspected because solid masses, which were partially enhanced, were detected (Figure 1), although fat was also seen, and her serum squamous cell carcinoma (SCC) level was 50.6 ng/ml. There were no abnormalities found for peripheral blood, biochemistry or coagulation testing. The tumor marker levels were high with SCC of 50.6 ng/ml, CA125 of 86 U/ml, CA19-9 of 699 U/ml and carcinoembryonic antigen (CEA) of 19.7 ng/m. Although the initial pathological diagnosis was struma ovarii, simple total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy were performed due to the patient's age and suspected malignant transformation. No apparent dissemination was found in the greater omentum or abdominal cavity. Macroscopic findings were that the tumors were bilateral and that solid masses, as well as fat and hair were recognized (Figure 1). Histopathological findings indicated that most of the right ovarian tumor was MCT, and adenosquamous cancer was partially detected (Figure 2). Microscopic dissemination was seen in the greater omentum, and was Stage IIIA according to the FIGO classification. The left ovarian tumor was a MCT without malignant transformation. Postoperative chemoradiation was performed, with a total of 45 Gy administered over the entire pelvis. With the radiation therapy, 30 mg/m^2 of cisplatin (CDDP) was administered once weekly for five times. The serum SCC level normalized after treatment and recurrence was not found during five years follow-up after the initial surgery.

Case 2

A 36-year-old patient, gravida 1 and para 1, with no relevant family or medical history, was diagnosed with an ovarian tumor during a gynecological examination in December 2009. Laparoscopic surgery had been performed for the 12 cm diameter ovarian MTC at a previous hospital and, due to a solid mass within the tumor suggestive of malignancy found during this surgery, right salpingo-oophorectomy had been performed. The tumor had ruptured during surgery, and after a postoperative pathological examination indicated that the solid mass was squamous cell cancer, the patient was referred to the department. There were no abnormalities detected on hematology, peripheral blood, biochemistry or coagulation testing. Tumor marker levels were as follows: CA125 25.2 U/ml, CA19-9 58.6 U/ml, and serum SCC was high at 12.3 ng/ml. Careful observation of the images from preoperative pelvic MRI indicated that the 12-cm MCT was accompanied by a solid mass measuring six cm diameter above the tumor. Macroscopic findings were

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Fig. 1A

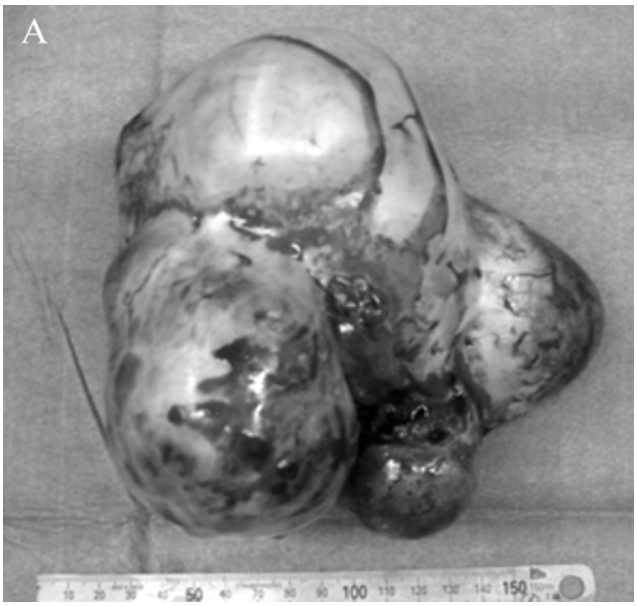

Fig. 1B

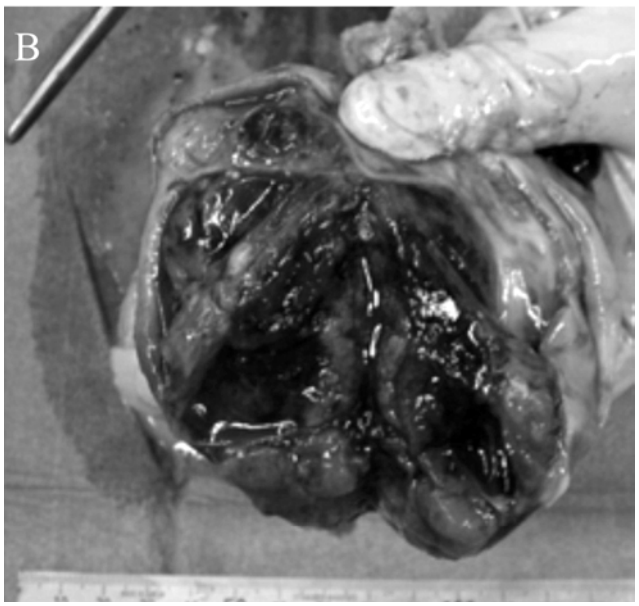

Fig. 2A

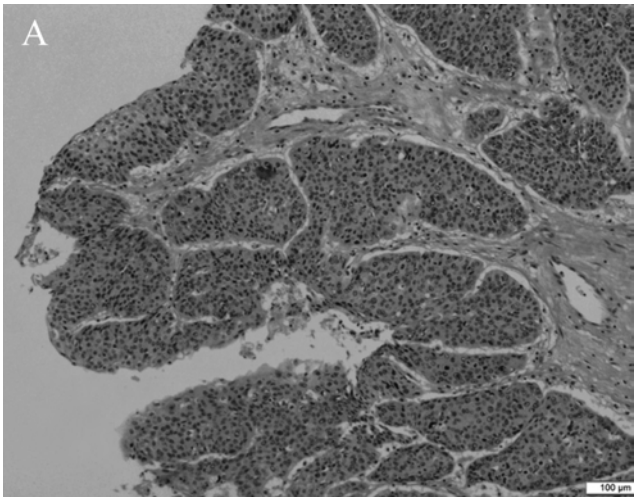

Fig. 2B

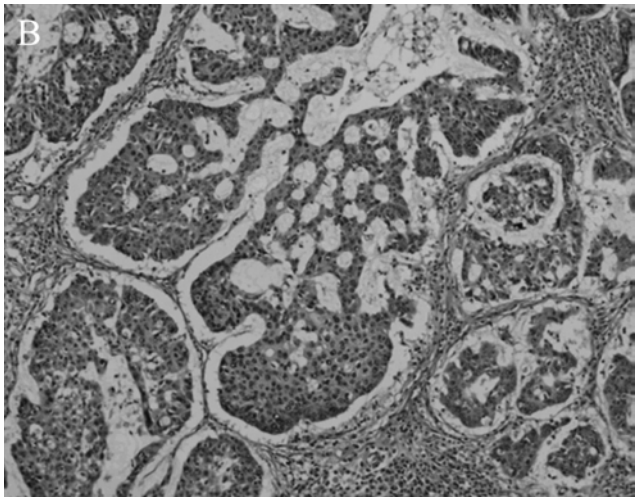

Fig. 3

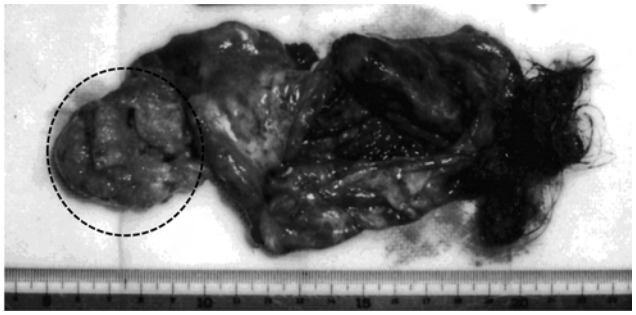

Figure 1. — A: The resected ovarian tumor; B: The resected surface. Solid masses along with hair and fat are found in the multilocular mass.
Figure 2. — Pathological findings from the ovarian tumor. A: Squamous cell cancer; B: adenocarcinoma.
Figure 3. — The resected ovarian tumor. The tumor is comprised mostly of fat and hair, with a partial solid mass (black circle).

that the MCT was comprised mostly of fat and hair but there was also a partial solid mass (Figure 3). On the basis of the pathological findings, the lesion was diagnosed as a transitional cell cancer accompanied by squamous metaplasia (Figure 4). Our department additionally performed staging laparotomy, which gave a staging of Stage IC according to the FIGO classification. Postoperative treatment comprised of three cycles of combined paclitaxel and carboplatin therapy. During three years follow-up, no recurrence was detected.

Materials and Methods

Age, maximum tumor diameters, tumor marker levels (serum SCC and CA19-9), the presence of solid tumor masses, and the presence or absence of contrast enhancement in pelvic MRI were investigated in two cases of MCT with malignant transformation and 76 cases of benign MCT in which surgery was performed, and a pathological diagnosis was given by the department during 2004 to 2010.

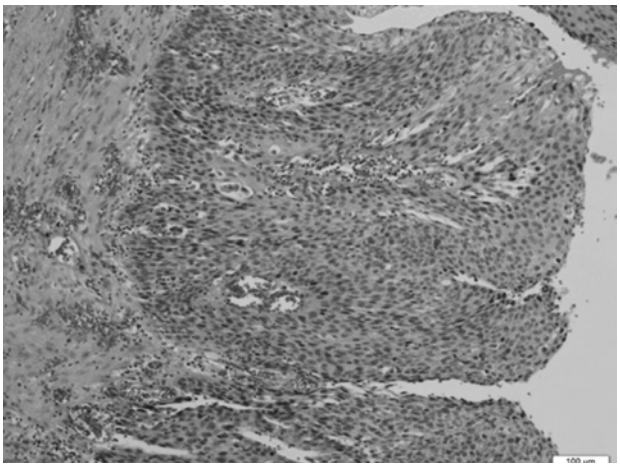

Figure 4. — Pathological findings from the ovarian tumor. Transitional cell cancer accompanied by squamous metaplasia was diagnosed.

Table 1. — *Comparison of mature cystic teratoma with malignant transformation and mature cystic teratoma.*

Histology	Mean age (years)	Maximum diameter of tumor (mm)	Value of serum SCC (ng/ml)	Value of serum CA19-9 (ng/ml)	Solid parts within tumor (%)	Enhancement of the image (%)
Mature cystic teratoma with malignant transformation (n = 2)	42.5	130	31.5	378.8	100	100
Mature cystic teratoma (n = 76)	34.2	73.8	0.92	69.8	1.3	12.5

Results

A summary is shown in Table 1. The mean ages of the two cases with malignant transformation and the cases of benign MCT were 42.5 years and 34.2 years, respectively. The mean maximum tumor diameter in the two cases with malignant transformation and the cases of benign MCT were 130 mm and 73.6 mm, respectively. The mean levels of serum SCC in the two cases with malignant transformation and the cases of benign MCT were 31.5 ng/ml and 0.92 ng/ml respectively, with mean levels of CA19-9 of 377.8 U/ml and 69.8 U/ml, respectively. The number of cases that showed enhancement in pelvic MRI in the two cases with malignant transformation and the cases of benign MCT were 1/1 case (100%) and 11/76 cases (14.7%) respectively, with solid masses detected in two cases (100%) and 2/76 cases (2.6%), respectively. Thickening of the tumor wall and a septal wall were enhanced in the contrasted benign MCT images.

Discussion

MCT accounts for 10% to 20% of ovarian tumors. However, malignant transformation is thought to occur in only 1% to 2% of MCT cases [1, 2]. Histologically, SCC accounts for the largest percentage of cases where malignant transformation occurs at 75% [3].

As malignant transformation of MCT is rare and there are only a few reports that cover a large number of cases, while many individual cases have been reported. Reports by single institutions that have relatively large numbers of patients and reports by multiple institutions working together cover several dozens of cases (7 to 37 cases) [3-5]. Three reviews on malignant transformation in MCT have been published so far [6-8]. These reviews are the accumulation of 30 years of experience. Therapies and surgical methods have inevitably changed during these 30 years. Therefore these reviews lack sufficient data to establish methods for the prediction and treatment of MCT that transform into malignancy.

As the authors had only two cases of MCT with malignant transformation in their department, the data may again be insufficient for establishing a definitive method. However, by comparing these cases with those of benign MCT, the authors were able to establish the following: (1) patients with MCT with malignant transformation were not particularly old but did appear to have a mean age higher than that of cases of benign MCT; (2) the diameter of MCT that transformed into malignancy was greater than that of benign MCT; (3) serum SCC may be an indicator of malignancy, whereas CA19-9 varies widely and may be elevated in both malignant and benign MCT; (4) While benign MCT rarely shows enhancement, malignant transformation may be characterized by enhanced solid masses.

The authors looked at previously published reports to further investigate these four points. First, concerning age, Hackethal *et al*. [7] reported a mean age of 55 years, with other reports having similar results. In these reports, the ages when MCT transformed into malignancy ranged from 19 to 87 years, with a standard deviation of 14.1 years. These findings suggest that careful consultation is required for patients aged 30 years and older. One patient treated in the department was 36 years old. It may be assumed that malignant transformation of MCT occurs in elderly patients, but this is not always true.

Second, concerning tumor diameter, Hackethal *et al*. [7] reported that 70% of cases of MCT with malignant transformation had tumors 100 mm or larger in diameter. Chen *et al*. [8] reported a diameter range of 137 mm ± 57 mm. Both cases treated in the department had tumors with a diameter of at least 100 mm, which is consistent with the report by Kikkawa *et al*. [4] that by assuming the cutoff value for tumor diameter at 99 mm, sensitivity is 86%, specificity 74%, and diagnostic yield 64%. However, prediction based on the tumor diameter alone may be difficult, as MCT with a tumor diameter exceeding 100 mm is not frequently seen in clinical practice. The mean tumor diameter in cases with benign MCT in this department was 73.6 mm ± 34.6 mm. Tumor diameter of at least 100 mm was observed in 10/76 cases (13.2%).

Which tumor marker should be measured when MCT is suspected in the ultrasound exam? The most likely choic-

es would be CA19-9 and CA125. SCC is unlikely to be routinely measured due to economic considerations. In the review by Hackethal *et al*. [7], SCC was measured only in 52 cases (18.8%), CA125 in 51 cases (18.4%), CA19-9 in 39 cases (14.1%), and CEA in 24 cases (8.7%) among a total of 277 cases. In order to justify measurement with these markers, malignant transformation of MTC should be suspected. Tumor images, discussed later, tumor diameter, and patient age should be carefully considered before measurement.

What is the best tumor marker to predict MCT that will transform into malignancy? When considering that SCC accounts for 75% of MCT with malignant transformation, SCC is considered the best choice. Kikkawa *et al*. [4] reported that when MCT with malignant transformation was screened using SCC (< 2.0 ng/ml), CA125 (< 35 U/ml), CA19-9 (< 37 U/ml), and CEA (< 5.0 ng/ml), diagnostic yields were 63%, 50%, 28%, and 45%, respectively. The sensitivity of CEA was low at 45%, but its specificity was 100%. Based on the previous statement, SCC and CEA are considered appropriate to screen MCT for malignant transformation.

The last point for discussion is whether pelvic MRI can identify MCT that has transformed into malignancy? Only a limited number of reports on this issue are available [9]. Most medical institutions perform preoperative pelvic MRI, and laparoscopic surgery is widely performed in cases where MCT is suspected. Not many institutions, however, evaluate MCT using contrast agents. In case 2 the authors reported a patient that did not undergo contrast studies. Contrast agents, of course, will rarely be used when malignant transformation is not suspected. However, if the presence of solid masses is confirmed by pelvic MRI, re-examination, such as performing tumor marker tests and contrast studies, will be performed. If there is strong suspicion of malignant transformation, laparotomy rather than laparoscopy, will be performed. The order of these procedures is considered ideal at present [8]. This present investigation suggests it important to focus on the presence or absence of solid masses, on the basis of the finding that among cases of benign MCT, only 2.6% had solid masses, and only 14.7% showed contrast enhancement on pelvic MRI.

The way to detect all cases of malignant transformation of MCT is to perform pelvic MRI to check for the presence of solid masses in patients 30 years and older and with a tumor at least 100 mm in diameter. If solid masses are enhanced, at least serum SCC and CEA should be measured. The findings of this investigation, along with the existing literature, suggest that in order to avoid missing cases of malignant transformation, that these procedures are considered prudent.

Conclusion

It must be noted that it is difficult to honestly answer the question of whether malignant transformation of MCT can be predicted preoperatively on the basis of the results of this investigation. Prognosis, which has not been discussed in this paper, is particularly unfavorable in many advanced cases. A treatment strategy has not been established for malignant transformation of MCT, and a relevant therapy is likely to be found by accumulating data on cases of MCT with malignant transformation.

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