

Mature Cystic Teratoma of the Ovary; Clinicopathological Evaluation of 143 Cases in our Series, 5 Years Experience

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ABSTRACT

OBJECTIVE: Mature cystic teratoma, also known as a dermoid cyst, is the most common germ cell tumor of the ovary. In this retrospective study, it is aimed to evaluate clinicopathological findings of the patients who were operated on due to the preliminary diagnosis of dermoid cyst.

STUDY DESIGN: Between May 2013 and May 2018, the findings of a total of 143 patients who were operated on with a preliminary diagnosis of dermoid cyst in our institution were analyzed retrospectively. In addition to demographic characteristics such as age, parity number and tumor size, lateralization, pre-operative tumor markers, surgical procedure, presence of other pathological findings, and the rate of malignant transformation were analyzed.

RESULTS: The median age of patients was 35.4 years and the ratio of nulliparous, primiparous, and multiparous patients was 46.9%, 25.2%, and 28%, respectively. The median tumor diameter was 6.7 cm, 50.3% of which were right-sided, 46.9% were left-sided and the remaining 2.8% were bilateral. Intraoperative torsion was found in 15 (10.5%) cases. The treatment consisted of 60.1% cystectomy by laparoscopy, 3.5% unilateral salpingo-oophorectomy by laparoscopy, 9.8% unilateral salpingo-oophorectomy by laparotomy, while the rate of 16.1% cases underwent hysterectomy with bilateral salpingo-oophorectomy by laparotomy, 10.5% of the cases, cysts were excised during cesarean section. As the final pathology report revealed, of 143 patients, immature teratoma was observed in five cases (3.5%), in one of them (0.7%) mixed germ cell tumor and in three of them (2.1%) borderline mucinous cancer, squamous cell carcinoma, and carcinoid tumor on mature cystic teratoma base were observed.

CONCLUSION: Torsion is the most common complication with mature cystic teratoma. The size of the tumor is an important prognostic factor in terms of the malignant transformation of teratoma. Fertility sparing surgery with a minimally invasive surgical approach is available for fertility patients diagnosed with Mature cystic teratoma.

Keywords: Dermoid cyst, Malign transformation, Mature cystic teratoma, Size, Torsion

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Introduction

Mature cystic teratoma (MCT), also recognized as dermoid cyst, is the most common germ cell tumor of the ovary. It constitutes 10-20% of all ovarian tumors and is the most common benign ovarian tumor (1). These tumors originating from three germ layers are frequently observed between the ages of 20-40 (2). Teratomas developed from three germ layers such as ectoderm, endoderm, and mesoderm are classified according to mature and immature cells; immature, mature, and monodermal teratoma are subtypes (3). Most of them are asymptomatic until symptoms such as pain and abdominal mass are seen due to torsion, rupture, infection, or malignant transformation. It can be detected incidentally during routine physical examination, radiological evaluation, and abdominal surgery for different reasons (4). Transvaginal ultrasonography is the most important diagnostic method for early detection of teratomas and the image is pathognomonic due to the fatty component (5). The detection rate of mature cystic teratomas by tumor markers is low (6). The bilaterality ratio of

MCTs is 10% and torsion is the most common complication in 15% of cases. The rate of malignant transformation varies between 1-2% and occurs in older ages.

The most common malignant transformation in MCT is squamous cell carcinoma and it is seen at a rate of 70-80% in mature teratomas (7,8). Although the exact cause of malignant transformation is unknown, it is assumed that the presence of long-term mature cystic teratoma and squamous metaplasia in the columnar epithelium result from the malignant change. Rarely, adenocarcinoma, small cell carcinoma, carcinoid tumor, various sarcomas, and malignant melanoma can be observed together (8,9). Malignant transformation of MCT may show local invasion and peritoneal implantation, and the clinical symptoms of affected organs can be observed (10,11). MCTs should be surgically removed due to the growth of sizes and complications such as rupture, torsion, infection, and malignant transformation. Standard treatment is ovarian cystectomy with laparotomy or laparoscopic methods or oophorectomy for perimenopausal and postmenopausal women. Cystectomy should be performed by laparoscopic method especially in young patients (12).

Material and Method

Between May 2013 and May 2018, 143 patients were operated on with the preliminary diagnosis of dermoid cyst in our institution. The findings of those 143 patients were analyzed retrospectively in this cross-sectional study. Besides the demographic characteristics such as age, the number of pregnancy and parity and tumor size, lateralization, preoperative tumor markers, surgical procedure and methods, the presence of other pathological findings (such as endometrioma, fibroid, serous cyst), malignant transformation rates was analyzed, too. The data of evolution are obtained from patients' pathology reports and electronic files. SPSS software version 22.0 is used for statistical analysis of the research data.

We used descriptive statistics as categorical and continuous variables. Categorical variables were represented by number and percentage and continuous variables were presented as mean \pm standard deviation for normally distributed data and median (minimum-maximum value) for non-normally distributed data. As a result of the analysis, it was found that the continuous variables in this study were not coherent with the normal distribution. The Mann-Whitney U test was used to compare these inconsistent analyses among double grouped results. ROC analysis was performed to determine whether the cyst diameter has a valuable cut-off in predicting malignancy in cases with teratoma. Values of $p < 0.05$ were considered statistically significant.

Ethics committee approval was received by the ethics committee of our faculty (727 date 08.10.2018). All procedures were performed according to the declaration of Helsinki.

Results

The median age of patients was 35.4 years (ranging from 15 up to 81 years old). The rate of the patients with nulliparous, primiparous, and multiparous was respectively 46.9%, 25.2%, and 28%. The average diameter of the tumors is 6.7 cm, ranging in size from 2 cm to 20 cm. While 50.3% of the tumors were right-sided, 46.9% of them were left-sided. The remaining 2.8% were also bilateral localization. Intraoperative torsion was found in 15 (10.5%) cases (Table I). Torsion was the most common complication among all other complications. Considering the benign pathological rate of the findings, 5.6% endometrioma, 4.2% myoma, 0.7% serous cyst, 0.7% mucinous cyst, 1.4% corpus luteum cyst, and 0.7% Morgagni cyst were detected simultaneously with teratomas. 60.1% of the patients were treated by cystectomy, 3.5% unilateral salpingo-oophorectomy by laparoscopy, 9.8% unilateral salpingo-oophorectomy by laparotomy. While 16.1% of the cases underwent hysterectomy with bilateral salpingo-oophorectomy, in one of the cases diagnosed as immature teratoma with pathology, pelvic and paraaortic lymphadenectomy and omentectomy were performed. In addition, appendectomy was performed for one which was reported as a borderline mucinous tumor. In fifteen (10.5%) cases, cysts were excised during cesarean section. In 2 (1.4%) cases, cysts were detected in antenatal follow-up and 13 (9.1%) cases were incidentally observed during cesarean section (Table II). Malignant pathological results were reported in 10 of 143 patients operated on with a preliminary diagnosis of dermoid cyst. Five cases (3.5%) were reported with immature teratoma by the final pathology, one of them (0.7%) was with mixed germ cell tumor and one of them (0.7%) was with rectal carcinoma besides teratoma. One of them was reported with borderline mucinous tumor, one was with squamous cell carcinoma, and one was with carcinoid tumor observed on mature cystic teratoma base. The last three cases constitute (2.1%) of the total cases. The average age of patients with and without malignancy was respectively, 38 ± 24.5 (min=17-max=81), 33 ± 12 (min=15-max=74) and there were no statistically significant differences (Mann-Whitney test; $p=0.313$).

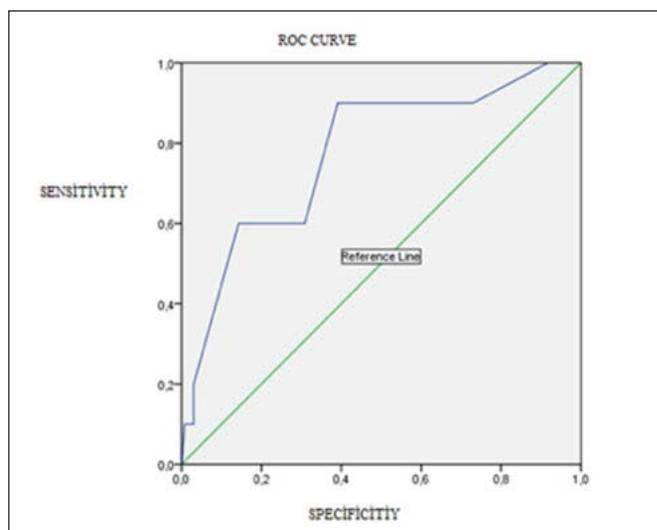
Table I: Evaluation of demographic and clinical data of mature cystic teratoma cases

Demographic features	n (mean; %)
Age(min-max)	35.4 \pm 13.4 (15-81)
Cyst diameter (min-max)	6.7 \pm 3.0 (2-20 cm)
Nulliparous	67 (46.9)
Primiparous	36 (25.1)
Multiparous	40 (28)
Localization	
Right-sided	72 (50.3)
Left-sided	67 (46.9)
Bilateral	4 (2.8)
Torsion	15 (10.5)
Total(n)	143 cases

Table II: Distribution of applied surgical methods in mature cystic teratoma cases

Surgical method	n (%)
Laparoscopy cyst excision	86 (60.1)
Laparoscopy salpingo-oophorectomy	5 (3.5)
Laparotomy salpingo-oophorectomy	14 (9.8)
TAH+BSO	23 (16.1)
C /S + Cyst excision	15 (10.5)
Total	143

As a result of ROC analysis, cyst diameter had a diagnostic value to predict malignancy in patients with teratoma (AUC=0.775; %95CI=0.620-0.929; $p=0.004$), and the cut-off value was determined as 6.5 cm (sensitivity 90%, specificity 61%, Figure1).

**Figure 1:** Receiver operating characteristic analysis to evaluate sequence matching, analysis curve of cyst diameter of 143 individuals included in the study.

The effect of risky conditions on malignancy in teratomas was investigated by univariate binary logistic regression analysis. It was determined after the result of the analysis that cyst diameter ≥ 6.5 cm, the value of AFP level ≥ 9 ng/mL, and the

value of CA-125 level ≥ 35 U/mL were found to be effective on the malignancy diagnosis (Table III).

Discussion

Mature cystic teratoma is accepted as the most frequently seen benign ovary tumor that constitutes 10-20% of the total (13). Teratomas could exist in any age but it is frequently seen between the ages 20-40 (14). In this study, the average interval of age is 35.4 ± 13.4 , which is coherent with previous studies. It is important to diagnose MCT in the early phase so that conservative ovary operation could be used easily and it has less effect on puberty and fertility because MCTs are often seen in the reproductive period (15). It is presumed that MCTs are seen in this age group because it comes out of only the primordial germ cell that completes meiosis 1 and represses meiosis 2 (16). More than 90% of mature cystic teratomas are unilateral and located on the right side. Bilaterality is between 8% and 15% (17). In this study, 50.3% of the tumors were on the right ovary and 46.9% were on the left. 2.8% were bilateral and this rate was lower than in the literature. Patients with mature cystic teratoma could have pain, menstrual disorder, and some other urinary and gastrointestinal complaints due to the pressure caused by the diameter of the mature cystic teratoma, and they are mostly asymptomatic and seen during the gynecological examination or incidentally during the surgery (18-20). In this study, 25 of the patients (17.4%) had a tumor over 10 cm diameter and pain along with complaints related to the pressure while 15 (10.5) of the cases were urgently operated on because of torsion, and in 13 (9.1%) patients, MCT was incidentally seen during the cesarean section.

The most frequently seen complications of mature cystic teratoma are torsion, rupture, and malignant transformation. The torsion frequency changes between 3.5% and 9.2% interval in literature, and the torsion frequency was 10.5% in this study (21). Ayhan et al. determined 4.9% torsion in their study which includes 501 patients (1). The size of the tumor in torsioned cases is usually bigger than the average but it is thought

Table III: Evaluation of the effect of cyst diameter and tumor markers on malignancy transformation

	Malignite Positive n*	Malignite Positive %	OR (95 % CI)**	p
Cyst diameter (n=143)	1/82	1.2	1	0.004
<6.5 cm (reference)	52/61	85.2	14.02 (1.73-113.93)	
≥ 6.5 cm				
AFP (n=92)	5/88	5.7	1	0.011
<9 (reference)	2/4	50	16.60(1.10-143.62)	
≥ 9				
Ca-125(n=104)	4/91	4.4	1	0.024
<35 (reference)	10/13	76.9	6.53 (1.27-33.43)	
≥ 35				

*Number of patients with malignancy/number of all patients. **OR: Odds Ratio

that the increase in dimension may not be the reason but could be the result (22). In this study, the average cyst diameter in torsioned cases is 8 ± 4 while it is 6 ± 2.7 in the ones without torsion, the fact that the diameter of the cyst is increasing while the torsion rate is increasing (Mann-Whitney test; $p=0.014$) was found statistically significant.

Rupture is a very rare complication that causes granulomatous peritonitis via leaking the liquefying sebaceous cyst ingredient into the peritoneal gap (23). Rupture is not found in this study.

Malignant transformation is usually seen in postmenopausal women, it is rare and its incidence changes between 0.2% and 4%. Peterson determined 1.8% malignant transformation among 8000 patients with MCT, Hurwitz et al. determined 1-2%, and Kim et al. 0.6% (24-26). The Taiwan Oncology Group that includes Chiang et al. determined 0.2% that comes from the results of ten different studies which constitute metanalysis (27). Sherpa et al. determined 3%, Rathore 3.5%, and Bedir et al. determined 4% (28-30).

Squamous cell carcinoma could come out of any component of mature cystic teratoma, which is seen in almost 80% of malignant cases (31). Less often than squamous cell carcinoma; thyroid carcinomas, adenocarcinomas, and carcinoid tumors could be seen (26). In this study, in only one case (0.7%), squamous cell carcinoma in teratoma was seen, in one case (0.7%) borderline mucinous tumor in teratoma, and in one case (0.7%) on teratoma base, carcinoid tumor was seen (Figure 2). The malignant transformation rate of these cases was 2.1%, which supports the relevant literature. About MCT, the ages of the patient and the dimension of the tumor are important for the development of malignant transformation (17). In the studies done by Chiang, Sherpa, and Rathore, et al, the average age of the patients was 52, 47.5, and 40, respectively. The dimension of the tumors was determined as 10.5, 10.8, and 10 cm (27-29). The average age was 55 and the average dimension of the tumor was 10 and over in the study in which 277 patients with squamous cell carcinomas, the malignant transformation was researched in 126 articles published between 1978 and 2007 (31,32). In this study, the average age was 38 ± 24.5 among the patients with malignant transformation while it was 33 ± 12.0 in the one without malignant transformation, which was not statically significant (Mann-Whitney test; $p=0.313$). In this study, 3 patients aged 53, 37, and 81 were diagnosed with malignant transformation on teratoma base. Immature teratoma was determined in 5 patients who were diagnosed with MCT operated by the researchers, in another patient, a mixed germ cell tumor was seen and all malign cases were evaluated together while statistics were done. The average dimension of the tumors was 10 ± 4.3 cm in the cases with malignant transformation while it was 6 ± 2.8 cm in the ones without malignant transformation. The difference was found significant (Mann-Whitney test; $p=0.003$). ROC

analyses showed that the dimension of the cyst of the patients who have teratoma diagnosis is valuable in predicting malignancy and the limit value is determined as 6.5 cm (sensitivity 90 % specificity 61%) (AUC: 0.775; %95 GA=0.620-0.929; $p=0.004$). No certain correlation was seen between malignant transformation and serum tumor indicators but in some cases, high levels of CA-125 or CA19-9 were accompanied (31,33). In this study, serum AFP level ≥ 9 ng/mL and CA-125 level ≥ 35 U/ml were found to be effective on malignancy.

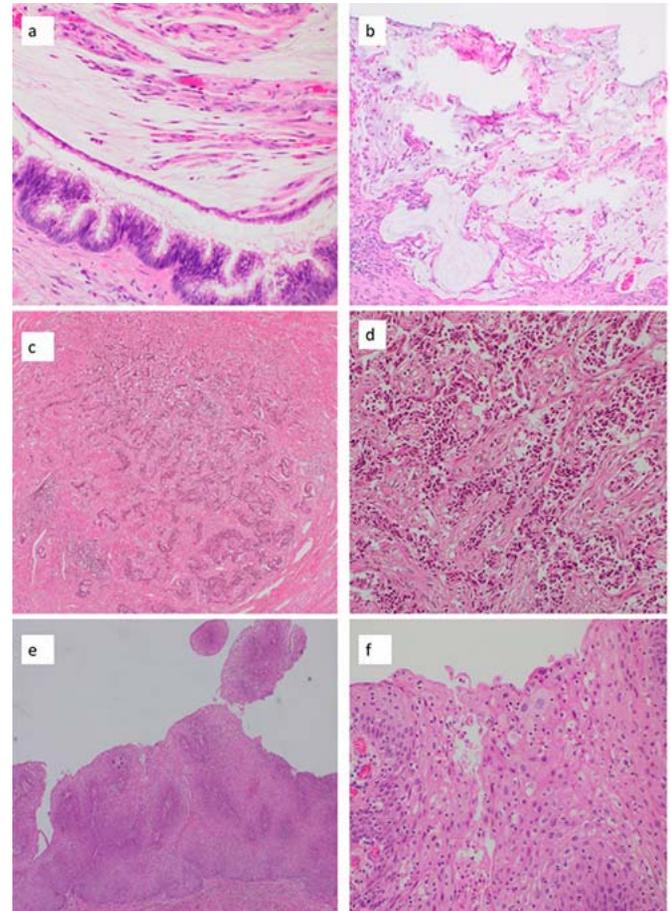


Figure 2a: Mucinous borderline tumor lining with proliferating pseudostratified epithelium (H&E stain, x100). **b:** Myxoid infiltration associated with pseudomyxoma peritonei (H&E stain x200). **c,d:** Carcinoid tumor infiltration in cyst wall (H&E stain x40 and x400, respectively) **e,f:** Squamous cell carcinoma in situ in cyst wall (H&E stain x100 and x200, respectively).

Ultrasonography is mostly used to diagnose MCT (34). In this study, apart from 9.1% incidentally diagnosed cases, all cases of MCT were diagnosed via ultrasonography in the preoperative era.

Oophorectomy was the most used principal procedure for MCT in the previous period (35). Because MCTs are usually seen in women in the reproductive period, the operative approach should be as conservative as possible. Oophorectomy or salpingo-oophorectomy is suitable for young patients who have suspicious malignancy or for the women in postmenopausal period (1). In 101 (70.6%) of our cases, cyst ex-

cision (60.1% of them laparoscopy, 10.5% of them laparotomy) was applied, for 13.3% of them salpingo-oophorectomy and for 16.1% of them, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed.

Considering the cases in which total abdominal hysterectomy and bilateral salpingo-oophorectomy were used, malignancy, myoma, cyst, descensus, and other gynecologic problems were indications for surgery. Age, fertility desire, and additional pathologies must be considered in deciding how to treat MCT.

Mature cystic teratoma is the most seen benign ovary tumor in the reproductive period and preoperative ultrasonography is the most important indicator. They are usually unilateral and the risk of malignant transformation is low and the incidental diagnosis during the operation is high. Additionally, torsion is the most seen complication of these tumors. Older age and the dimension of the cyst are the most risk factors in malignant transformation. The most suitable operative approach is laparoscopic cyst excision if it is not malignant.

Declarations: Ethics approval and consent to participate
All participants signed informed written consent before being enrolled in the study.

The informed consent was taken from patients before surgery that the study was conducted in accordance with the Declaration of Helsinki.

Availability of data and materials: The data supporting this study is available through the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: FK., OE., and AO: Raised the presented idea. FK., BO., and DY: Designed the study. DY: Conducted the analyses. FK., OE., and BO: Developed the first draft of the manuscript. All authors contributed to the writing of the paper, and have read and approved the final manuscript.

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