Is Presence Time of Dermoid Cysts a Risk Factor for Malignancy Potential in Advanced Age?

6 authors, including:

Bugra Coskun
Ankara Liv Hospital
43 PUBLICATIONS 29 CITATIONS

SEE PROFILE

Bora Çoşkun
40 PUBLICATIONS 38 CITATIONS

SEE PROFILE

Mehmet Ferdi Kinci
Mugla Sıtkı Kocman University Education and Research Hospital
49 PUBLICATIONS 28 CITATIONS

SEE PROFILE

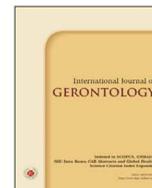Some of the authors of this publication are also working on these related projects:

Project

The opinions and thoughts of the women who had applied hysterosalpingography for the first time: Letter to editor View project

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Is Presence Time of Dermoid Cysts a Risk Factor for Malignancy Potential in Advanced Age?

Çoşkun Buğra [a *], Salman-Özgü Burçin [b], Kısa Burcu [b], Çoşkun Bora [a], Kıncı Mehmet Ferdi [b], Çolak Eser [c], Evliyaoğlu Özlem [b]

[a] *Department of Obstetrics and Gynecology, Gülhane Education and Research Hospital, Ankara, Turkey,* [b] *Department of Obstetrics and Gynecology, Zekai Tahir Burak Women's Health Education and research Hospital, Ankara, Turkey,* [c] *Department of Obstetrics and Gynecology, Baskent University Research Center, Konya, Turkey*

ARTICLE INFO

SUMMARY

Background: We have aimed to identify the markers for malignant transformation and also determine the differences between the reproductive age and postmenopausal mature cystic teratoma (MCT) patients.

Methods: Between 2008 and 2015, totally 246 patients informations diagnosed as MCT have been examined retrospectively. Demographic characteristics of the patients, preoperative examinations, final pathology results have been evaluated.

Results: It is included 246 patients with a total of 117 postmenopausal, 129 reproductive age in the study. When demographic characteristics, tumor markers and mass size were compared, only Carcino Embryogenic Antigen (CEA) values were found to be statistically significantly higher in postmenopausal patients. Malignancy was detected in 5 patients (2.03%), all of them were in the postmenopausal period, also CA125 and CA15-3 were determined statistically high in malignant patients.

Conclusions: We think that CA125 can be use as marker for MT in MCT as well as on epithelial ovarian tumors. The duration of mass inside the abdomen without being operated can be a risk factor for malignant transformation. Because of this reason even if it is asymptomatic, after MCT diagnose we think that it will be good to operate the patients without losing time for prevention of malignant transformation.

1. Introduction

Mature cystic teratoma (MCT), also known as dermoid cyst, is one of the most common ovarian tumors, accounting for 11–20% of such tumors.[1] In the second and third decades of life, MCT is the most common ovarian tumor in women.[2] It is most commonly seen in reproductive-age patients, and sometimes it can be seen in the postmenopausal period.[3]

Most women with dermoid cysts are asymptomatic.[4] Symptoms usually depend on the size of the mass. Torsion is not uncommon. Dermoid cyst rupture may also result in the spillage of sebaceous material in the abdominal cavity, but this is rare. Shock and bleeding are early signs of rupture; a marked granulomatous reaction (chemical peritonitis) may develop later and lead to the formation of dense adhesions.[2] Preoperative diagnosis of MCT can be provided easily with ultrasonography, computed tomography, and magnetic resonance imaging; the bony tissues, including teeth, bones, and cartilage, can be easily identified by these imaging methods.[5] MCT is always benign in pure form; however, as a rare complication, malignant transformation (MT) is seen in approximately 1–2% of MCTs.[1] MT frequency is related to age and usually appears in advanced-age patients, such as those between ages 45 and 60.[6] Many MTs are squamous carcinoma. The prognosis of MT is worse than that of epithelial ovarian cancer. Additionally, the management of patients with MT naturally differs from that of patients with benign MCTs. For this reason, diagnosis of MT prior to surgery will benefit the prognosis of the disease.[7]

The extant literature does not provide enough information about MCT prognosis with advancing age. In this study, we aimed to determine possible markers that could be used in predicting malignancy in patients with an MCT diagnosis and to investigate the differences between patients with reproductive-age and postmenopausal MCT.

2. Material and methods

A total of 246 patients were included in our retrospective planned study; all were reported with final pathologic MCT diagnoses between 2008 and 2015. Our study plan was reviewed and approved by our hospital's Civilian Expertise and Ethics Committee. Demographic data of the patients and operation and pathology results were obtained via the hospital registry system. Patients with

* Corresponding author. Department of Obstetrics and Gynecology, Gülhane Education and Research Hospital, Ankara, Turkey.

E-mail address: drbugracoskun@gmail.com (Ç. Buğra)

deficiencies in the data available in the hospital operating system were excluded from the study.

The demographic characteristics of patients, preoperative complaints, preoperative values for CA125, CA19-9, carcino embryogenic antigen (CEA), CA15-3, and alpha feto protein (AFP), mass diameters, and final pathology results were evaluated. Data of patients diagnosed with MT as well as data of patients diagnosed with benign postmenopausal and premenopausal MCT were compared using statistical methods. The operations performed with demographic and tumor marker values of patients with MT and the stage and grade status of the tumor were examined and recorded.

Statistical analysis was performed using SPSS Version 22 (SPSS Inc., Chicago, IL). Numerical variables are described with mean and standard deviation values and categorical variables were shown as a median also minimum and maximum values were described for all variables. The differences between the groups were compared using chi-square or Mann-Whitney U tests. The receiver operating characteristics (ROC) area under the curve (AUC) was used to determine the sensitivity and specificity of each marker, either alone or in combination. The optimal cutoff values were calculated by ROC analysis and the Youden index. P < 0.05 was considered statistically significant.

3. Results

A total of 246 patients, 117 postmenopausal and 129 reproductive-age patients with MCT, were included in the study. All were present in our gynecology clinic between 2008 and 2015 and had a final pathology report of MCT.

The mean age of the premenopausal patients was 39.02, while the mean age of the postmenopausal patients was 55.24. The vast majority of the patients in our study detected MCT incidentally. In the whole population, 84 patients (34%) were asymptomatic. The most common complaint was abdominal pain during admission to the hospital, seen in 75 patients (30%). Other leading causes were bloating in 16%, menstruation irregularity in 14%, and mass in 5%.

Of the 129 patients in the premenopausal period, 39% (51 patients) were asymptomatic, while 28% (36 patients) had abdominal pain, and 19% (25 patients) had bleeding disorders. In the

postmenopausal period, 35% of the 117 patients (38 patients) were admitted to the hospital with complaints of abdominal pain, while 29% were asymptomatic and MCT was incidentally detected. In this group, 17% (19 patients) complained of swelling in their abdomens. Malignancy, seen in five of the patients, was asymptomatic in two of the patients and presented with abdominal pain in two patients and swelling in the abdomen in one patient.

The mean mass size of the pathologic specimen was 5.79 cm in the premenopausal age group and 6.60 cm in the postmenopausal age group; there was no statistical difference between the two groups. The mean mass of patients with malignancy was 5.70 cm, and there was no statistically significant difference between this group and the non-malignancy group. Malignancy was observed in 2% of all patients, and all were postmenopausal. Serological carcinoma was observed in three patients, borderline mucinous tumor in one, and carcinoid tumor in one patient with malignancy. The characteristics of patients with MT as a result of the ultimate pathology are shown in Table 3. When demographic features, tumor markers, and mass size were compared, only CEA values were found to be statistically significantly higher in postmenopausal patients, compared to premenopausal MCT patients (0.91 ng/ml vs. 1.94 ng/ml; p < 0.001) (Table 1).

Malignancy was detected in five patients (2.03%). All patients with malignancy were in the postmenopausal period (Table 2). When the preoperative findings of malignant and benign patients were compared, it was determined that Ca 125 and Ca 15-3 values were statistically higher in malignant patients: respectively, 165.2 U/ml vs. 15.37 U/ml and 56.04 U/ml vs. 14.5 U/ml (Table 3).

The ROC analysis of the CA125 and CA15-3 values among patients with the diagnosis of malignancy is shown in Figure 1. The AUC for CA125 and CA15-3 were 0.873 and 0.803 respectively. (95% confidence interval 0.85–0.94; p < 0.001) with a cutoff value of 34.45 U/ml for CA125, a sensitivity of 80.0%, a specificity of 94.1% and with a cutoff value of 16.80 U/ml a sensitivity of 80.0%, a specificity of 66.6% (Figure 1).

4. Discussion

Although MCT can be seen in all age groups, it is most fre-

Table 1

Comparison of menopausal and non-menopausal mature cystic teratoma patients.

	Nonmenopozal (n = 129)	Menopozal (n = 117)	p
Age	39.02 ± 7.436 (22–50)	55.24 ± 7.092 (46–77)	*< 0.001*
Gravida	4 (0–8)	5 (0–14)	0.059
Parite	3 (0–8)	4 (0–14)	0.096
CA125	16.34 ± 13.174 (2.2–113.0)	20.76 ± 353.941 (3.3–383.3)	0.16
CA19-9	40.71 ± 17.749 (0.6–58.1)	45.97 ± 86.085 (1.07–700)	0.19
CA15-3	14.06 ± 8.095 (0.5–37.3)	16.82 ± 17.749 (0.5–182.9)	*0.18*
CEA	0.91 ± 1.595 (0.5–16.4)	1.94 ± 5.585 (0.3–58.1)	*< 0.001*
AFP	2.85 ± 4.392 (0.7–40.5)	2.41 ± 1.923 (0.5–14.2)	0.48
Diameter (cm)	5.79 ± 2.751 (1.0–13.0)	6.60 ± 3.401 (1.5–20.0)	0.10
Malignancy (n)	0	5	*< 0.001*

Table 2

Characteristics of mature cystic teratoma patient swith malignancy.

Pt.	Age (year)	AC	Histological type	TS (cm)	CA 125 (U/ml)	CA 19-9 (U/ml)	CEA (ng/ml)	CA 15-3 (U/ml)	AFP (ng/ml)	Stage
1	46	AP	BMT	7	119.8	167.6	58.13	16.9	2.24	1c2
2	59	AB	SC	9.7	383.4	154.4	2.16	40.8	1.38	3b
3	63	AP	SC	6.1	34.9	19.45	1.29	27.7	2.11	3a2
4	77	N	SC	3	278	12.01	0.01	182.9	2.3	3b
5	71	N	CT	2.7	10.6	24.4	1.64	11.9	3.14	1a

P: Patient no, AC: Application complaint, AP: Abdominal pain, AB: Abdominal bloating, N: None, BMT: Borderline mucinous tumor, SC: Serous carcinoma, CT: Carcinoid tumor, TS: Tumor size.

Table 3
Comparison of mature cystic teratoma patients with and without malignancy.
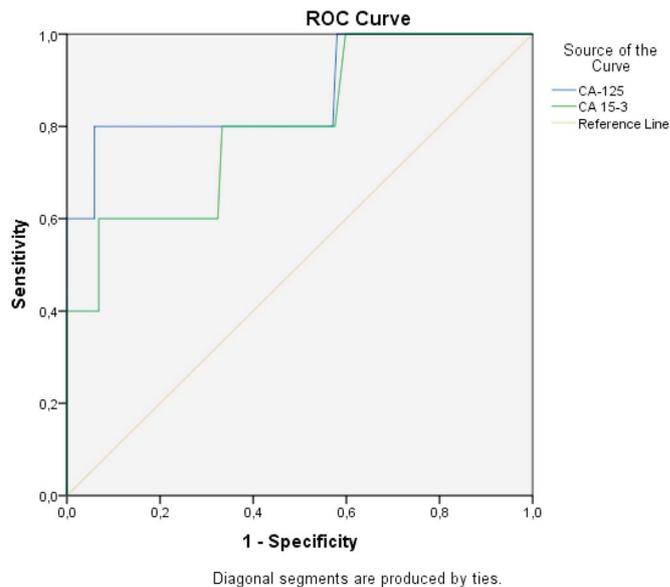
	Malign (n = 5)	Benign (n = 241)	p
Age	63.2 ± 11.866 (46–77)	46.41 ± 10.652 (22–77)	***0.007***
Gravida	4 (2–12)	5 (0–14)	0.20
Parite	3 (2–12)	3 (0–14)	0.437
CA125	165.20 (10.6–383.8)	15.37 (2.2–113.0)	***0.004***
CA19-9	75.56 (12.01–167.56)	42.61 (2.2–700)	0.152
CA15-3	56.04 (11.9–182.9)	14.50 (0.5–37.3)	***0.020***
CEA	12.64 (0.0–58.1)	1.14 (0.0–16.4)	0.170
AFP	1.84 (1.4–2.3)	2.66 (0.7–40.5)	0.657
Diameter (cm)	5.70 (3.0–10.0)	6.19 (1.0–20.0)	0.808

Figure 1. Receiver operating characteristic analysis of Ca125 and Ca15-3 to diagnose malignancy in mature cystic teratoma patients.

quently observed in women in the reproductive age.[4,8] Most MCT is asymptomatic, and for the majority of patients diagnosed, MCT is incidentally detected during routine gynecologic examinations or ultrasonography. In rare cases, hyperthyroidism can cause symptoms due to the inside of the thyroid tissue.[4] The majority of patients in our study were asymptomatic patients (34%) with incidental MCT detected in accordance with the literature. Of the 129 patients in the premenopausal period, the majority (39%) were asymptomatic, while in the postmenopausal period, 29% of the 117 patients were asymptomatic. In symptomatic cases, abdominal pain, abdominal mass, abdominal bloating, and menstrual irregularities were the most common complaints. The most common complaint in the postmenopausal period was abdominal pain (35%).

A specific symptom indicative of MT was not identified. In our study, two out of five patients with MT were asymptomatic, two presented with abdominal pain, and one patient with swelling in the abdomen. Patients with MT compatible to the literature are likely to be asymptomatic or to suffer from complaints such as headache, pelvic pain, abdominal mass, and distention.[6,9]

In the diagnosis of dermoid cysts, ultrasonographic examination is accepted as the gold standard because it is noninvasive and effective.[10,11] Mass screening of all the patients in our study was also performed by ultrasonography. While MCTs are usually 5–10 cm in size, approximately 10% of cases find tumors larger than 15 cm in size. In a study conducted between the body and the tumor size, it was found that dermoid cysts that were detected under the age of 20 years were more susceptible to being thick.[4] However, in our study, the size of the mass in the pathologic specimen was 5.79 cm (1.0–13.0 cm) in the premenopausal patients and 6.60 cm (1.5–20.0 cm) in the postmenopausal patients; statistically no difference was detected between the two groups. There are also studies suggesting that the diameter of the tumor may predict malignancy. Additionally, some studies have stated that a mass above 10 cm may be associated with a high risk of malignancy.[12,13] In our study, there was no significant difference in tumor size between the groups with MT detected and undetected. This may be due to the limitation of our sample size.

Tumor markers are widely used in the differential diagnosis of MCT, as in the distinction of ovarian masses. There is no specific tumor marker to diagnose dermoid cyst. However, tumor markers such as CA125, CA19-9, CA15-3, and AFP are frequently used.[14,15] In our study, only CEA values were found to be statistically significantly higher in postmenopausal MCT patients, compared to premenopausal patients (0.91 ng/ml vs. 1.94 ng/ml; p < 0.001). Although there are many studies on the search for a marker to predict MT in patients with MCT, there is no clear result yet.[9] In our study, when preoperative findings of malignant and benign MCT patients were compared, it was determined that CA125 and CA15-3 values were statistically higher in malignant patients (respectively, 165.2 U/ml vs.

15.37 U/ml, 56.04 U/ml vs. 14.5 U/ml). MT is seen in 0.2–2% of MCTs.[16,17] Malignant transformed MCTs constitute 2.9% of all malignant ovarian germ cell tumors. Although any components of the MCT can undergo malignant degeneration, squamous cell carcinoma originating from the ectoderm is the most common secondary neoplasm.[2] Serous carcinoma, adenocarcinoma, melanoma, immature teratoma, and granulosa cell tumor are common malignancies.[18] Serous carcinoma was observed in our case in three patients, borderline mucinous tumor in one, and carcinoid tumor in one. When MT exists in MCT, the treatment should be adapted to the converted histology. In parallel, as in our series, expanded surgical procedures are needed for patients with MT. Among the risk factors for malignant neoplasm in MCT is an age over 45 years, as the mean age for MT was 50 years, compared to a mean age of 33 years for benign teratomas.[2] Other risk factors include tumor size greater than 10 cm, rapid growth and imaging findings.[2] In our study, all patients with MT were in the postmenopausal period, and the mean age was 63.2 (range 46–77), which was statistically significantly higher than the mean age of the benign group.

5. Conclusions

Dermoid cysts are usually benign ovarian tumors frequently found in women in the reproductive age group. MT is the most catastrophic complication of MCTs. The type of operation, life expectancy, quality of life parameters, and overall survival rates all differ between patients with MT and benign MCTs. For this reason, it would be useful to diagnose MT prior to operation. Ultrasonography is a useful diagnostic tool for MCT because of its easy accessibility and diagnostic sensitivity. However, there is no specific diagnostic tool for pre-operative diagnosis of malignant transformation. According to the current literature and data from our study, CA125 may be accepted as a marker for MT in MCT as well as in epithelial ovarian tumors.

Despite the small number of patients in our study, we found a relatively high incidence of malignancy in MCT patients with advancing age. This could be due to the peak incidental age of ovarian cancer, but presence of MCT tissue for a long period of time could also be a cause for malignant transformation. For this reason, we think that operating on patients after an MCT diagnosis without

delay will be useful for avoiding malignancy, even if the patient is asymptomatic. A wider series of studies focusing on dermoid cysts in the postmenopausal period may better elucidate the causes and long-term malignancy potential of dermoid cysts.

Conflicts of interest

Authors declarate that we have no potential financial and non-financial conflicts of interest.

References

1. Park JY, Kim DY, Kim JH, et al. Malignant transformation of mature cystic teratoma of the ovary: Experience at a single institution. *Eur J Obstet Gynecol Reprod Biol.* 2008;141(2):173–178.
2. Zalel Y, Piura B, Elchalal U, et al. Diagnosis and management of malignant germ cell ovarian tumors in young females. *Int J Gynaecol Obstet.* 1996;55(1):1–10.
3. Goudeli C, Varytimiadi A, Koufopoulos N, et al. An ovarian mature cystic teratoma evolving in squamous cell carcinoma: A case report and review of the literature. *Gynecol Oncol Rep.* 2017;19:27–30.
4. Kim MJ, Kim NY, Lee DY, et al. Clinical characteristics of ovarian teratoma: Age-focused retrospective analysis of 580 cases. *Am J Obstet Gynecol.* 2011;205(1):32.e1–32.e4.
5. Kido A, Togashi K, Konishi I, et al. Dermoid cysts of the ovary with malignant transformation: MR appearance. *AJR Am J Roentgenol.* 1999;172(2):445–449.
6. Koc S, Tapisiz OL, Turan T, et al. Malignant transformation of mature cystic teratoma of the ovary: A case series. *J Exp Ther Oncol.* 2015;11(1):11–16.
7. Mori Y, Nishii H, Takabe K, et al. Preoperative diagnosis of malignant transformation arising from mature cystic teratoma of the ovary. *Gynecol Oncol.* 2003;90(2):338–341.
8. Naqvi KZ, Abdullah A, Jabeen M, et al. Ovarian dermoid causing pilimiction. *J Coll Physicians Surg Pak.* 2015;25(1):71–72.
9. Tseng CJ, Chou HH, Huang KG, et al. Squamous cell carcinoma arising in mature cystic teratoma of the ovary. *Gynecol Oncol.* 1996;63(3):364–370.
10. Cakmak B, Nacar M, Ozsoy Z, et al. Mature cystic teratomas: Relationship between histopathological contents and clinical features. *Niger J Clin Pract.* 2015;18(2):236–239.
11. Tekin YB, Altınbaş ŞK, Dede FS, et al. The parameters affecting accuracy of e ultrasonographic diagnosis in dermoid cysts. *Dicle Med J.* 2014;41(1):64–70. [In Turkish, English abstract]
12. Kikkawa F, Nawa A, Tamakoshi K, et al. Diagnosis of squamous cell carcinoma arising from mature cystic teratoma of the ovary. *Cancer.* 1998;82(11):2249–2255.
13. Kimura T, Inoue M, Miyake A, et al. The use of serum TA-4 in monitoring patients with malignant transformation of ovarian mature cystic teratoma. *Cancer.* 1989;64(2):480–483.
14. Park CH, Jung MH, Ji YI. Risk factors for malignant transformation of mature cystic teratoma. *Obstet Gynecol Sci.* 2015;58(6):475–480.
15. Suh DS, Moon SH, Kim SC, et al. Significant simultaneous changes in serum CA19-9 and CA125 due to prolonged torsion of mature cystic teratoma of the ovary. *World J Surg Oncol.* 2014;12:353.
16. Singh P, Yordan EL, Wilbanks GD, et al. Malignancy associated with benign cystic teratomas (dermoid cysts) of the ovary. *Singapore Med J.* 1988;29(1):30–34.
17. Westhoff C, Pike M, Vessey M. Benign ovarian teratomas: A population-based case-control study. *Br J Cancer.* 1988;58(1):93–98.
18. Hursitoglu BS, Demirtas GS, Demirtas O, et al. A clinico-pathological evaluation of 194 patients with ovarian teratoma: 7-year experience in a single center. *Ginekol Pol.* 2013;84(2):108–111.