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ORIGINAL RESEARCH

Incidental risk of malignancy in mature cystic teratoma: experience of a single tertiary center

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Abstract

We aimed to evaluate the incidental risk of malignancy in mature cystic teratomas (MCT) and check the management. We retrospectively reviewed records of patients diagnosed and treated with MCT and divided patients into two groups as pure MCT and malignant transformation of MCT. In our clinic incidence of incidental malignant transformation of ovarian MCTs was 2.7%. Median age ($p = 0.005$) and mass size ($p = 0.027$) were statistically higher in malignant group. The most common histological type of malignant transformations was malignant struma ovarii (35.7%). In malignant group, five-year disease-free survival was 66.7% and five-year overall survival was 86.7%. Although the risk of malignancy in mature cystic teratomas is rare, it should not be ignored. Age, mass size, and preoperative imaging should all be evaluated with suspicion and if available, frozen section should be used. Management is inconsistent as a result of its rarity. New management practices should be developed with further studies.

Keywords

Dermoid cyst; Mature cystic teratoma; Malignancy; Malignant transformation

1. Introduction

Ovarian germ cell tumors that originated from primordial germ cells can be malignant or benign. Dermoid cyst, also called mature cystic teratoma (MCT), accounts for 10 to 20% of all ovarian tumors and is the most common ovarian germ cell tumor and is almost always benign [1]. Because of MCT's contents like teeth, bone, and cartilage as bony tissues, detecting it by using radiographic tools is simple and because of its benign nature, operations may be scheduled for a later date. Unfortunately, as a rare complication, MCT transforms to malignancy in about 1.2% of all cases [2]. Malignancy can be developed from all of three germ cell layers. Several types of malignancy have already been reported. These reported malignancy types are malignant thyroid struma, carcinoid tumor, melanoma, a variety of soft tissue sarcomas, squamous cell carcinoma, clear cell carcinoma [2]. Because of the rarity of these tumors, their clinicopathologic features, prognostic variables and treatment options have not been known yet. However, according to reports, the prognosis for these malignancies is poor [3]. Preoperative identification of malignant transformation is not easy as MCT. It is obvious that if there is a malignancy, the operation cannot be postponed. Thus, we must be aware of and prepared for the risk of malignancy.

We reported our experience about the patients treated for MCT and incidentally detected malignancy and discussed our current management protocols and survival statistics.

2. Material and methods

Total of 577 patients who were diagnosed with ovarian teratoma and undergone surgery between March 2000 and March 2015 at Department of Obstetrics and Gynecology, Ege University Faculty of Medicine, İzmir, Turkey, were included in the study. The records of the cases were retrospectively reviewed from the clinic's database. The only exclusion criterion was the detection of "immature teratoma" in the final pathology. When we observed the pathology results; pathology reports of 555 patients were resulted as MCT and of the other 22 patients as immature cystic teratoma. We excluded patients diagnosed with immature teratoma and investigated patients whose final pathology was reported as MCT. Out of 555, there were 15 patients diagnosed with MCT who had another malignancy in the ovarian cyst as well as the mature teratoma.

We divided the patients into two groups as pure mature cystic teratoma and malignant transformation of MCT. Age, size of tumor, bilaterality, presence of torsion, another ovarian pathology, type of operation, tumor marker values, recurrence, follow up time and necessity of second operation were checked retrospectively and recorded for two groups. Adjuvant chemotherapy, lymph node dissection rate and number of removed lymph nodes, progression free survival (PFS) and overall survival (OS), pregnancy after operation were checked for malignant transformation of MCT group and recorded. All these data were compared within each group and between two

groups.

Comparisons between and within groups were made with Mann Whitney U tests for continues variables and Chi-Square or with Fisher's exact tests for nominal variables. Kaplan-Meier method was used for survival analysis.

p values were the result of two-sided tests, and a p value, 0.05 was considered to indicate a statistically significant difference. Statistical analyses were done using Statistics Software Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc, Chicago, IL, USA).

3. Results

We reviewed 555 patients with ovarian MCTs, and there were 15 patients (2.7%) with malignant transformation out of 555 patients with ovarian MCTs. The median age was 50 years in patients with malignancy, which was statistically higher than the patients with pure MCT whose median age was 31 years ($p = 0.005$). The median ovarian mass size in patients with malignancy was 8 cm, which was statistically higher than the patients with pure MCT whose median ovarian mass size was 5.5 cm ($p = 0.027$). Tumor markers (cancer antigen 125 (CA125), cancer antigen 15-3 (CA15-3), carcinoembryonic antigen (CEA), cancer antigen 19-9 (CA19-9)) and preoperative abdominal cytology were statistically same between two groups (Table 1).

There was no bilaterality, torsion of ovary or mass, preoperative abdominal malignant cytology and another ovarian pathology in malignant group.

Two patients in the malignant group had laparoscopy, whereas the others had laparotomy. Two of them had cystectomy, five of them had unilateral oophorectomy, and eight of them had both hysterectomy and bilateral oophorectomy. Because of their ages, five of them had fertility preserving surgery, but no one gave birth after treatment throughout the follow-up period. No one had lymphadenectomy. The most common histological type was malignant struma ovarii (35%). The least common histological types were dysgerminoma (7.1%) and squamous cell carcinoma (SCC) (7.1%). Two of them had cancer recurrence. None of them had a second operation. Four of them were treated with adjuvant chemotherapy and five of them died because of malignancy (Table 2). Five-year disease-free survival was 66.7%, five-year overall survival was 86.7% in malignant group.

4. Discussion

In this retrospective analysis, the incidence of malignant transformation of ovarian MCTs was found to be 2.7%, which is slightly higher than in prior investigations. This rate has been estimated to range between 0.17% and 1.6% in several researches [3–6]. Due to the rarity of malignant transformation, limited evidence from studies with a small number of cases can make it difficult to determine the true rate.

Age and mass size may be sign of malignancy. The majority of research concluded that malignancy suspicion should be raised if a postmenopausal woman has MCT more than 9.9 cm [7–10]. According to Black et al. [11], the average tumor size was 18 cm. This can be about long-term presence of the dermoid cyst in the ovary. In our study, average tumor size was found to be 8 cm in malignant group and 5.5 cm in MCT group. Although age and mass size are significantly higher in malignant group than in pure MCT in our study, we should be aware that these results belong to an incidentally found malignant transformation. The youngest age in the malignant transformation group was 21, and the smallest mass size was 1.1 cm in our study. This means that all mature cystic teratomas should be diagnosed and managed with caution.

The most common histological type was found to be SCC in previous studies, and they focused on the diagnosis and treatment of this malignancy. In these studies, serum SCC antigen levels were found to be useful for preoperative diagnosis [8, 12, 13]. In our study, the most common histological type was malignant struma ovarii (35%). Only one of our cases was SCC (7.1%). In our study, preoperative blood SCC antigen levels were not examined, while tumor markers (CA125, CA15-3, CEA and CA19-9) were not different between two groups. This demonstrates that the rarity of the malignancy and the variability of histologic types can lead to preoperative misdiagnosis.

TABLE 1. Comparison of the two groups.

	Malignant group (n: 15/555 2.7%)	Pure mature cystic teratoma group (n: 540/555 97.3%)	p value	OR (95% CI)
Age median (range)	50.00 (21.00–75.00)	31.00 (6.00–94.00)	0.005*	8.81 (3.08–25.13)
Ovarian mass size (cm) median (range)	8.00 (1.10–22.50)	5.50 (1.00–25.00)	0.027*	3.11 (1.10–8.73)
CA125 (U/mL)	18.00	18.00	0.944	
CA19-9 (U/mL)	11.65	22.50	0.108	
CA15-3 (U/mL)	13.00	15.10	0.680	
AFP (ng/mL)	1.55	2.10	0.253	
CEA (ng/mL)	1.60	1.45	0.410	

*Indicates for statistically significance. CA125, cancer antigen 125; CA19-9, cancer antigen 19-9; CA15-3, cancer antigen 15-3; AFP, alfa feto-protein; CEA, carcinoembryonic antigen.

TABLE 2. Demographic and clinical data of the patients with malignant transformation.

#	Age	Tumor size (cm)	Tumor marker level					Histology of malignant transformation	Operation	Adjuvan Chemo Cure	Cancer recurrence	Died because of malignancy
			CA125	CA15-3	CEA	CA19-9	AFP					
1	21	4.5	29.0	26.6	0.8	30.2	1.8	Dysgerminoma	cystectomy	1	+	+
2	43	8.0	18.0	9.0	0.3	0.6	1.5	Malignant struma ovarii with thyroid papillary microcarcinoma	hysterectomy and bilateral oophorectomy	0		
3	50	10.5	16.0	41.0	8.4	6539.0	1.2	Malignant struma ovarii with thyroid papillary microcarcinoma	hysterectomy and bilateral oophorectomy	0		
4	21	9.5	12.0	15.6	1.4	1.9	1.2	Malignant struma ovarii with thyroid papillary microcarcinoma	unilateral oophorectomy	0		
5	75	8.0	20.0	8.1	4.3	19.0	1.3	Malignant struma ovarii with thyroid papillary microcarcinoma	hysterectomy and bilateral oophorectomy	0		
6	56	6.0	31.5	16.9	2.6	1.8	3.5	Malignant struma ovarii with thyroid papillary microcarcinoma	hysterectomy and bilateral oophorectomy	0		
7	26	-	9.0	4.0	1.4	0.6	1.1	Carcinoid tumor	unilateral oophorectomy	0	+	+
8	34	1.1	15.0	8.0	1.6	25.6	1.2	Carcinoid tumor	cystectomy	0		
9	52	12.0	11.0	7.2	2.6	0.8	1.6	Mucinous carcinoid tumor	unilateral oophorectomy	5	+	+
10	52	22.5	20.0	-	-	-	-	Mucinous adenocarcinoma	hysterectomy and bilateral oophorectomy	0		
11	54	6.5	15.0	26.5	3.0	61.7	2.7	Squamous cell carcinoma	hysterectomy and bilateral oophorectomy	0		
12	69	7.6	34.5	33.5	1.6	83.6	4.8	Carcinoid tumor	unilateral oophorectomy	0		
13	54	8.0	29.0	11.0	1.8	14.8	-	Endometrioid adenocarcinoma with neuroendocrine differentiation	hysterectomy and bilateral oophorectomy	6	+	+
14	25	20.0	12.3	25.2	1.4	7.7	-	Mucinous adenocarcinoma and signet ring cell carcinoma	unilateral oophorectomy	3	+	+
15	46	3.0	20.0	9.3	0.7	8.5	1.6	Carcinoid tumor	hysterectomy and bilateral oophorectomy	0		

CA125, cancer antigen 125; CA15-3, cancer antigen 15-3; CEA, carcinoembryonic antigen; CA19-9, cancer antigen 19-9; AFP, alfa feto-protein.

On computerized tomography (CT) and magnetic resonance imaging (MRI), the invasive development of massive irregularly marginated soft tissue lesions at or inside the tumor's wall, as well as nearby organ invasion in some cases, and the presence of solid masses increased in a pelvic MRI test are imaging findings indicating malignant transformation [14, 15]. In our retrospective study, we could not reach all the preoperative imaging examinations of the patients. This is the limitation of our study. However, it is clear that there can be cases that cannot be diagnosed preoperatively without pathological examination.

There is no agreed treatment for this disease. Benefits of chemotherapy and radiotherapy are not clear. Due to the cisplatin's efficacy in ovarian cancer and gynecological squamous-cell carcinomas, platinum-based regimens were most widely employed in previous studies. Some studies report that adjuvant chemotherapy can improve survival [16]. On the other hand, several studies reported that radiotherapy and chemotherapy had no apparent favorable impact [17, 18]. Most of the previous studies focused on treatment of histologic type of squamous-cell carcinoma. Therefore, their results may not be valid for other types. Another limitation of our study is the interpretation of the efficacy of the treatment. According to our records, only four patients were treated with chemotherapy. There were no squamous-cell carcinomas among patients treated with chemotherapy. Three of them died because of the malignancy, so we can't make a clear interpretation of the effectiveness of the adjuvant chemotherapy.

5. Conclusions

In conclusion, malignant transformation of mature cystic teratoma is a rare entity and it is difficult to diagnose preoperatively. We should suspect malignancy if a patient is over 50 and has an ovarian mass predicted as a mature cystic teratoma greater than 8 cm. Although clinical symptoms, preoperative imaging, and tumor markers may all lead to a correct diagnosis, they can also be deceiving. In this context, intraoperative frozen sections may help to achieve correct diagnosis early and allow proper staging in the same operation and proper treatment after operation. With further studies, advanced management and treatment plans could be elaborated further.

AVAILABILITY OF DATA AND MATERIALS

The data are contained within this article.

AUTHOR CONTRIBUTIONS

CS, ŞG, NY, GS, NÖ, OZ, LA and MCT—performed data curation. CS, ŞG, NY—conceptualized the study. AAÖ, MCT—performed formal analysis. CS, NY—contributed the writing for the original draft. MCT, NÖ, GS, NY—with further editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by Ege University, Faculty of Medicine Research Ethics Committee with the decision number of 18-7/26. Written informed consent was taken from all patients.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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