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Clinical analysis of 12 cases of ovarian cystic mature teratoma with malignant transformation into squamous cell carcinoma

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Abstract

Objective: This study aimed to examine the clinicopathological characteristics, treatment, and prognostic factors in 12 cases of malignant transformation of mature cystic teratoma of the ovary (MCTO).
Methods: We performed a retrospective study of 12 patients with malignant transformation of MCTO who were admitted to the Affiliated Hospital of Qingdao University from 2003 to 2019. We examined case records, clinical parameters, and biological assessments.
Results: The median age of the patients was 56.5 years and seven of them were postmenopausal. The average tumor size was 18.5 cm. All patients had pelvic masses at their first hospital visit. Nine of the patients had discomfort in the lower abdomen, two presented with a lower abdominal palpable mass, and three were complicated by fever. The median follow-up time was 73 months (12–193 months). Ten patients survived with a disease-free status and two died.
Conclusions: There is a low incidence of malignant transformation of MCTO, and its most common histological type is squamous cell carcinoma. Age and tumor size are important factors in malignant transformation of teratomas. While there is a lack of treatment guidelines for malignant transformation of MCTO, early diagnosis and treatment may be beneficial for these patients.

Keywords

Ovarian neoplasm, mature cystic teratoma of the ovary, malignant transformation, tumor size, squamous cell carcinoma, pelvic mass

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Introduction

Mature cystic teratoma of the ovary (MCTO) is a common benign ovarian tumor in women. MCTO can occur at any age, but the most common time is at the child-bearing age, when it comprises 10% to 20% of ovarian tumors and 85% to 97% of germ cell tumors. MCTO is relatively more common in postmenopausal women and the chance of malignancy increases with age. Ovarian teratoma originates from primordial germ cells. Ovarian teratoma is generally composed of two to three mesodermal tissues, and is occasionally found in the monodermal component. Any of the components in the teratoma may be malignant, but this is rare, with a malignant rate of approximately 1% to 2%. Squamous cell carcinoma is the most common type of ovarian teratoma, comprising approximately 80%,[1–3] followed by adenocarcinoma, sarcoma, carcinoid tumor, and melanoma.[4,5] Most of these patients do not have obvious clinical symptoms, and this disease is discovered in routine pelvic and abdominal physical examinations or imaging examinations. Therefore, MCTO is often missed in diagnosis. This study aimed to examine the clinicopathological characteristics, treatment, and prognostic factors in malignant transformation of MCTO.

Materials and methods

A total of 1043 patients suffering from MCTO were admitted to The Affiliated Hospital of Qingdao University from January 2003 to July 2019. A retrospective analysis was conducted on 12 cases of MCTO with malignant transformation combined with squamous cell carcinoma. The rate of malignant transformation of MCTO was 1.15%.

We examined the patients' clinical characteristics, diagnostic treatment, and prognostic factors. This study was approved by the ethics committee of the Affiliated Hospital of Qingdao University (approval number: QYFYWZLL 26077). Informed consent was acquired from the patients before the study started.

Results

Clinical data

The median age of the patients was 56.5 years (42–77 years) and seven of them were postmenopausal (Table 1). When the patients visited the hospital for the first time, all 12 patients had pelvic masses. Nine patients visited the hospital owing to discomfort in the lower abdomen, two visited owing to a lower abdominal palpable mass, and one visited because of discovering a pelvic mass in a routine gynecological examination. Three of these patients also had a fever. The shortest course of disease was half a month and the longest was more than 27 years.

Imaging examinations, and diagnosis

Twelve patients were examined by B-ultrasound before the operation, among whom nine showed ovarian or pelvic solid-cystic lesions with uneven density. There was an uneven internal echo with an unclear boundary inside. Gas-fluid levels were likely to be observed in the surrounding cystic area and a blood flow signal was observed inside the lesions. The possibility of malignancy was not eliminated. In six patients, the tumor not only infiltrated into adjacent tissues, but it also had typical features of teratoma. Therefore, diagnosis of probable malignant transformation of teratoma by B-ultrasound was feasible. Six patients had computed tomography or magnetic resonance imaging performed before the operation, and a cystic mass in the abdominopelvic cavity was observed.

Table 1. Clinicopathological characteristics in patients with mature cystic teratoma of the ovary.

Patient	Age (years)	Symptoms at diagnosis	Tumor size (cm)	Side	Tumor marker (mmol/L)	Operation	Grade	FIGO stage	Adjuvant therapy	F/U after the operation (months)
1	42	Abd/pel. pain	17	Right	CA19-9: >1000 CA125: 261.3	TAH, BSO, PLND, PALND, TO, App	3	IA	TP×4	Alive, 90
2	62	Abd/pel. pain	20	Left	CA19-9, CA125, AFP, NSE (−)	TAH, BSO, PLND, PALND, TO	1	IB	PVB×6	Alive, 104
3	55	Abdominal mass-fever	16	Left	CA125: 135.5 SCC-Ag: 31.34	TAH, BSO, PLND, PALND, TO	2	IIC	TP×4+RT	DOD, 12
4	50	Abdominal mass-Abd/pel. discomfort	10	Left	CA125, SCC-Ag (−)	TAH, BSO, PLND, PALND, TO	1	IC	TP×6	Alive, 23
5	72	Abdominal mass	18	Left	CA19-9: >1000, AFP: 13.43 SCC-Ag, CEA, CA125 (−)	TAH, BSO, PLND, PALND, TO	2	IA	PE×4	Alive, 20
6	43	Abdominal mass	8	Right	AFP, CA125 (−)	TAH, BSO, PLND, PALND, TO	2	IA	PVB×4	Alive, 102
7	77	Abd/pel. discomfort	15	Left	CA19-9: 101.60 CA125: 68.75 CEA: 12.67	Left USO	3	NA	/	DOD, 35
8	64	Abd/pel. pain	30	Right	CA125: 100.7 CA199: 118.4 SCC-Ag: 3.7	TAH, BSO, PLND, PALND, TO, App, partial bowel resection	2	IIIC	TP×6	Alive, 56
9	65	Abd/Pel. pain-fever	13	Left	SCC-Ag: 1.8 CA19-9: 146.8 CEA, AFP, CA125 (−)	TAH, BSO, PLND, PALND, partial colo-proctectomy, left hem-icolectomy, TO	1	IIIC	TP×6	Alive, 26
10	58	Abd/pel. pain-fever	15	Left	CA125 (−)	TAH, BSO, PLND, PALND, TO	1	IIA	BEP×4	Alive, 166
11	50	Abdominal mass-Abd/pel. discomfort	30	Left	CA199: 201.5 CA125 (−)	TAH, BSO, PLND, PALND, TO, App	2	IC	/	Alive, 193
12	44	Abdominal mass-Abd/pel. pain	30	Right	CA125: 484.9 CA199: 140.4 CEA: 26.6	TAH, BSO, PLND, PALND, TO	2	IA	PVB×4	Alive, 119

FIGO, International Federation of Gynecology and Obstetrics; F/U, follow-up; Abd/pel., abdomino-pelvic; CA, carbohydrate antigen; TAH: total abdominal hysterectomy, BSO, bilateral salpingo-oophorectomy; PLND, pelvic lymph node dissection; PALND, para-aortic lymph node dissection; TO, total omentectomy, App, appendectomy; TP, taxol+platinum; AFP, alpha fetoprotein; NSE, neurone-specific enolase; PVB, platinum+vincristine+bleomycin; SCC-Ag, squamous cell carcinoma antigen; RT, radiotherapy; DOD, died of disease; PE, platinum+etoposide; USO, unilateral salpingo-oophorectomy; NA, not available; CEA, carcinoembryonic antigen; BEP, bleomycin+etoposide+platinum.

In these patients, enhanced scanning showed that the solid component was enhanced, with unclear demarcation of the lesions. We considered that the tumors were malignant, without excluding the possibilities of ovarian epithelial carcinoma and malignant transformation of teratoma.

Pathological examination

All patients underwent a postoperative pathological examination, which showed that 2 patients had cystic mature teratoma in contralateral ovaries, and the remaining 10 patients had unilateral tumors. Eight cases were left ovarian malignancy, while the remaining four were right ovarian malignancy. The mean (standard deviation) size of the tumors was 18.5±7.7 cm and all of them were solid-cystic. Surgical pathological sections of all patients were rechecked by staff at the Pathology Department of the hospital, who confirmed the diagnosis of MCTO with malignant transformation into squamous cell carcinoma (Figure 1). No lymphatic metastasis was found in 11 patients who underwent a comprehensive staging operation or cytoreductive surgery. International Federation of Gynecology and Obstetrics staging was as follows: IA stage for three cases, IB stage for one case, IC stage for two cases, IIA stage for one case, IIB stage for one case, IIC stage for one case, and IIIC stage for two cases. One patient did not have a staging operation performed.

Treatment and follow-up

Surgical treatment was performed in all patients (Table 1). Eleven patients had a comprehensive staging operation or cytoreductive surgery performed, and no remaining lesions were observed by the naked eye. Ten patients had adjuvant therapy performed and eight had combination chemotherapy with platinum. Four to six courses of treatment were provided. One patient was administered combined chemotherapy with platinum + pelvic irradiation. The remaining two patients did not have adjunctive therapy performed. Five patients who had no ruptured ovarian tumor were tumor-free and survived, with a median tumor-free time for survival of 72 months. Only one of these patients had surgical treatment, and the other four patients had four courses of treatment of combination chemotherapy with platinum after surgery. The follow-up period of the 12 patients ended in July 2017. The follow-up time ranged from 12 to 193 months and the median follow-up time was 73 months. Two of the 12 cases died.

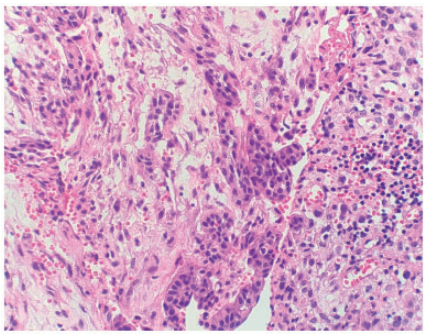

Figure 1. Histopathological image showing that tumor cells are arranged in nests, and proliferating fibrous tissue can be seen between the nests. Poorly differentiated squamous cell carcinoma has no obvious keratinizing beads or cell bridges (hematoxylin and eosin, ×400).

Discussion

Malignancy of MCTO is rare, with a rate of 1% to 2%,[1,6] and malignant transformation into squamous cell carcinoma is the most common type.[1] The clinical manifestations of malignant transformation of MCTO into squamous cell carcinoma are mostly unspecific. The average age of MCTO ranges from 32.7 to 37.5 years,[1,7,8] whereas the average age of malignancy of MCTO is

50.8 to 55.2 years. Kashimura et al.[8] believed that the patient's age was a factor determining whether MCTO is malignant. Malignant teratomas are often large, mostly unilateral, and have a diameter of 10 to 20 cm.[9] When the tumor's diameter is greater than 9.9 cm, its sensitivity to forming cancer is 86%. Therefore, some scholars believe that the size of the tumor has an association with malignant transformation into squamous cell carcinoma.[10] Chen et al.[11] studied 188 patients with malignancy of MCTO in whom the diameter of 78.7% of tumors was greater than 10 cm, and they were usually lager than non-malignant ovarian mature teratoma. These findings suggest that, when a patient is older than 45 years (especially postmenopause), the diameter of the tumor is greater than 9.9 cm, and there are clinical symptoms caused by rapid short-term growth of the tumor or adherence with surrounding tissues, the occurrence of malignant transformation should be highly suspected.

Making a definite diagnosis before an operation for malignant transformation of MCTO is difficult. Reports have shown that an imaging examination of patients with a malignant change in the tumor shows certain characteristic manifestations.[2,12] The diagnostic value of computed tomography and magnetic resonance imaging examinations is important when identifying malignant manifestations, such as bleeding, necrosis, cyst wall growth, invasion of surrounding structures, or the occurrence of pelvic abdominal metastases. MCTO lacks tumor markers with high specificity and strong sensitivity. In previous studies, the preoperative diagnostic value of multiple tumor markers, such as carbohydrate antigen 125, carbohydrate antigen 19-9, carcinoembryonic antigen, squamous cell carcinoma antigen, and alpha fetoprotein, was limited in mature ovarian teratoma with malignant transformation into squamous cell carcinoma.[1] Studies have shown that the surgical pathological stage, pathological grading, and the presence of a residual tumor after the operation are the most important factors affecting the prognosis.[2]

There is still no unified treatment program for adjunctive therapy of squamous cell carcinoma. Many scholars believe that chemotherapy of an alkylating agent, including combination chemotherapy of platinum and combined paclitaxel, can improve the survival time of the patients with advanced ovarian mature teratoma with malignant transformation into squamous cell carcinoma.[2] The platinum-based chemotherapy regimen was selected in adjuvant therapy in our study, and 10 patients had chemotherapy after the operation. Except for one patient who died from their disease, the other nine patients are tumor-free and still alive. Five patients who had no ruptured ovarian tumor were tumor-free and survived, with a median tumor-free time for survival of 72 months. Only one of these patients had surgical treatment performed, and the other four patients had four courses of treatment of combination chemotherapy with platinum after the operation. The limited number of patients may have affected the accuracy of our results. However, our findings could provide some reference for clinicians when they encounter patients with similar conditions.

In summary, physicians should be aware that the morbidity rate for MCTO with malignant transformation into squamous cell carcinoma is relatively low. At present, there are still many problems to be solved in terms of diagnosis and treatment of this disease. There should be awareness of the malignant possibility of teratoma if the teratoma has been present for a long time; the patient is an older woman, particularly if she is postmenopausal; the tumor diameter is greater than 10 cm; or there is thickening of the cyst wall or papillary growth occurs,

as well as an increase in tumor markers. In this situation, a prompt operation and intraoperative frozen pathological examination should be performed. The early prognosis of MCTO with malignant transformation is mostly good. In most cases, adjunctive therapy may not be performed in the IA stage. For patients who are young and have not had a child, their reproductive ability should be preserved. However, when the prognosis in the advanced stage is poor, satisfactory cytoreductive surgery and combination chemotherapy based on platinum may improve the prognosis. Accumulation of more cases and more detailed studies is required to formulate a standard therapeutic regimen.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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