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Case Report

Undifferentiated carcinoma arising in ovarian mature cystic teratoma: a case report and literature review

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Abstract: Malignant transformation is a rare complication of the mature cystic teratoma of the ovary. Most of these histologic types are squamous cell carcinoma, and other types are exceptionally rare. Here, we present an extremely rare histology of malignant transformation, an undifferentiated carcinoma, arising in mature cystic teratoma of the ovary. A 48-year-old woman was referred due to abdominal distension and palpable pelvic mass. Computed tomography showed 16- and 12-cm-diameter mixed solid and cystic tumors in bilateral ovaries. Surgical exploration revealed bilateral ovarian tumors with multiple nodules on the whole peritoneum, liver capsule, and diaphragm. Cytoreductive surgery was performed, leaving <1 cm tumors. On pathologic review, the tumor was confirmed as undifferentiated with an adenosquamous carcinoma component arising in mature cystic teratoma. The patient died 7 days postoperatively due to uncontrolled malignant ascites and pleural effusion. We report a case of undifferentiated carcinoma arising from mature cystic teratoma, and we review the clinicopathologic features of this rare case.

Keywords: Teratoma, carcinoma, ovarian neoplasms, malignant transformation

Introduction

Mature cystic teratoma (MCT) accounts for 10-20% of all ovarian tumors and is the most common germ cell ovarian tumor. It is a benign tumor, but malignant transformation (MT) occurs in 1-2% of cases [1]. MT in MCT usually occurs in postmenopausal women aged 45-60 years [1]. Various histological types can develop from MCT, with MT to squamous cell carcinoma (SCC) being the most common. The prognosis for MT in MCT has been reportedly poor in previous studies, with majority of cases dying within 12 months of diagnosis [2]. Therefore, early detection is important. However, in contrast to benign MCT, MT in MCT is nearly impossible to diagnose preoperatively and usually diagnosed during the postoperative pathologic review. Furthermore, owing to its rarity, the optimal management remains to be established yet. Although several studies of MT in MCT have been published to date, undifferentiated carcinoma arising in ovarian MCT is extremely rare, with only few cases reported. Here, we describe a case of undifferentiated carcinoma arising in ovarian MCT.

Case report

A 48-year-old, gravida 1, para 0 woman was referred to our gynecologic oncology department due to abdominal distension. She had right hemiplegia due to cerebral infarction. Her body mass index was 16.0 kg/m^2 with cachectic general appearance. Physical examination revealed a large pelvic mass with abdominal distention. Computed tomography (CT) showed 16 and 12 cm bilateral ovarian masses, omental infiltration, massive ascites, and large amounts of bilateral pleural effusions (**Figure 1**). Pelvic masses were predominantly cystic, but solid component was also identified. On whole-body positron emission tomography-computed tomography, intense 18-fluorodeoxyglucose uptake in the solid portion of bilateral ovarian masses was noted. Serum CA-125 and CA-19-9 levels were elevated to 396.1 U/ml and 228.5 U/ml, respectively. With the presumed diagnosis of advanced ovarian cancer, two cycles of neoadjuvant chemotherapy with paclitaxel and carboplatin were initiated; however, tumors had slightly increased in size on the follow-up CT.

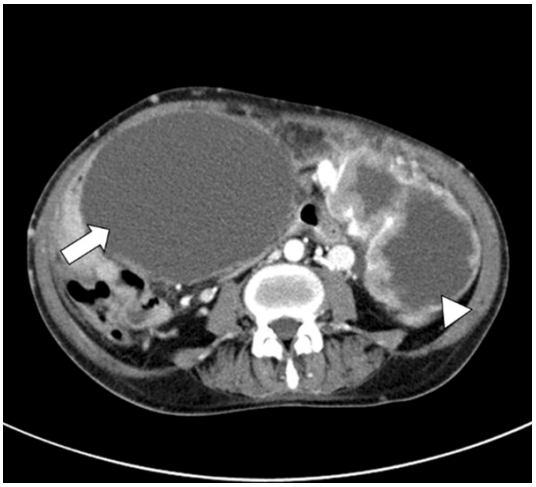

Figure 1. Contrast-enhanced computed tomography scan showing 16 cm (arrow) and 12 cm (arrowhead) sized cystic and solid ovarian masses with enhanced solid tissue components.

On surgical exploration, 18- and 13-cm bilateral ovarian tumors and multiple small nodules in the whole abdominal peritoneum, liver capsule, and diaphragm were detected. In addition, enlarged right pelvic lymph nodes were observed. Cytoreductive surgery was performed including total abdominal hysterectomy with bilateral salpingo-oophorectomy, infracolic omentectomy, both pelvic lymph node dissection, appendectomy, and multiple peritoneal excision; however, multiple tumors of <1 cm in diameter were left in the colon, liver, diaphragm, and peritoneum.

Grossly, both ovaries had been entirely replaced by the tumor with solid and cystic components. Right and left adnexal tumors measured 18.5×13.5×10.7 cm and 13×12.5×4 cm, respectively. The cut surface showed grayish solid mass with extensive internal necrosis (**Figure 2**). Microscopically, tumors showed a biphasic pattern (**Figure 3A**). Most of them, especially extraovarian metastatic tumors, were composed of small round cells (**Figure 3B**). Various immunohistochemical studies including cytokeratin (AE1/AE3), vimentin, WT-1, p63, CD99, Fli-1, CD56, and synaptophysin were performed to determine the tumor differentiation. However, these tumor cells only showed cytokeratin positivity, indicating an undifferentiated carcinoma. Another tumor component was well-differentiated adenosquamous carcinoma (**Figure 3C**), showing cystic basaloid squamous carcinoma components with central keratinization, necrosis, and focal glandular differentiation. Adenosquamous carcinoma components only were identified in both ovaries.

Benign glial tissues were focally observed only in the right ovary, which can be frequently observed in MCT (**Figure 4**), indicating that the tumor can be diagnosed as undifferentiated carcinoma with adenosquamous carcinoma component, arising in MCT.

The patient's postoperative condition deteriorated due to uncontrolled malignant ascites and pleural effusion. She died on the 7th postoperative day before the initiation of adjuvant chemotherapy.

Discussion

MCT is one of the most common ovarian neoplasms, especially during reproductive age. MT in MCT generally occurs after 40 years old. SCC comprises approximately 85% of MT in MCT cases, whereas adenocarcinoma accounts for 7% [3]. Other MTs include melanoma, sarcoma, basal cell carcinoma, and papillary carcinoma of the thyroid. Several reports have described cases of MT with various histological types from MCT. However, ovarian undifferentiated carcinoma arising in MCT is extremely rare, and this is the fourth report in English literature based on our literature review.

The first case was reported in 1961 [4]. The patient was 75 years old, who complained of palpable mass, abdominal pain, and constipation. Because of the 14-cm right ovarian tumor, she underwent hysterectomy and bilateral salpingo-oophorectomy. The tumor was diagnosed as undifferentiated carcinoma arising in MCT. The patient developed pulmonary metastasis and died 27 months postoperatively. The second case was reported in 1979 [5]. A 33-year-old woman underwent unilateral oophorectomy due to ovarian tumor. On pathology, the tumor was diagnosed as undifferentiated carcinoma originated in MCT. Despite a stage IA tumor, she received adjuvant chemotherapy, but died 9 months later due to tumor progression. The third case was reported in 2003 [6]. She was 70 years old and complained of abdominal distension. The tumor size was up to 30 cm. Left salpingo-oophorectomy

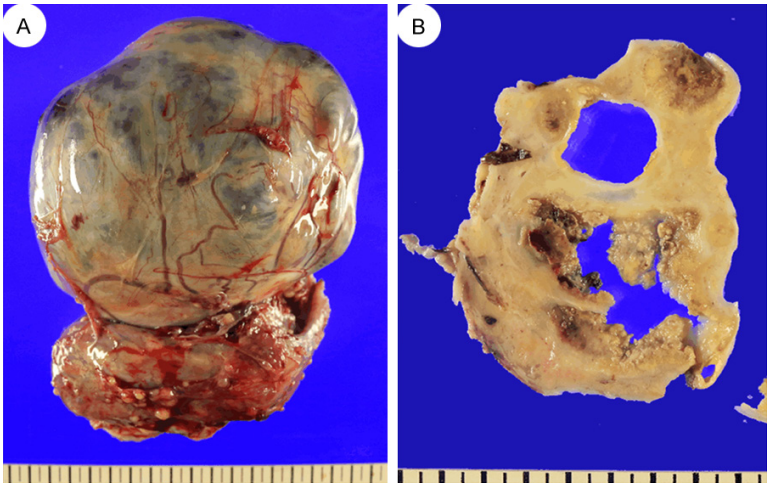

Figure 2. Gross appearance of the left adnexa. A. The tumor measures 13 cm; B. The cut surface shows grayish solid mass with extensive internal necrosis.

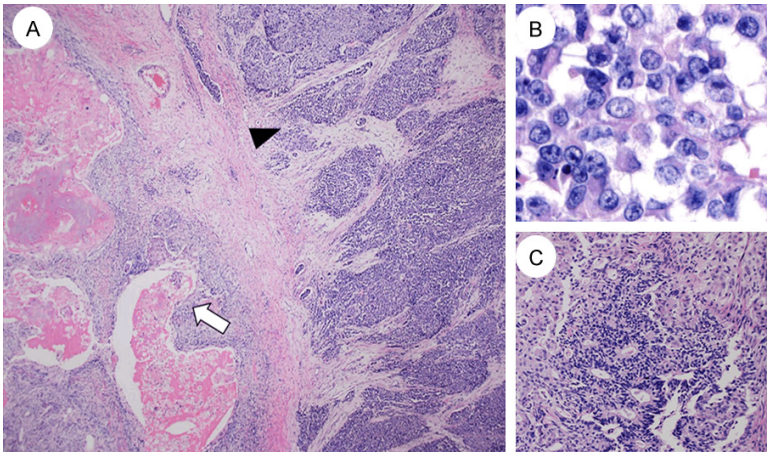

Figure 3. Microscopic findings of the right ovarian tumor. A. Along with the cystic portion, the tumors showed biphasic patterns of adenosquamous cell carcinoma (arrow) and undifferentiated carcinoma components (arrowhead). Majority of adenosquamous carcinoma was composed of large cystic squamous cell carcinoma components with central keratinization (haematoxylin-eosin staining, ×40 magnification); B. Undifferentiated carcinoma composed of small round cells (×400 magnification); C. Adenocarcinoma component identified at the periphery of the tumor (×200 magnification).

and infracolic omentectomy were performed, but the patient died 5 weeks postoperatively due to rapidly growing residual tumors. Histology revealed undifferentiated carcinoma containing osteoclast-like multinucleated giant cells arising in MCT. Thus, the prognosis of undifferentiated carcinoma arising in MCT seems to be very poor.

MT arising in MCT is very difficult to diagnose preoperatively. Similar to epithelial ovarian cancer, no specific symptoms are observed. Common presentation includes abdominal pain, abdominal distension, and palpable mass. Imaging features of MCT with MT have been difficult to evaluate for several reasons. First, their rare occurrence makes a large-scale study impossible. In addition, malignant changes located in a tiny area can cause difficulties in the preoperative diagnosis of MT. Third, the appearance of MT covers a broad spectrum ranging from an entirely solid to a predominantly cystic mass [7]. Nevertheless, some preoperative imaging characteristics may be helpful in detecting MT. An irregular border forming an obtuse angle with the inner wall of the cyst would more likely suggest MT. Kido et al. reported that MT arising from MCT tends to have a contrast-enhanced solid component, transmural extension, and direct invasion through the septa to the adjacent pelvic area [8]. In a study reviewing 37 cases of MT, Kikkawa et al. reported that the tumor size could be used as a predictor of MT. Although MCT presents in wide range of sizes, larger tumors (>9.9 cm) were associated with high risk of malignancy, and the mean size of SCC arising from MCT was 15.2 cm as compared to 8.8 cm in benign MCT [9].

The use of tumor markers in diagnosing MT arising in ovarian MCT is unclear. SCC antigen has been reported as a useful marker for SCC arising in ovarian MCT. Mori et al. reported that younger patients (<40 years) and patients with low serum SCC antigen level (<2.5 ng/mL) had benign MCT [10]. The sensitivity of combination of age and serum SCC antigen level for MT in MCT was 77% and specificity was 96%. However, the role of the SCC antigen in diagnosis remains controversial, and furthermore, no study has found a useful serum marker for non-SCC tumors of MT.

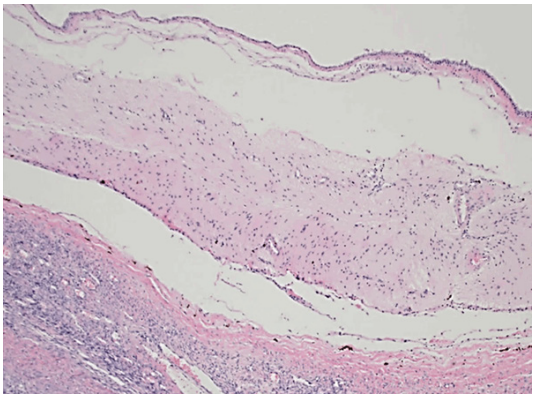

Figure 4. Microscopic findings of the right ovarian tumor. Benign glial tissue was identified, indicating that the cancer originated from mature teratoma (×100 magnification).

Histologically, undifferentiated ovarian carcinoma is composed predominantly of diffuse solid areas lacking a specific pattern. Undifferentiated carcinoma usually showed immunoreactivity for both epithelial and mesenchymal markers such as cytokeratin, EMA, and vimentin [11]. In this case, a small portion of the tumor was composed of glial cells, and both epithelial and mesenchymal components were observed in the solid portion of the tumor. Therefore, the histomorphology and immunohistochemistry profiles were consistent with undifferentiated carcinoma arising from MCT.

Similar to epithelial ovarian cancers, the treatment of MT in MCT might be an optimal cytoreductive surgery. For stage IA SCC arising in MCT, conservative unilateral oophorectomy without further postoperative treatment has been proposed for young and nulliparous patients [12]. However, a recent case series reviewing ovarian endometrioid carcinoma associated with undifferentiated carcinoma showed that stage IA tumors recurred despite the initial complete staging surgery in patients who did not receive adjuvant treatment [13]. Therefore, early diagnosis, complete resection, and adjuvant treatment may be necessary, even for the early-stage of MT in MCT.

Due to the rarity of this disease, its optimal adjuvant treatment has not been established. In Park et al.'s study, patients who received adjuvant chemotherapy or concurrent chemoradiation therapy had longer survival than those who received radiation alone or had no adjuvant therapy [14]. Similarly, Sakuma et al. suggested platinum-based chemotherapy with radiotherapy for SCC arising in MCT [15]. In case of adenocarcinoma arising in MCT, treatment similar to that of an epithelial ovarian cancer has been proposed. However, Sakuma et al. recommended platinum/taxane as the standard regimen for MT of MCT, regardless of histological type.

In conclusion, MT of MCT is a rare malignancy with poor prognosis. Particularly, undifferentiated carcinoma arising in MCT is extremely rare. Although the treatment strategy has not been standardized according to the tumor histology, early detection and complete cytoreduction may be important for better survival. Therefore, further knowledge and experience of this rare tumor should be acquired, because most cases are diagnosed postoperatively and associated with poor postoperative survival.

Disclosure of conflict of interest

None.

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