Case Report

Undifferentiated pleomorphic sarcoma arising in a mature cystic teratoma of ovary: a case report and review of the literature

Chi Yue1,2, Xiaoxia Wei3, Ranhong Li4, Jiangyan Lou1,2, Hui Liu1,2

1Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Chengdu 610041, Sichuan, China; 2Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu 610041, Sichuan, China; 3Department of Pathology, West China Second Hospital of Sichuan University, Chengdu 610041, Sichuan, China; 4Department of Obstetrics and Gynecology, The People’s Hospital of Henan Province, Zhengzhou 450003, China

Received July 18, 2017; Accepted June 1, 2018; Epub September 15, 2018; Published September 30, 2018

Abstract: Mature cystic teratoma is the most common type of ovarian germ cell tumor, while malignant transformation rarely occurs. Here, we report a case of a 19-year-old female patient presenting with abdominal pain. Computed tomography revealed an approximately 9 cm wide complex cystic and solid adnexal mass in the left ovary. After surgery, histopathological examination determined that the left ovarian neoplasm was a germ cell derived tumor, with the cystic part as a mature teratoma and with the solid part as an undifferentiated pleomorphic sarcoma (UPS). To our knowledge, this is the fourth case, reported so far, of undifferentiated pleomorphic sarcoma arising in a mature cystic teratoma of the ovary. Currently, there is limited information about the history or the prognosis of this disease and there is no general consensus on the optimal surgical approach and the postoperative treatment required. Therefore, to better comprehend this disorder, here we present the patient’s pathophysiological symptoms, briefly discuss the diagnosis, treatment, and prognosis of this disease, and further review literature for similar cases.

Keywords: Undifferentiated pleomorphic sarcoma, mature cystic teratoma, malignant transformation, ovary

Introduction

Mature cystic teratoma (MCT) is the most common type of germ cell tumor among women of reproductive age, accounting for approximately 10% to 20% of all the ovarian tumors. Malignant transformation of mature cystic teratoma of the ovary is relatively rare, with an incidence rate ranging from 1% to 2% [1]. The histology of malignant transformation teratomas is variable, with squamous cell carcinoma being the most common type, accounting for 80% of the cases [2]. Less common malignancies include adenocarcinoma, carcinoid, carcinosarcoma, angiosarcoma, thyroid carcinoma, and malignant melanoma [3-8]. However, the occurrence of sarcoma is extremely rare in comparison to other types of malignancies and therefore, there is a lack of information concerning this disease and its treatment. Here, we present a case of a patient with undifferentiated pleomorphic sarcoma (UPS) arising in a mature cystic teratoma of the ovary.

Case report

A 19 year-old female patient with no history of sexual intercourse was presented with abdominal pain at the West China Second University Hospital, Sichuan University on February 14th, 2017. Computerized tomography scan revealed a large complex cystic and solid adnexal mass in the left ovary, which mainly consisted of solid parts, was irregular in shape and with unclear boundaries, measuring 6.9 × 8.9 × 7.8 cm, and showing the “Ovarian Vascular Pedicle” sign. A small amount of fluid accumulation was also noted in the pelvis. The symptomatic diagnosis was possible left ovarian germ cell tumor.

The level of the serum tumor markers was 40.2 U/mL for CA19-9 (reference range: < 30.9 U/
Malignant transformation of the ovarian mature cystic teratoma

The left ovary was entirely replaced with a multilocular tumor mass, grossly measuring 10 × 9 × 8 cm. After the operation, the mass was dissected. The cut surface of the tumor was pale yellow in color, solid, soft, and included hair, fat, and bony tissue. Further analysis of sliced sections showed that the tumor was cystic and that the thickness of the cystic wall was 0.3 to 0.5 cm (Figure 1). Histological staining of tissue slices revealed that the tumor contained both solid and cystic areas; highlight with black arrows; H&E stain; original magnification, 100 ×. The cystic part of the tumor is composed of skin and its appendages and part of the osseous tissue; highlighted with black arrows; H&E stain, original magnification, 100 ×. The neoplastic cells are obvious pleomorphic, atypical, and arranged in a storiform growth pattern; H&E stain, original magnification, 100 ×.

Figure 1. Light microscopy image of the tumor mass. The tumor mass was 10 × 9 × 8 cm in size. The cut surface of the tumor was pale yellow in color, solid, soft, and included hair, fat, and bony tissue.

The blood test analysis results were as follows: the white blood cell count was 21.4 × 10⁹/L with 75.2% neutrophils, the red blood cell count was 3.37 × 10¹²/L, the hemoglobin levels were 73 g/L, the hematocrit was 24.2%, the platelet count was 544 × 10⁹/L, and the serum ferritin was 606.9 ng/mL. Electrocardiography revealed sinus tachycardia with the resting heart rate fluctuations ranging from 120 to 134 beats per minute. Plasma prothrombin time was 16.8 seconds (reference range 8.5-14.5 seconds) and the partial activated thromboplastin time was 48.2 seconds (reference range: 20.4-40.4 seconds). Liver, kidney, and the thyroid gland function were normal. The levels of serum electrolytes were also normal. Marrow bone aspiration smears showed an increased number of plasmocytes and a bone marrow biopsy indicated active cell proliferation, especially of the megakaryocytes.

A laparotomy was performed on February 16th, 2017. Intraoperatively, a large cystic and solid tumor could be seen protruding from the left ovary. The right ovary and the uterus appeared to be unaffected. No macroscopic metastases were observed. Histological examination of frozen tumor sections suggested a malignant neoplasm of the left ovary, with an indication that the malignant transformation arose from a teratoma. Because the patient was very young, only the left ovary was removed together with the left fallopian tube.
Malignant transformation of the ovarian mature cystic teratoma

and cystic areas (Figure 2A), and that the cystic part of the tumor was mainly composed of skin and its appendages, and partly of osseous tissue (Figure 2B). The solid part of the lesion mostly contained fibroblast-like and histocyte-like elements. The neoplastic cells were pleomorphic and atypical. The spindle-shaped fibroblast-like cells were mainly arranged in a storiform growth pattern (Figure 2C). A large number of gigantic cells with single or multiple bizarre nuclei were seen in the pleomorphic areas, some of which were undergoing mitosis (Figure 3A). The cytoplasm of the giant cells had an eosinophilic glassy or foamy appearance (Figure 3B), which was similar to rhabdomyoblastoma. Their nuclei were vesicular and had prominent nucleoli (Figure 3). Immunohistochemically, the tumor was positive for the expression of vimentin and CD68 (Figure 4A, 4B), and negative for SMA, desmin, S-100, EMA, HMB-45, Melan-A, GFAP, Sall-4 and CK-P.

The Ki-67 proliferation index was 80% (Figure 4C). Collectively, the histopathological tests determined that the left ovarian neoplasm was a germ cell derived tumor, in which the cystic part was a mature teratoma, and the solid part was an undifferentiated pleomorphic sarcoma.

Five days post-surgery, the white blood cell, neutrophil and platelet levels returned to normal. The plasma prothrombin time and the partial activated thromboplastin time normalized within 20 days. The patient received 3 cycles of adjuvant chemotherapy with bleomycin, etoposide and cisplatin. Follow-up examination after 10 months revealed full recovery of the patient, with no sign of tumor recurrence or metastasis.

**Discussion**

Undifferentiated pleomorphic sarcoma (UPS), formerly known as “malignant fibrous histiocytoma (MFH)”, was included in the quite separate and new category of undifferentiated/unclassified sarcomas for the first time in the 2013 classification of soft tissue tumors [9]. The term MFH was first conceived by Ozzello and Stout in 1963 [10], and further described by O’Brien and Stout in 1964 [11]. Later, Al-Agha OM reported five subtypes of MFH: storiform-pleomorphic, myxoid, inflammatory, giant cell, and angiomatoid [12]. In the 2002 World Health Organization (WHO) classification of soft tissue tumors, three subtypes of MFH/UPS were defined, the pleomorphic MFH/ high grade UPS, the giant cell MFH/UPS with giant cells, and the inflammatory MFH/UPS with prominent inflammation [13]. After the 2013 WHO classification, the concepts of so-called “MFH” were gradually replaced by the term of “UPS” [9]. Currently, the undifferentiated/unclassified sarcomas are sub-classified according to their predominant morphological features, which are round cell, spindle cell, pleomorphic, and epithelioid [14]. Based on these classifications and according to the Pubmed databases, from 1977 to 2017, only eleven cases of ovarian UPS, including malignant transformation of mature cystic teratoma and primary ovarian UPS, have been reported [15-25] (Tables 1 and 2).

The histogenesis of UPS remains controversial, although a recent study suggested that UPS arises from primitive mesenchymal cells which
Malignant transformation of the ovarian mature cystic teratoma

can differentiate into both fibrous and histiocytic cells [26]. UPS is the most common sarcoma of the soft tissue and can occur in any part of the body, but it is mainly found in the extremities and the deep soft tissue of the retroperitoneum [27]. However, UPS of the female tract, especially the ovary, is extremely rare. The first well-documented case of MFH, arising in a benign cystic teratoma of the ovary, was described in 1997 [23]. Although UPS of the ovary typically appears in patients of approximately 50-70 years of age, this patient was only 19 years old. The rate of misdiagnosis can be very high, because the etiology of this disease is not clear and there is a lack of specific clinical features of abdominal pain associated with large pelvic masses. In addition, UPS of the ovary is usually local, hematogenously aggressive, and highly malignant.

In this case, the white blood cell, neutrophil, and platelet counts were highly elevated at the time of admission, but they returned to normal levels soon after surgery. This indicated that the abnormal blood indexes were attributed to the presence of the tumor, which is consistent with findings of a similar patient case report [15]. UPS of the ovary is typically composed of a mixture of spindle cells admixed with pleomorphic or rounded cells, and arranged in a storiform pattern. A variable number of bizarre, multinucleated giant cells are also commonly present. Marked cellularity and nuclear pleomorphisms with abundant atypical mitoses are usually evident in these high-grade tumors. At present, the pathologic diagnostic criterion for UPS of the ovary is high-grade sarcoma without any specific differentiation direction. Accurate diagnosis requires exclusion of other definitive sarcomas, and this should be based on sufficient sampling and careful histopathological and biochemical analysis of various tumor markers. The application of immunohistochemistry can prevent misdiagnosis of UPS. In this case, the immunohistochemical markers were positive for vimentin and CD68, but were negative for -SMA, desmin, S-100, EMA, HMB-45, Melan-A, GFAP, Sall-4 and -CK-P. Collectively, these findings confirmed the diagnosis of UPS.

Currently, there is a lack of sufficient number of reported cases of UPS of the ovary to make any concrete conclusion about the optimal treatment option. Dilek and colleagues reported an ovarian MFH (or UPS) in a 22-year-old patient who’s right ovary had a storiform-pleomorphic-type MFH and the left ovary had an inflammatory-type MFH [16]. After surgery, the patient received six cycles of adjuvant chemotherapy, including cisplatinum and cyclophosphamide, and fully recovered 10 months post-surgery. Furthermore, Savitchi and Rao reported a case of squamous cell carcinoma and pleomorphic sarcoma arising in a mature cystic teratoma of the ovary in a 58-year-old woman [25]. The patient also received two rounds of chemotherapy with cisplatin post-surgery, but developed

Figure 4. Immunohistochemical staining results of tumor cells that were positive for vimentin and CD68. A. vimentin IHC stain; original magnification 200 ×. B. CD68 IHC stain; original magnification 200 ×. C. Ki-67 IHC stain; original magnification 200 ×.
Malignant transformation of the ovarian mature cystic teratoma

<table>
<thead>
<tr>
<th>Authors and years</th>
<th>Age</th>
<th>Presentation</th>
<th>Variant of UPS</th>
<th>Tumor size (cm)</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ueda G 1977</td>
<td>42</td>
<td>Abdominal mass; Pelvic mass; Pyrexia</td>
<td>Unclear</td>
<td>30 × 25 × 20 (right ovary)</td>
<td>Surgery</td>
<td>Recurrence at 5 months</td>
</tr>
<tr>
<td>Hanada M 1981</td>
<td>75</td>
<td>Abdominal pain; Pelvic mass</td>
<td>Myxiod</td>
<td>21 × 15 × 8 (right ovary)</td>
<td>Surgery</td>
<td>Alive and well at 21 months</td>
</tr>
<tr>
<td>Savitchi E 2012</td>
<td>58</td>
<td>Abdominal pain; Urinary tract infection</td>
<td>Giant cell with squamous cell</td>
<td>30 × 20 × 7 (left ovary)</td>
<td>Surgery + adjuvant chemotherapy with cisplatin (2 rounds) and doxorubicin (2 doses)</td>
<td>Developed acute renal failure, and died at 5 months</td>
</tr>
<tr>
<td>Current</td>
<td>19</td>
<td>Abdominal pain; Pelvic mass; Leukocytosis of unknown origin</td>
<td>Pleomophic</td>
<td>10 × 9 × 8 (left ovary)</td>
<td>Surgery + adjuvant chemotherapy with bleomycin, etoposide and cisplatin (3 cycles)</td>
<td>Alive and no evidence of disease now</td>
</tr>
</tbody>
</table>
### Table 2. Primary UPS of the ovary: summary of the case reports

<table>
<thead>
<tr>
<th>Authors and years</th>
<th>Age</th>
<th>Presentation</th>
<th>Variant of UPS</th>
<th>Tumor size (cm)</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamakawa Y 1999</td>
<td>43</td>
<td>Leukocytosis of unknown origin, pyrexia</td>
<td>Inflammatory</td>
<td>5.3 × 4.0 × 3.8 (right ovary)</td>
<td>Surgery</td>
<td>Recurrence at 6 months with secondary surgery, no evidence of disease at 14 months</td>
</tr>
<tr>
<td>Dilerk TU 2006</td>
<td>22</td>
<td>Abdominal pain, suspected appendicitis</td>
<td>Inflammation (left ovary), storiform-pleomorphic (right ovary/terminal ileum)</td>
<td>9.5 × 6.0 × 4.0 (left ovary)</td>
<td>Surgery + adjuvant chemotherapy with cisplatinum (75 mg/m²) and cyclophosphamide (750 mg/m²) (6 cycles)</td>
<td>Alive and well at 10 months</td>
</tr>
<tr>
<td>Mukherjee S 2009</td>
<td>49</td>
<td>Abdominal pain,</td>
<td>Pleomorphic coexistence with rhabdomyosarcomatous</td>
<td>7 × 6 × 3 (right ovary)</td>
<td>Surgery + chemotherapy of unspecified regimen</td>
<td>Lost to follow up</td>
</tr>
<tr>
<td>Roque DM 2010</td>
<td>69</td>
<td>Abdominal pain</td>
<td>Pleomorphic with giant cell</td>
<td>18.5 × 12 × 9 (right ovary)</td>
<td>Surgery + adjuvant chemotherapy with gemcitabine and docetaxel (2 cycles)</td>
<td>No evidence of disease at 12 months</td>
</tr>
<tr>
<td>Chen G 2011</td>
<td>22</td>
<td>Pelvic mass</td>
<td>Angiomatoid</td>
<td>6 (right ovary)</td>
<td>Surgery</td>
<td>Well at 8 months</td>
</tr>
<tr>
<td>Choi SY 2011</td>
<td>46</td>
<td>Whole abdominal discomfort</td>
<td>Myxoid</td>
<td>3 × 3 (right ovary)</td>
<td>Surgery + adjuvant chemotherapy with cisplatin and ifosfamide (2 cycles)</td>
<td>Lost to follow up</td>
</tr>
<tr>
<td>Stefanovi A 2012</td>
<td>67</td>
<td>Pelvic mass</td>
<td>Storiform-pleomorphic</td>
<td>Unknown (right ovary)</td>
<td>Surgery + chemotherapy + radiotherapy</td>
<td>Recurrence at 4 months with secondary surgery and died one year later</td>
</tr>
<tr>
<td>Kurtoglu E 2016</td>
<td>46</td>
<td>Abdominal pain and distention</td>
<td>Pleomorphic coexistence with rhabdomyosarcomatous</td>
<td>18 × 11 × 6 (left ovary), 12 × 10 × 9 (right ovary)</td>
<td>Surgery + adjuvant chemotherapy with cisplatinum and doxorubicin (1 cycle)</td>
<td>Died 15 days later</td>
</tr>
</tbody>
</table>
Malignant transformation of the ovarian mature cystic teratoma

acute renal failure during the procedure. After dialysis, 2 more doses of doxorubicin were administered but the patient was diagnosed with tumor recurrence and died five months later. UPS with prominent inflammation is characterized by an intense inflammatory infiltrate that consists predominantly of neutrophils, lymphocytes, and foamy histiocytes. In 1999, Yamakawa and colleagues reported a patient case with inflammatory MFH of the ovary, which was positive for interleukin-6 expression [15]. The patient was a 43-year-old and presented with fever. The white blood cell, neutrophil and platelet counts were increased while the red blood cell, hemoglobin, and hematocrit levels were decreased. The patient became afebrile the day after surgery, and the blood indexes returned to normal levels soon after surgery. Finally, a case of primary UPS of the ovary with multinucleated giant cells was reported in 2010 [18]. After surgery, the patient was subjected to 2 cycles of adjuvant chemotherapy, and at 12 months post-diagnosis, the patient had no evidence of the disease.

According to the preceding reports and our case study, the cornerstone of the treatment of UPS is complete surgical resection with a tumor-free resection margin, followed by adjuvant chemotherapy and radiotherapy. However, the effectiveness of an adjuvant chemotherapy regimen remains unclear. Metastasis and local recurrence are the main determinants of the prognosis of this disease [28]. The prognosis is unfavorable due to the tumor’s high tendency for malignancy, aggressive metastasis, recurrence potential, and unclear chemotherapy regimen. In our patient case, we only removed the left ovary together with the left fallopian tube because of the young age of the patient and the requirement to maintain her reproductive ability. In addition, the patient received 3 cycles of adjuvant chemotherapy. This treatment approach was effective for this particular case since 10 months later, the patient had recovered well and there were no sign of tumor recurrence or metastasis. However, the patient’s long-term survival needs to be assessed further.

Acknowledgements

This study was not supported financially by any funding agency.

Disclosure of conflict of interest

None.

Address correspondence to: Hui Liu, Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, No. 20, 3rd Section, South Renmin Road, Chengdu 610041, Sichuan, China. Tel: +86 13982180233; E-mail: lh666888@163.com

References

Malignant transformation of the ovarian mature cystic teratoma


