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REVIEW ARTICLE

Clinicopathological characteristics and treatment of carcinosarcoma of the female genital tract

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Abstract

Carcinosarcomas of the female genital tract are highly aggressive and rare tumors, differing from other malignant gynecological tumors in that they contain both malignant carcinomatous and sarcomatous elements. Because carcinosarcomas are rapidly progressive, less sensitive to chemotherapy or radiotherapy, and have a high probability of recurrence, patients with advanced uterine and ovarian carcinosarcomas have poorer survival than those with endometrial or high-grade serous carcinomas. Although the treatment strategies are controversial, a comprehensive management approach is recommended, which involves complete debulking surgery followed by adjuvant chemotherapy and/or radiotherapy. Molecular-targeted therapies are promising for the management and improvement in the overall survival of patients with carcinosarcomas.

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Carcinosarcomas, also called malignant mixed mullerian tumors (MMMTs), are highly aggressive and rare tumors of the female genital tract. Uterine carcinosarcoma (UCS) is a common gynecological carcinosarcoma, accounting for 2%–5% of all uterine tumors [1]. Ovarian carcinosarcoma (OCS) is less common than UCS, accounting for only 1%–2% of all ovarian malignancies [2]. Primary carcinosarcomas of the cervix, fallopian tube, and vagina have only been reported in several cases in the literature. This review focuses on the clinicopathological characteristics and treatment of carcinosarcomas.

Pathological features

Carcinosarcomas are tumors containing malignant epithelial as well as mesenchymal components [3]. These two components are interlaced or independent on microscopic observation. The malignant epithelial component is mainly composed of serous endometrial adenocarcinoma [4], clear cell carcinoma, squamous basal cell carcinoma, adenosquamous carcinoma, and undifferentiated carcinoma [5]. The mesenchymal component is either homologous or heterologous. Homologous sarcoma contains tissue native to the mullerian duct, such as endometrial stromal sarcoma, fibrosarcoma, or leiomyoma. However, cartilaginous, osteosarcomatous, liposarcomatous, and rhabdomyosarcomatous differentiation, which are commonly seen in the heterologous elements, are not native to mullerian duct tissues. Studies showed that approximately one-third of carcinosarcomas have two or more sarcomatoid components, and advanced stromal sarcoma is the most common component [6]. Sood *et al* [7] showed that the heterologous subtype was more common than homologous subtype, and the heterologous subtype revealed poorer survival. However, other studies suggest that the histologic subtype of carcinosarcoma is not a predictive/prognostic factor for survival [8].

The histogenesis of female genital tract carcinosarcomas has been a subject of debate and several theories have been proposed. Among these are the collision theory (also called polyclonal origin theory), based on the collision of epithelial and mesenchymal stem cells, and the combination theory (also called monoclonal origin theory), in which both components are thought to arise from a single stem cell clone, with dominance of the carcinomatous element. Conversely, the conversion theory postulates that the sarcomatous element is derived from the carcinoma during tumor development. That is, an original stem cell differentiates into one cell type, which, in turn, differentiates into a second cell type. Jin *et al* [9] showed that

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2 cases of OCS and 10 cases of UCS had monoclonal origin, while another 2 cases of UCS had polyclonal origin. Similarly, Schipf *et al* [10] supported the monoclonal origin theory using comparative genomic hybridization and fluorescence in situ hybridization to evaluate 30 cases of OCS. They found that genetic aberrations in OCS were similar to those in serous carcinomas – an indication of metaplasticity – giving support to the conversion theory. The conversion theory is also supported by the findings of 2 cases of primary serous epithelial carcinomas recurring as OCS. After loss of heterozygosity, *p53* mutation status, and microsatellite analyses, Gallardo *et al* [11] found that both the primary and recurrent tumors had identical characteristics. In one study of 25 cases of UCS, chromosomal aberrations were found in 2 components of most UCS. Meanwhile, *p53* and *K-ras* mutations and *X* chromosome inactivation were identical, lending support for the monoclonal origin of UCS. Nevertheless, few studies have reported the correlation between UCS and a polyclonal origin [12].

Many studies have described the biological characteristics of carcinosarcomas based on their molecular characteristics. High cytokeratin and epithelial membrane antigen (EMA) expression was noted on carcinosarcomas, which can predict pathogenesis by immunohistochemical staining [13]. Epidermal growth factor receptor (*EGFR*), estrogen or progesterone receptor (*ER/PR*), and insulin-like growth factor 1 and 2 (*IGF1/2*) have critical roles in regulating the cell cycle. Targeted genes such as *EGFR* and *Her2* have been found to be aberrantly expressed in carcinosarcoma, and *EGFR* overexpression was associated with increased *AKT* activation [14]. Abnormal expression of these tyrosine kinase receptors, which are key kinases in cellular signal transduction, will set foundation for the potential targeted therapies of carcinosarcoma [15].

Clinical features

The clinical presentation of UCS is similar to that of other uterine carcinomas. Typically, UCS presents with postmenopausal vaginal bleeding, watery discharge, abdominal pain, or an abdominal mass. About 50%–95% of patients with UCS experience dilatation of the uterine cavity, and 50% are found to have a vaginal mass on examination [16]. High preoperative levels of CA125 are seen in some patients.

National Comprehensive Cancer Network (NCCN) guidelines recommend a staging system of UCS that is the same as that applied to the endometrial system [17]. The biological characteristics and invasiveness of UCS are relevant to its pathological stage and sarcomatous histological subtype, and 53% of UCS cases are diagnosed in the advanced stages [6].

The symptoms of OCS are similar to those of high-grade serous ovarian cancer, and the staging system is the same as that applied to ovarian carcinomas [International Federation of Gynecology and Obstetrics (FIGO 2014)]. OCS FIGO stage III or IV has been reported to be associated with older age and faster disease progression in women [18]. Typical symptoms of OCS include abdominal pain and distention, early satiety, and gastrointestinal complaints; the performance status of OCS is usually poorer than that of epithelial ovarian cancer. A palpable abdominal mass may be found on initial physical examination. More than 90% of patients are estimated to have metastatic foci, and 30% present with abundant ascites. Serum CA125 levels tend to be elevated in OCS patients [19].

Only few cases of cervical carcinosarcoma have been reported in the literature. Philip *et al* [20] reported that 8 of 9 patients with cervical carcinosarcoma had FIGO stage I or II, with clinical symptoms of abnormal vaginal bleeding or spotting, postmenopausal bleeding, and abnormal Papanicolaou smear results. A cervical mass indicates advanced disease. Serum CA125 levels may be elevated in cervical carcinosarcoma patients [20]. Carcinosarcoma of the vagina is much more uncommon, and only few cases have been reported in the literature. Pelvic radiotherapy has been reported as a risk factor for carcinosarcoma of the vagina, with 50% of patients having a history of radiotherapy [21].

Treatments

The optimal treatment regimens for carcinosarcomas of the female genital tract have not been established. According to the NCCN guidelines, routine treatment of OCS and UCS is similar to that of advanced endometrial carcinoma and high-grade serous ovarian cancer [17, 22].

Surgery

Surgery is the primary treatment, and is the mainstay therapy for gynecological carcinosarcomas. In patients with early stage disease (especially stage I and II), radical surgery should be performed as soon as possible, which includes peritoneal lavage for cytology, total abdominal hysterectomy and bilateral salpingo-oophorectomy, dissection of the pelvic and para-aortic lymph nodes, and omentectomy and multi-peritoneal biopsies. For patients with advanced disease, maximal tumor debulking surgery is recommended with optimal cytoreductive surgery, which is defined as surgery after which there is no measurable residual disease. Rutledge *et al* [23] showed that postoperative residual disease correlated with survival in 31 advanced carcinosarcoma patients who underwent cytoreductive surgery. Similarly, Edward *et al* [24] studied 44 advanced UCS patients and found a trend toward improved survival after optimal debulking surgery compared to that after tumor excision alone [overall survival

(OS): 52.3 vs. 8.6 months; $P < 0.0001$]. Several studies have suggested that lymphadenectomy is correlated with improved survival. Gunjal *et al* [25] analyzed 2758 UCS and 924 OCS cases in the SEER database, and found that lymphadenectomy reduced that mortality rates by 33% [hazard ratio (HR) = 0.67,95% confidence interval (CI), 0.61–0.74] and 34% (HR = 0.66,95% CI, 0.56–0.78) in the UCS and OCS cases, respectively.

Radiation therapy

Radiation therapy has been utilized as a treatment approach for UCS. However, its impact on patient survival remains controversial. In an European Organization for Research and Treatment of Cancer (EORTC) study [26], 224 FIGO stage I–II uterine sarcomas, 91 of which were carcinosarcomas, were randomized between an observation arm (OA) and a radiation therapy arm (RT). All patients underwent a hysterectomy and bilateral salpingo-oophorectomy, but peritoneal lavage for cytology and pelvic lymph node sampling were optional. The results showed no difference in either the OS (RT vs. OA, 8.5 vs. 6.8 years) or disease-free survival (RT vs. OA, 6.2 vs. 4.9 years) but increased local control for the carcinosarcoma patients receiving radiation (RT vs. OA, 61% vs. 47%). In a study of 1819 patients in the SEER database, Wright *et al* [27] reported a 21% reduction in the mortality rate for the patients who underwent radiotherapy. Thus, radiation reduced the mortality rate by 25% in carcinosarcoma patients who did not undergo node dissection, but had only a marginal effect on survival in patients who underwent node dissection.

However, a phase III trial performed by the Gynecologic Oncology Group (GOG) [28] from 1993 to 2005 showed no advantage for radiotherapy in 206 stage I–IV UCS patients. All patients underwent a hysterectomy, bilateral salpingo-oophorectomy and maximal debulking surgery, and optional peritoneal cytology and/or pelvic lymph node dissection with residual disease ≤ 1 cm. Abdominal radiotherapy was performed in 105 patients and ifosfamide-cisplatin-mesna was administered to 101 patients after complete resection. The chemotherapy group showed an improved recurrence rate (21% lower; HR = 0.789, 95% CI 0.530–1.176) and death rate (29% lower; HR = 0.79, 95% CI 0.53–1.18), although there was no statistically significant survival benefit.

There has been little use or rationale for radiotherapy in OCS patients, and thus far, no studies have reported that radiation therapy may improve survival in early-stage OCS patients [29].

Chemotherapy

Although surgery remains the mainstay of treatment for early-stage carcinosarcoma patients, postoperative recurrent tumors are common in most patients. For women with advanced disease, adjuvant chemotherapy and/or radiotherapy is not recommended owing to the high risk of abdominopelvic recurrence. Therefore, postoperative adjuvant chemotherapy has a significant role in preventing recurrence. However, there is no consensus recommendation of chemotherapy for carcinosarcoma patients. Most studies recommended chemotherapy as a postoperative adjuvant therapy in patients with stage I or II disease, or as a palliative treatment for advanced and recurrent diseases. Several single chemotherapeutic agents have been investigated, including ifosfamide [response rate (RR) = 29%–36%], cisplatin (RR = 28%–42%), doxorubicin (RR = 10%–25%) or paclitaxel (RR = 18%) [30] for UCS; and doxorubicin (RR = 10%) [31] or cisplatin (RR = 20%) [32] for OCS.

Several studies have noted the increasing value of combination chemotherapy over single chemotherapeutic agents, but a consensus regimen has not been established. Carcinosarcomas are often responsive to platinum-based chemotherapies and may be tested in combination with other agents. Combination chemotherapeutic agents are recommended as summarized below.

(1) Paclitaxel and carboplatin. Powell *et al* [30] reported an overall RR of 54% (95% CI, 37%–67%) in a series of 46 UCS patients with advanced and/or recurrent disease. Most of the patients received 3–6 cycles of paclitaxel (175 mg/m^2, >3 h) and carboplatin (AUC = 6) chemotherapy; the main toxicities were hematologic, fatigue, and peripheral neuropathy. Similar results were found in a phase II prospective study by Lacour *et al* [33]. A time to progression (TTP) of 9.5 months and an OS of 21.1 months were reported in 23 advanced/recurrent UCS patients. Common toxicities included fatigue, neutropenia, and alopecia. Rauh *et al* [18] demonstrated an overall RR of 62% in 50 OCS patients treated with carboplatin and paclitaxel after surgery. In contrast, among 100 matched controls with serous epithelial ovarian cancer, the RR was 83% ($P = 0.03$).

(2) Ifosfamide and cisplatin. Sutton *et al* [34] reported an RR of 34.8% using ifosfamide alone in a phase II trial of UCS. In a later phase III trial, the RR of the combination of ifosfamide and cisplatin was shown to be significantly greater than that of ifosfamide alone (54% vs. 36%). However, there was no statistically significant difference in the median survival between the combination and single-agent treatment (4.0 vs. 6.0 months, $P > 0.05$) [35]. Advantages of the combination of ifosfamide and cisplatin can also been found in the treatment of OCS. A retrospective study of 27 OCS patients conducted by Rutledge *et al* [24] found that ifosfamide-cisplatin improved progression-free survival (PFS) ($P = 0.05$) and OS ($P = 0.03$), but was associated with more toxicities, including alopecia and neutropenia, compared to paclitaxel and carboplatin.

(3) Ifosfamide and paclitaxel. The advantage of com-

bination chemotherapy consisting of ifosfamide and paclitaxel in 179 advanced/recurrent UCS patients was discussed by Homesley *et al* [36]. A significant difference was noted in the PFS (5.8 vs. 3.6 months) and OS (13.5 vs. 8.4 months) between the combination chemotherapy and ifosfamide alone. Further, the estimated death rate was 31% lower in the combination chemotherapy group (HR = 0.69, 95% CI 0.49–0.97, $P = 0.03$). Alopecia and severe sensory neuropathy were the most common toxicities in the combination chemotherapy group.

(4) Paclitaxel, carboplatin, and ifosfamide. Forty patients, 34 with primary UCS and 6 with fallopian tube or OCS, with no prior chemotherapy, were treated with this combination in the series studied by Kosmas [37]. The chemotherapy regimen was administered at the following doses: paclitaxel, 175 mg/m^2 day 1; ifosfamide, 2.0 g/m^2 on days 1 and 2; carboplatin, AUC = 5 mg/mL/min on day 2; and prophylactic G-CSF from day 3. The RR was 67.5% (20/40), with 11 complete responses and 16 partial responses, while 10 patients had stable disease, and 3 developed progressive disease. The median response duration was 9 months, median PFS was 13 months, and median OS was 18 months. Grade 3/4 neutropenia was recorded in 55% of patients, which was endurable.

Additional chemotherapeutic agents include topotecan, cisplatin/ifosfamide/mesna, gemcitabine, and docetaxel. However, outcomes did not differ among these agents, and more toxic effects were reported.

Targeted therapy

Recently, molecular-targeted therapy has been utilized in the treatment of gynecological tumors. ABL gene, fibroblast derived growth factor receptor-β (FDGFR-β) and Her-2 are overexpressed in up to 45%, 100%, and 19% of gynecological carcinosarcomas, respectively, and that other molecules, including PR, ER, VEGF, and EGFR, have slightly high expression levels [38]. The overexpression of certain proteins could be a focus for potential therapeutics in a number of studies. A phase II trial of sorafenib, an oral agent that inhibits VEGFR, demonstrated that 5% of patients with uterine carcinoma had a partial response and 42.5% achieved stable disease; the median OS was 11.4 months. However, no patient had an objective response, with 25% achieving stable disease [39]. In a phase II trial of imatinib, a tyrosine kinase inhibitor, 1 of 23 UCS patients had a PFS ≥ 6 months, while all other patients had progressive disease or tumor response could not be assessed [40]. Trastuzumab, a humanized monoclonal antibody that acts through the HER2/neu extracellular domain, exhibits therapeutic efficacy in HER2/neu-overexpressing cancers *in vitro* and *in vivo* [41]. The effect of treatment with trastuzumab on patient survival needs to be explored in further studies.

Prognosis

Female genital tract carcinosarcomas have very poor prognosis. UCS has significantly worse prognosis than endometrial carcinoma (6.660 vs. 17.760 months; $P < 0.001$) [42] and the overall prognosis for early-stage (stage I) OCS is worse than that for high-grade serous ovarian carcinomas of a similar FIGO stage [5-year OS: 65.3% (95% CI, 58.0%–71.4%) vs. 80.6% (95% CI, 58.0%–71.4%)]. Meanwhile, 5-year OS of advanced carcinosarcomas and serous carcinomas is 18.2% and 33.3% [43], respectively. Carcinosarcoma of the vagina has a poor prognosis with a 5-year OS of only 17% [44]. Recurrence of carcinosarcomas occurs in 56% of patients after primary surgical and adjuvant therapy [45]. Even in early-stage disease, the recurrent rate is estimated between 47% and 64%, and up to 80% of cases will develop distant metastases [46]. The most common sites of metastatic foci include the lung (49%), peritoneum (44%), pelvic or para-aortic lymph nodes (35%), adrenal gland or bone (19%), heart or pericardium (9%), and/or the brain (7%) [47]. Lymph node metastasis, tumor size, lymphovascular invasion, histological subtype, pathological subtype, cervical invasion, and myometrial invasion are considered prognostic factors for UCS [45]. OCS has a recurrent rate of up to 70%, and the major prognostic factors are stage/grade of tumor, pathological subtype, and myometrial invasion [48].

Conclusions

In conclusion, carcinosarcoma of the female genital tract is a rare, rapidly progressing neoplasm with a poor prognosis. Although the optimal management modality remains controversial, maximal cytoreductive surgery and adjuvant therapy may improve survival outcomes. Thus, further research is needed to improve the understanding and management of these tumor subtypes. Novel therapies associated with less severe adverse effects and higher efficacy need to be established.

Conflicts of interest

The authors indicated no potential conflicts of interest.

References

1. Cimbaluk D, Rotmensch J, Scudiere J, *et al*. Uterine carcinosarcoma: immunohistochemical studies on tissue microarrays with focus on potential therapeutic targets. Gynecol Oncol, 2007, 105: 138–144.
2. Siegel R, Ward E, Brawley O, *et al*. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. CA Cancer J Clin, 2011, 61: 212–236.
3. Brown L. Pathology of uterine malignancies. Clin Oncol (R Coll Radiol), 2008, 20: 433–447.
4. El-Nashar SA, Mariani A. Uterine carcinosarcoma. Clin Obstet Gynecol, 2011, 54: 292–304.

5. Ahuja A, Safaya R, Prakash G, *et al*. Primary mixed mullerian tumor of the vagina – a case report with review of the literature. Pathol Res Pract, 2011, 207: 253–255.
6. Kernochan LE, Garcia RL. Carcinosarcomas (malignant mixed mullerian tumor) of the uterus: advances in elucidation of biologic and clinical characteristics. J Natl Compr Canc Netw, 2009, 7: 550–556.
7. Sood AK, Sorosky JI, Gelder MS, *et al*. Primary ovarian sarcoma: analysis of prognostic variables and the role of surgical cytoreduction. Cancer, 1998, 82: 1731–1737.
8. Ariyoshi K, Kawauchi S, Kaku T, *et al*. Prognostic factors in ovarian carcinosarcoma: a clinicopathological and immunohistochemical analysis of 23 cases. Histopathology, 2000, 37: 427–436.
9. Jin Z, Ogata S, Tamura G, *et al*. Carcinosarcomas (malignant mullerian mixed tumors) of the uterus and ovary: a genetic study with special reference to histogenesis. Int J Gynecol Pathol, 2003, 22: 368–373.
10. Schipf A, Mayr D, Kirchner T, *et al*. Molecular genetic aberrations of ovarian and uterine carcinosarcomas – a CGH and FISH study. Virchows Arch, 2008, 452: 259–268.
11. Gallardo A, Matias-Guiu X, Lagarda H, *et al*. Malignant mullerian mixed tumor arising from ovarian serous carcinoma: a clinicopathologic and molecular study of two cases. Int J Gynecol Pathol, 2002, 21: 268–272.
12. El-Nashar SA, Mariani A. Uterine carcinosarcoma. Clin Obstet Gynecol, 2011, 54: 292–304.
13. Euscher E, Wei C, Ramondetta L, *et al*. Reverse-phase protein lysate array identified potential therapeutic targets in uterine carcinosarcoma. Supplement to Gynecologic Oncology: Abstracts Presented for the 42nd Annual Meeting of the Society of Gynecologic Oncologists, 2011, 120: S92.
14. Rice LW, Stone RL, Xu M, *et al*. Biologic targets for therapeutic intervention in endometrioid endometrial adenocarcinoma and malignant mixed mullerian tumors. Am J Obstet Gynecol, 2006, 194: 1119–1126.
15. Menczer J, Schreiber L, Sukmanov O, *et al*. COX-2 expression in uterine carcinosarcoma. Acta Obstet Gynecol Scand, 2010, 89: 120–125.
16. Kuyumcuoğlu U, Kale A. Homologous type of malignant mixed Mullerian tumor of the uterus presenting as a cervical mass. J Chin Med Assoc, 2009, 72: 533–535.
17. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasm, 2014.
18. Rauh-Hain AJ, Grodwon WB, Rodriguez N, *et al*. Carcinosarcoma of the ovary: a case-control study. Gynecol Oncol, 2011, 121: 477–481.
19. Brown E, Stewart M, Rye T, *et al*. Carcinosarcoma of the ovary: 19 years of prospective data from a single center. Cancer, 2004, 100: 2148–2153.
20. Clement PB, Zubovits JT, Young RH, *et al*. Malignant mullerian mix tumor of the uterine cervix: A report of nine case of a neoplasm with morphology often different from its counterpart in the corpus. Int J Gynecol Pathol, 1998, 17: 211–222.
21. Creasman WT, Phillips JL, Menck HR. The national cancer data base report on cancer of the vagina. Cancer, 1998, 83: 1033–1040.
22. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Ovarian Cancer including fallopian tube cancer and primary peritoneal cancer, 2014.
23. Rutledge TL, Gold MA, McMeekin DS, *et al*. Carcinosarcoma of the ovary – a case series. Gynecol Oncol, 2006, 100: 128–132.
24. Tanner EJ, Leitao MM Jr, Garg K, *et al*. The role of cytoreductive surgery for newly diagnosed advanced-stage uterine carcinosarcoma. Gynecol Oncol, 2011, 123: 548–552.
25. Garg G, Shah JP, Kumar S, *et al*. Ovarian and uterine carcinosarcomas: a comparative analysis of prognostic variables and survival outcomes. Int J Gynecol Cancer, 2010, 20: 888–894.
26. Reed NS, Mangioni C, Malmström H, *et al*. Phase III randomized study to evaluate the role of adjuvant pelvic radiotherapy in the treatment of uterine sarcomas stages I and II: an European Organisation for Research and Treatment of Cancer Gynaecological Cancer Group Study (protocol 55874). Eur J Cancer, 2008, 44: 808–818.
27. Wright JD, Seshan VE, Shah M, *et al*. The role of radiation in improving survival for early-stage carcinosarcoma and leiomyosarcoma. Am J Obstet Gynecol, 2008, 199: 1–8.
28. Wolfson AH, Brady MF, Rocereto T, *et al*. A gynecologic oncology group randomized phase III trial of whole abdominal irradiation (WAI) vs. cisplatin-ifosfamide and mesna (CIM) as postsurgical therapy in stage I-IV carcinosarcoma (CS) of the uterus. Gynecol Oncol, 2007, 107: 177–185.
29. Mano MS, Rosa DD, Azambuja E, *et al*. Current management of ovarian carcinosarcoma. Int J Gynecol Cancer, 2007, 17: 316–324.
30. Powell MA, Filiaci VL, Rose PG, *et al*. Phase II evaluation of paclitaxel and carboplatin in the treatment of carcinosarcoma of the uterus: a Gynecologic Oncology Group study. J Clin Oncol, 2010, 28: 2727–2731.
31. Morrow CP, Bundy BN, Hoffman J, *et al*. A Gynecologic Oncology Group Study. Adriamycin chemotherapy for malignant mixed mesodermal tumor of the ovary. Am J Clin Oncol, 1986, 9: 24–26.
32. Thigpen JT, Blessing JA, DeGeest K, *et al*, Gynecologic Oncology Group study. Cisplatin as initial chemotherapy in ovarian carcinosarcoma. Gynecol Oncol, 2004, 93: 336–339.
33. Lacour RA, Euscher E, Atkinson EN, *et al*. A phase II trial of palitaxel and carboplatin in women with advanced or recurrent uterine carcinosarcoma. Int J Gynecol Cancer, 2011, 21: 517–522.
34. Sutton GP, Blessing JA, Rosenshein N, *et al*. Phase II trial of ifosfamide and mesna in mixed mesodermal tumors of the uterus (a Gynecologic Oncology Group study). Am J Obstet Gynecol, 1989, 161: 309–312.
35. Sutton G, Brunetto VL, Kilgore L, *et al*. A phase III trial of ifosfamide with or without cisplatin in carcinosarcoma of the uterus: A Gynecologic Oncology Group Study. Gynecol Oncol, 2000, 79: 147–153.
36. Homesley HD, Filiaci V, Markman M, *et al*. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma: a gynecologic oncology group study. J Clin Oncol, 2007, 25: 526–531.
37. Kosmas C, Vorgias G, Tsakonas G, *et al*. Paclitaxel-ifosfamide-carboplatin combination chemotherapy regimen in advanced uterine and adnexal malignant mixed Mullerian tumours. Br J Cancer, 2011, 105: 897–902.
38. Ulbricht LJ, Kunert M, Gremmler B, *et al*. Intracardiac metastasis of a Malignant Mixed Mullerian tumor (MMMT): progressive dyspnea due to obstruction of the left atrium and the left ventricle without left ventricular dysfunction or primary lung disease. Wien Med Wochenschr, 2009, 159: 355–358.
39. Nimeiri HS, Oza AM, Morgan RJ, *et al*. A phase II study of sorafenib in advanced uterine carcinoma/carcinosarcoma: a trial of the Chicago, PMH, and California Phase II Consortia. Gynecol Oncol, 2010, 117: 37–40.
40. Huh WK, Sill MW, Darcy KM, *et al*. Efficacy and safety of imatinib mesylate (Gleevec) and immunohistochemical expression of c-Kit and PDGFR-beta in a Gynecologic Oncology Group Phase II Trial in women with recurrent or persistent carcinosarcomas of the uterus. Gynecol Oncol, 2010, 117: 248–254.
41. Guzzo F, Bellone S, Buza N, *et al*. HER2/neu as a potential target

for immunotherapy in gynecologic carcinosarcomas. Int J Gynecol Pathol, 2012, 31: 211–221.
42. Mahendraraj K, Moore I, Chamberlain RS, *et al*. Demographics and Clinical Outcomes of Carcinosarcoma of the Uterus: A Population Based Clinical Outcomes Study From the Surveillance Epidemiology and End Results (SEER) Database (1973–2010). J Surg Res, 2014, 186: 569–570.
43. George EM, Herzog TJ, Neugut AI. Carcinosarcoma of the ovary: natural history, patterns of treatment, and outcome. Gynecol Oncol, 2013, 131: 42–45.
44. Peters WA, Kumar NB, Andersen WA, *et al*. Primary sarcoma of the adult vagina: a clinicopathologic study. Obstet Gynecol, 1985, 65: 699–704.
45. El-Nashar SA, Mariani A. Uterine carcinosarcoma. Clin Obstet Gynecol, 2011, 54: 292–304.
46. Genever AV, Abdi S. Can MRI predict the diagnosis of endometrial carcinosarcoma?. Clin Radiol, 2011, 66: 621–624.
47. Ho KC, Lai CH, Wu TI, *et al*. 18F-fluorodeoxyglucose positron emission tomography in uterine carcinosarcoma. Eur J Nucl Med Mol Imaging, 2008, 35: 484–492.
48. Barnholtz-Sloan J, Bryant C, Morris R, *et al*. Epidemiology and survival of women diagnosed with malignant mixed mullerian tumors of the ovary (OMMMT). Gynecol Oncol, 2004, 93: 506–512.

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