

# World Journal of *Clinical Cases*

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## OPINION REVIEW

- 4280 Role of monoclonal antibody drugs in the treatment of COVID-19  
*Ucciferri C, Vecchiet J, Falasca K*

## MINIREVIEWS

- 4286 Review of simulation model for education of point-of-care ultrasound using easy-to-make tools  
*Shin KC, Ha YR, Lee SJ, Ahn JH*
- 4303 Liver injury in COVID-19: A minireview  
*Zhao JN, Fan Y, Wu SD*

## ORIGINAL ARTICLE

## Case Control Study

- 4311 Transanal minimally invasive surgery vs endoscopic mucosal resection for rectal benign tumors and rectal carcinoids: A retrospective analysis  
*Shen JM, Zhao JY, Ye T, Gong LF, Wang HP, Chen WJ, Cai YK*
- 4320 Impact of *mTOR* gene polymorphisms and gene-tea interaction on susceptibility to tuberculosis  
*Wang M, Ma SJ, Wu XY, Zhang X, Abesig J, Xiao ZH, Huang X, Yan HP, Wang J, Chen MS, Tan HZ*

## Retrospective Cohort Study

- 4331 Establishment and validation of a nomogram to predict the risk of ovarian metastasis in gastric cancer: Based on a large cohort  
*Li SQ, Zhang KC, Li JY, Liang WQ, Gao YH, Qiao Z, Xi HQ, Chen L*

## Retrospective Study

- 4342 Predictive factors for early clinical response in community-onset *Escherichia coli* urinary tract infection and effects of initial antibiotic treatment on early clinical response  
*Kim YJ, Lee JM, Lee JH*
- 4349 Managing acute appendicitis during the COVID-19 pandemic in Jiaying, China  
*Zhou Y, Cen LS*
- 4360 Clinical application of combined detection of SARS-CoV-2-specific antibody and nucleic acid  
*Meng QB, Peng JJ, Wei X, Yang JY, Li PC, Qu ZW, Xiong YF, Wu GJ, Hu ZM, Yu JC, Su W*
- 4370 Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients  
*Wang L, He WB, Yu XM, Hu DL, Jiang H*

- 4380** Percutaneous radiofrequency ablation is superior to hepatic resection in patients with small hepatocellular carcinoma

*Zhang YH, Su B, Sun P, Li RM, Peng XC, Cai J*

- 4388** Clinical study on the surgical treatment of atypical Lisfranc joint complex injury

*Li X, Jia LS, Li A, Xie X, Cui J, Li GL*

- 4400** Application of medial column classification in treatment of intra-articular calcaneal fractures

*Zheng G, Xia F, Yang S, Cui J*

### Clinical Trials Study

- 4410** Optimal hang time of enteral formula at standard room temperature and high temperature

*Lakananurak N, Nalinthassanai N, Suansawang W, Panarat P*

### META-ANALYSIS

- 4416** Meta-analysis reveals an association between acute pancreatitis and the risk of pancreatic cancer

*Liu J, Wang Y, Yu Y*

### SCIENTOMETRICS

- 4431** Global analysis of daily new COVID-19 cases reveals many static-phase countries including the United States potentially with unstoppable epidemic

*Long C, Fu XM, Fu ZF*

### CASE REPORT

- 4443** Left atrial appendage aneurysm: A case report

*Belov DV, Moskalev VI, Garbuzenko DV, Arefyev NO*

- 4450** Twenty-year survival after iterative surgery for metastatic renal cell carcinoma: A case report and review of literature

*De Raffe E, Mirarchi M, Casadei R, Ricci C, Brunocilla E, Minni F*

- 4466** Primary rhabdomyosarcoma: An extremely rare and aggressive variant of male breast cancer

*Satală CB, Jung I, Bara TJ, Simu P, Simu I, Vlad M, Szodorai R, Gurzu S*

- 4475** Bladder stones in a closed diverticulum caused by *Schistosoma mansoni*: A case report

*Alkhamees MA*

- 4481** Cutaneous ciliated cyst on the anterior neck in young women: A case report

*Kim YH, Lee J*

- 4488** Extremely rare case of successful treatment of metastatic ovarian undifferentiated carcinoma with high-dose combination cytotoxic chemotherapy: A case report

*Kim HB, Lee HJ, Hong R, Park SG*

- 4494** Acute amnesia during pregnancy due to bilateral fornix infarction: A case report  
*Cho MJ, Shin DI, Han MK, Yum KS*
- 4499** Ascaris-mimicking common bile duct stone: A case report  
*Choi SY, Jo HE, Lee YN, Lee JE, Lee MH, Lim S, Yi BH*
- 4505** Eight-year follow-up of locally advanced lymphoepithelioma-like carcinoma at upper urinary tract: A case report  
*Yang CH, Weng WC, Lin YS, Huang LH, Lu CH, Hsu CY, Ou YC, Tung MC*
- 4512** Spontaneous resolution of idiopathic intestinal obstruction after pneumonia: A case report  
*Zhang BQ, Dai XY, Ye QY, Chang L, Wang ZW, Li XQ, Li YN*
- 4521** Successful pregnancy after protective hemodialysis for chronic kidney disease: A case report  
*Wang ML, He YD, Yang HX, Chen Q*
- 4527** Rapid remission of refractory synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome in response to the Janus kinase inhibitor tofacitinib: A case report  
*Li B, Li GW, Xue L, Chen YY*
- 4535** Percutaneous fixation of neonatal humeral physeal fracture: A case report and review of the literature  
*Tan W, Wang FH, Yao JH, Wu WP, Li YB, Ji YL, Qian YP*
- 4544** Severe fundus lesions induced by ocular jellyfish stings: A case report  
*Zheng XY, Cheng DJ, Lian LH, Zhang RT, Yu XY*
- 4550** Application of ozonated water for treatment of gastro-thoracic fistula after comprehensive esophageal squamous cell carcinoma therapy: A case report  
*Wu DD, Hao KN, Chen XJ, Li XM, He XF*
- 4558** Germinomas of the basal ganglia and thalamus: Four case reports  
*Huang ZC, Dong Q, Song EP, Chen ZJ, Zhang JH, Hou B, Lu ZQ, Qin F*
- 4565** Gastrointestinal bleeding caused by jejunal angiosarcoma: A case report  
*Hui YY, Zhu LP, Yang B, Zhang ZY, Zhang YJ, Chen X, Wang BM*
- 4572** High expression of squamous cell carcinoma antigen in poorly differentiated adenocarcinoma of the stomach: A case report  
*Wang L, Huang L, Xi L, Zhang SC, Zhang JX*
- 4579** Therapy-related acute promyelocytic leukemia with FMS-like tyrosine kinase 3-internal tandem duplication mutation in solitary bone plasmacytoma: A case report  
*Hong LL, Sheng XF, Zhuang HF*
- 4588** Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report  
*Zhang X, Gu X, Li JG, Hu XJ*



- 4595** Severe hyperlipemia-induced pseudoerythrocytosis - Implication for misdiagnosis and blood transfusion: A case report and literature review  
*Zhao XC, Ju B, Wei N, Ding J, Meng FJ, Zhao HG*
- 4603** Novel brachytherapy drainage tube loaded with double 125I strands for hilar cholangiocarcinoma: A case report  
*Lei QY, Jiao DC, Han XW*
- 4609** Resorption of upwardly displaced lumbar disk herniation after nonsurgical treatment: A case report  
*Wang Y, Liao SC, Dai GG, Jiang L*
- 4615** Primary hepatic myelolipoma: A case report and review of the literature  
*Li KY, Wei AL, Li A*
- 4624** Endoscopic palliative resection of a giant 26-cm esophageal tumor: A case report  
*Li Y, Guo LJ, Ma YC, Ye LS, Hu B*
- 4633** Solitary hepatic lymphangioma mimicking liver malignancy: A case report and literature review  
*Long X, Zhang L, Cheng Q, Chen Q, Chen XP*
- 4644** Intraosseous venous malformation of the maxilla after enucleation of a hemophilic pseudotumor: A case report  
*Cai X, Yu JJ, Tian H, Shan ZF, Liu XY, Jia J*
- 4652** Intravesically instilled gemcitabine-induced lung injury in a patient with invasive urothelial carcinoma: A case report  
*Zhou XM, Wu C, Gu X*
- 4660** Bochdalek hernia masquerading as severe acute pancreatitis during the third trimester of pregnancy: A case report  
*Zou YZ, Yang JP, Zhou XJ, Li K, Li XM, Song CH*
- 4667** Localized primary gastric amyloidosis: Three case reports  
*Liu XM, Di LJ, Zhu JX, Wu XL, Li HP, Wu HC, Tuo BG*
- 4676** Displacement of peritoneal end of a shunt tube to pleural cavity: A case report  
*Liu J, Guo M*
- 4681** Parathyroid adenoma combined with a rib tumor as the primary disease: A case report  
*Han L, Zhu XF*

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## Extremely rare case of successful treatment of metastatic ovarian undifferentiated carcinoma with high-dose combination cytotoxic chemotherapy: A case report

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### Abstract

#### BACKGROUND

Ovarian undifferentiated carcinomas are significantly rare and have an aggressive clinical course. Surgical resection is the only curative treatment in early-stage ovarian undifferentiated carcinomas that has a favorable prognosis. In case of recurrent and metastatic disease, palliative chemotherapy is the only available treatment. However, the effectiveness of standard chemotherapy regimen is not well-known, specifically in the case of extra-ovarian spread. We report an ovarian undifferentiated carcinoma of recurrent and inoperable advanced stage that was successfully treated with high-dose combination chemotherapy.

#### CASE SUMMARY

A 52-year-old woman presented with a 1-mo history of right lower quadrant and epigastric pain. A computed tomography (CT) scan of the abdomen revealed a multicystic mass with extensive internal necrosis of the right ovary without evidence of metastatic disease. A total hysterectomy with bilateral salpingo-oophorectomy and omentectomy was performed, but the surgery had a positive resection margin. Pathologically, it was diagnosed as ovarian undifferentiated carcinoma with sarcomatoid change. Although adjuvant chemotherapy was planned, it was delayed for 6 wk because of postoperative recovery, and the patient complained of abdominal pain. A CT scan and positron emission tomography-CT revealed a huge mass with multiple nodules in the pelvic cavity and para-aortic lymph node metastasis. Instead of standard therapy such as

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paclitaxel and platinum, combined chemotherapy with etoposide, ifosfamide, and cisplatin was administered. The patient experienced no recurrence for 5 years.

## CONCLUSION

This is a case of metastatic ovarian undifferentiated carcinoma with sarcomatoid change that was successfully treated with high-dose combination cytotoxic chemotherapy.

**Key Words:** Ovarian undifferentiated carcinoma; Sarcomatoid change; Chemotherapy; Etoposide, ifosfamide, cisplatin; Case report

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**Core Tip:** Palliative chemotherapy is the only available treatment for metastatic ovarian undifferentiated carcinoma. However, we used a high-dose combination chemotherapy of etoposide, ifosfamide, and cisplatin instead of the widely used paclitaxel and platinum and successfully treated an extremely rare case of inoperable metastatic ovarian undifferentiated carcinoma.

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## INTRODUCTION

Ovarian undifferentiated carcinomas do not classify into any type of carcinoma of the ovarian surface epithelium<sup>[1,2]</sup>.

Ovarian undifferentiated carcinomas account for approximately 5% of primary epithelial ovarian cancers and are clinically and significantly aggressive<sup>[1,3]</sup>. In most cases, this subtype spreads widely beyond the ovary at diagnosis; hence, complete tumor resection is considered difficult<sup>[4]</sup>. As in most other cancers, the detection of ovarian undifferentiated carcinomas in advanced stages is associated with poor prognosis<sup>[4,5]</sup>. A reported case of significantly rapid and fatal prognosis has been reported<sup>[6]</sup>. Furthermore, the efficacy of paclitaxel and platinum combination regimen that is generally used in epithelial ovarian cancer is unknown in the case of ovarian undifferentiated carcinoma<sup>[6]</sup>. Thus, there are no standard chemotherapy regimens available.

We report an interesting and rare case of metastatic ovarian undifferentiated carcinoma that was successfully treated with a high-dose combination cytotoxic chemotherapy.

## CASE PRESENTATION

### Chief complaints

Right lower quadrant and epigastric pain.

### History of present illness

A 52-year-old woman presented with a 1-mo history of right lower quadrant pain and epigastric pain.

### History of past illness

Her medical history and that of her family were otherwise unremarkable.

### Physical examination

Her abdomen was smooth and soft without any tenderness or palpable mass.

### Laboratory examinations

Complete blood count results were as follows (normal ranges in parentheses): White blood cell count,  $26.6 \times 10^3/\mu\text{L}$  ( $4.0\text{--}10.0 \times 10^3/\mu\text{L}$ ); hemoglobin, 10.8 g/dL (12–16 g/dL); and platelet count,  $674 \times 10^3/\mu\text{L}$  ( $150\text{--}400 \times 10^3/\mu\text{L}$ ). The results of blood biochemistry tests and urine analysis were normal. The serum C-reactive protein level was 4.26 mg/dL (0.0–0.5 mg/dL). The erythrocyte sedimentation rate was 41 mm/h (0–30 mm/h). The level of cancer antigen 125 was 58.5 U/mL ( $< 35$  U/mL), and both carcinoembryonic antigen (1.1 ng/mL; normal range 0.0–5.0 ng/mL) and carbohydrate antigen 19-9 (7.48 U/mL; normal range 0–33 U/mL) levels were normal.

### Imaging examinations

An abdominopelvic computed tomography (CT) scan revealed an 8 cm  $\times$  7 cm multicystic mass with extensive internal necrosis of the right ovary without evidence of metastatic lymphadenopathy and other organs (Figure 1). Our patient was clinically diagnosed with early-stage (less than the International Federation of Gynecology and Obstetrics Stage IC) ovarian cancer.

### Further diagnostic work-up

We performed debulking surgery with total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. At the time of surgery, the gross tumor measured 9 cm  $\times$  8 cm  $\times$  4 cm, and comprised solid and cystic areas. The tumor was significantly and severely adhesive to the pelvic wall and the intestine around the tumor. After surgery, macroscopic finding of the debulking tissue showed a multinodular cystic lesion filled with a yellowish liquid. Microscopic observation revealed tumor cell nests showing pleomorphic round-shaped nuclei with prominent nucleoli and high mitotic activity in the neutrophilic background. Areas of geographic necrosis are common, often with myxoid matrix. Sarcomatoid change of tumor cells was also identified, with areas showing immunohistochemically reactive for vimentin (Figure 2). The resection margin was positive because the mass was severely adhesive to the pelvic wall.

## FINAL DIAGNOSIS

The patient was diagnosed with ovarian undifferentiated carcinoma with sarcomatoid change and underwent incomplete surgical tumor resection.

## TREATMENT

We planned to administer adjuvant chemotherapy immediately because surgical resection margin was positive, and according to the literature review, this rare entity was known to have an aggressive course.

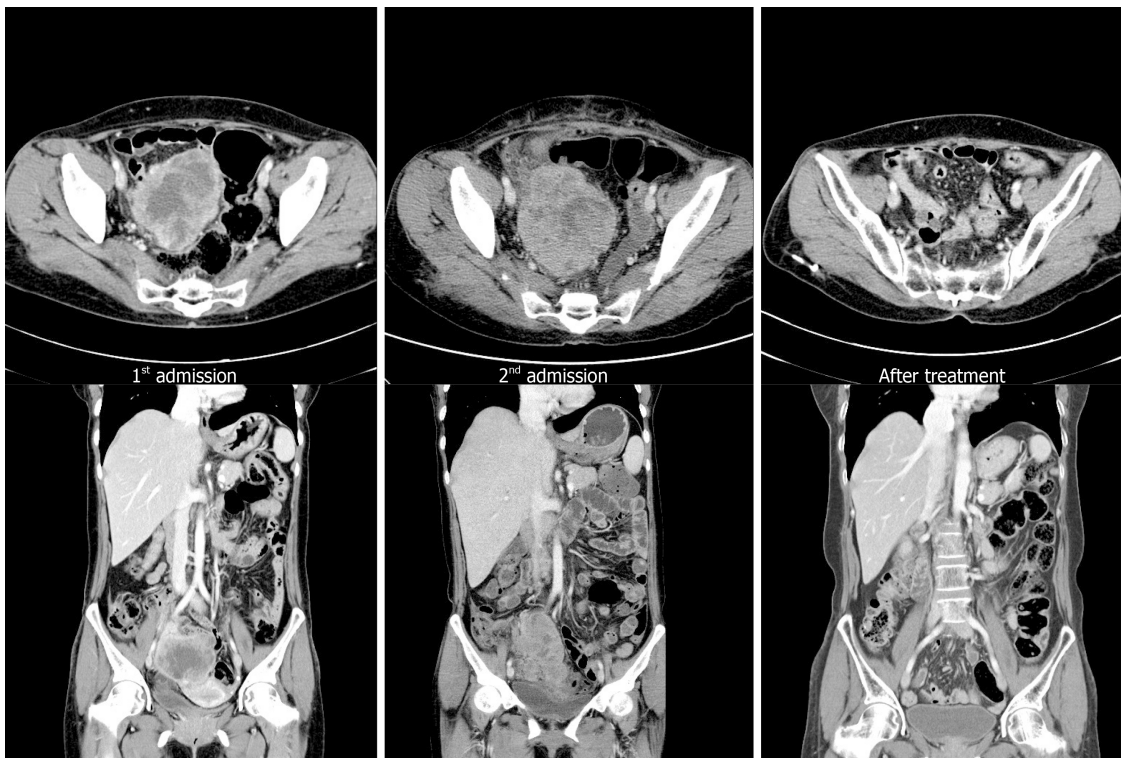
However, chemotherapy was delayed due to patient's general weakness and poor oral intake during the postoperative recovery period. Six weeks later, the patient suddenly complained of abdominal discomfort. A CT scan revealed an 11 cm  $\times$  7 cm mass with multiple nodules in the pelvic cavity, multiple peritoneal nodules, and enlargement of the para-aortic lymph nodes (Figure 1). Positron emission tomography-CT was performed for staging of the recurrent ovarian cancer, and it showed hypermetabolism in the lesions observed on CT scan (Figure 3). We strongly suspected metastatic and inoperable ovarian undifferentiated carcinoma due to the presence of multiple pelvic nodules and diffuse peritoneal seeding.

There is no standard chemotherapy regimen for ovarian undifferentiated carcinoma.

After reviewing various literature, we administered the etoposide, ifosfamide, and cisplatin (VIP) chemotherapy regimen with dose modification (cisplatin: 80 mg/m<sup>2</sup> on day 1, etoposide: 100 mg/m<sup>2</sup> on days 2–4, and ifosfamide: 1500 mg/m<sup>2</sup> on days 2–4) that targeted the sarcoma. We did not select the regimen commonly used for ovarian epithelial cancer (paclitaxel and platinum) since it was reported to have a poor response that led to rapid growth of recurrent tumor. After 2 cycles of aggressive combination chemotherapy, tumor size markedly decreased (from 10 cm  $\times$  7 cm to 4 cm  $\times$  3 cm). Furthermore, after 4 cycles of VIP regimen, almost the entire mass was no longer observed (Figures 1 and 3).

Therefore, we strongly recommend reoperation or definitive pelvic irradiation as a curative treatment option. Because the patient experienced the side effects of high-dose combination chemotherapy such as grade III febrile neutropenia,





**Figure 1 Computed tomography at admission and follow-up.** Computed tomography (CT) scan performed at first admission showing an 8 cm × 7 cm size mass only in the pelvic cavity. However, 6 wk after surgery (second admission), CT scan shows a mass that was larger than the initial mass in the pelvic cavity with peritoneal seeding and para-aortic lymphadenopathy (arrow). These lesions are almost no longer observed after chemotherapy.

thrombocytopenia, and mucositis, she strongly refused to perform additional chemotherapy and further definitive treatment. We recommended a short-term follow-up.

## OUTCOME AND FOLLOW-UP

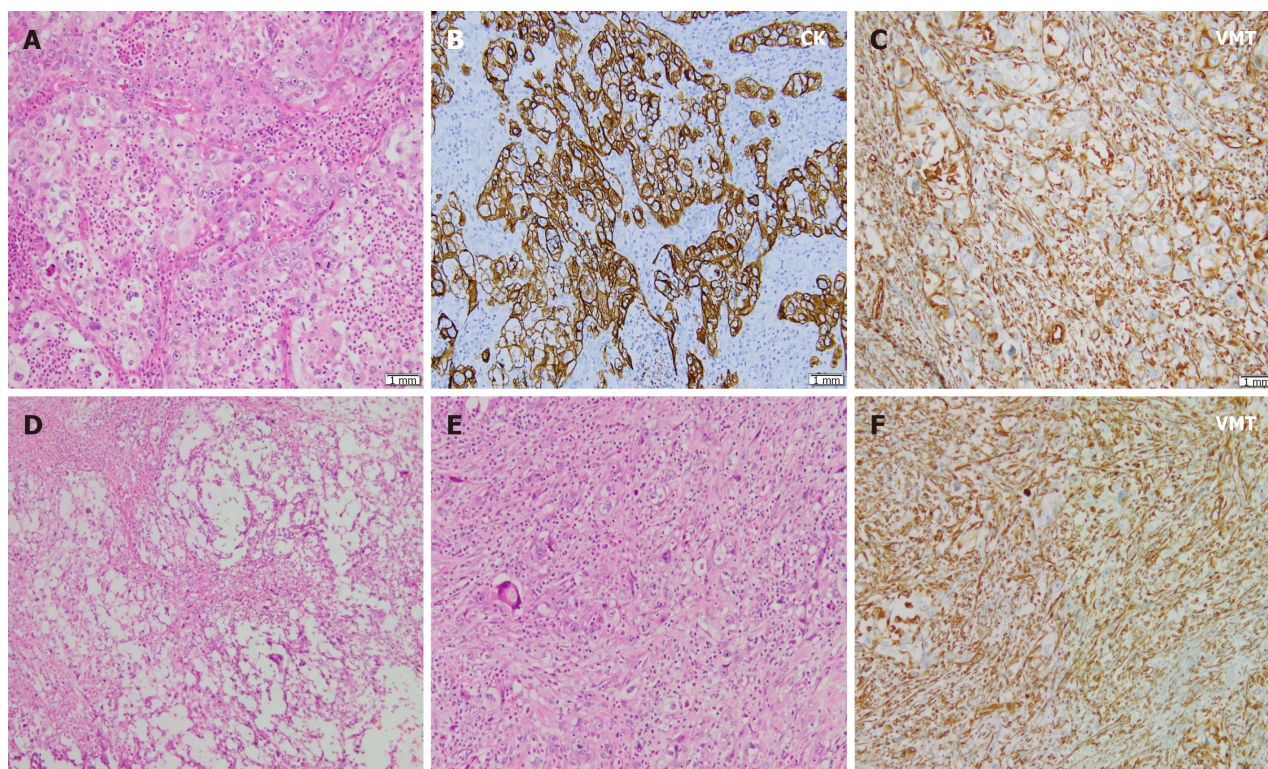
Fortunately, the tumor did not recur, and the patient is in complete remission. Five years after chemotherapy, this remission has been maintained, and the patient is alive without any tumor recurrence. Therefore, we had successfully treated the metastatic inoperable ovarian undifferentiated carcinoma.

## DISCUSSION

Ovarian undifferentiated carcinomas are rare. The World Health Organization classification describes ovarian undifferentiated carcinomas as a tumor showing solid growth of pleomorphic cells with no differentiation or only small foci of differentiation<sup>[7]</sup>. Similar to other epithelial ovarian cancers, it has a relatively favorable prognosis in its early stage<sup>[5,8]</sup>.

Traditionally, the prognosis of ovarian undifferentiated carcinoma is poor, and significantly rapid growth and fatal prognosis have been reported in advanced stage cases, such as this case. Furthermore, the cases with significantly rapid growth and fatal prognosis do not respond to paclitaxel and platinum treatment<sup>[6]</sup>.

In this case, instead of the standard regimen for the treatment of epithelial ovarian carcinoma (paclitaxel and platinum), we targeted the sarcomatous component of the ovarian undifferentiated carcinoma with the combined chemotherapy VIP regimen that is commonly used in sarcoma<sup>[9]</sup>. In sarcoma, anthracycline-based combination regimens (doxorubicin or epirubicin with ifosfamide and/or dacarbazine) have been generally used and have similar or severe side effects to VIP regimen<sup>[10]</sup>. Whole abdominal radiotherapy is rarely used for ovarian cancer. Palliative localized radiotherapy is an option for symptom control in patients with recurrent disease<sup>[11]</sup>. In our case, radiotherapy alone was insufficient to obtain therapeutic effect due to high



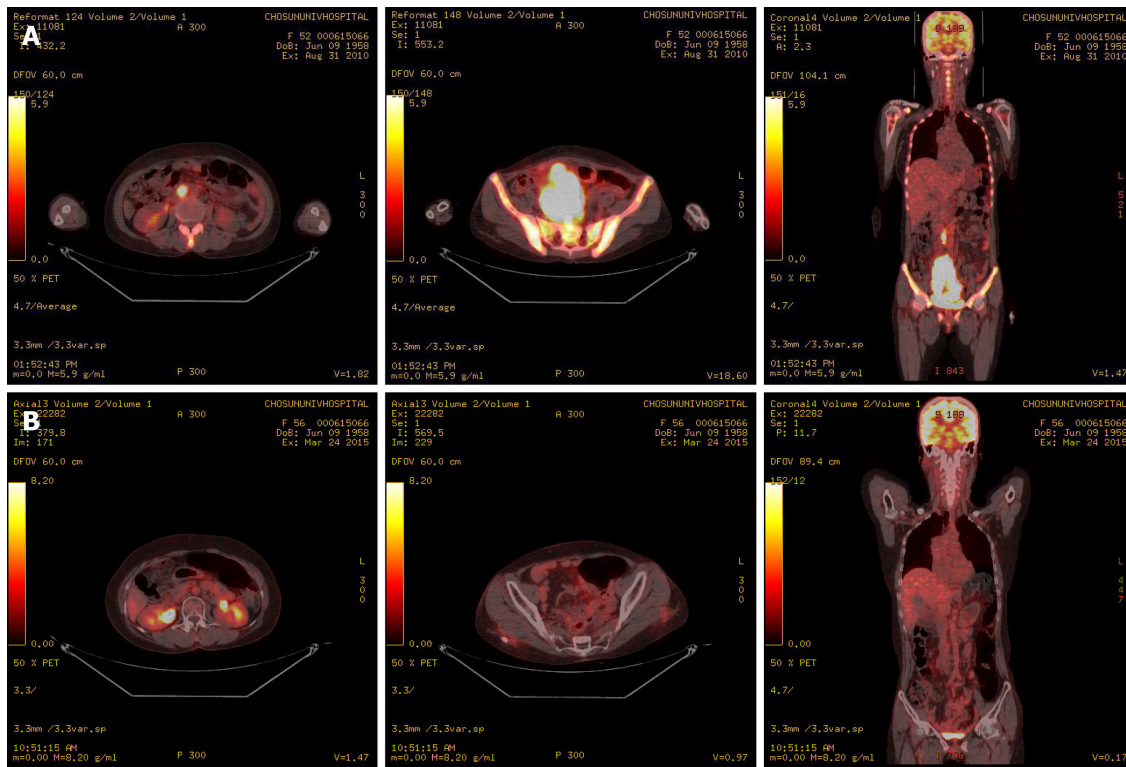
**Figure 2 Pathologic findings.** A: Tumor cell nests such as round to oval nuclei, prominent nucleoli, and many atypical mitotic figures are observed in the neutrophilic background; B and C: These cells are immunoreactive to pan-cytokeratin, but negative for vimentin (VMT) (B) and focally to VMT (C); D: Geographic necrosis is common with myxoid matrix; E: In some areas, sarcomatoid features are frequently observed; F: Tumor cells showing no organoid feature directly admixed with stromal components and were immunoreactive to VMT. CK: Cytokeratin; VMT: Vimentin.

tumor burden, and the patients at age of 52 years was relatively young to be able to tolerate the VIP chemotherapy. The patient was followed up at our outpatient department for 5 years after chemotherapy (4 cycles in 3 wk). After receiving an aggressive chemotherapy, the patient was free of the disease.

## CONCLUSION

We have successfully treated a metastatic inoperable case of ovarian undifferentiated carcinoma using high-dose combination chemotherapy. The effectiveness of the widely used chemotherapy regimen (paclitaxel and platinum) in treating inoperable ovarian undifferentiated carcinoma is uncertain. Therefore, aggressive combination chemotherapy can be used as an alternative treatment option. Moreover, ovarian undifferentiated carcinoma is a significantly rare disease with low clinical information. Thus, this case is an educational report that is considered beneficial in treating future patients.





**Figure 3 Positron emission tomography–computed tomography.** A: Positron emission tomography–computed tomography revealing hypermetabolism of the huge mass in the pelvic cavity, multiple peritoneal nodules, and para-aortic lymph nodes; B: Hypermetabolism of the huge mass in the pelvic cavity, multiple peritoneal nodules, and para-aortic lymph nodes showing improvement after chemotherapy.

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