



## Case Report

## Successful multidisciplinary treatment of uterine serous carcinoma in a patient who had previously undergone renal transplantation

I-Heng Chiu <sup>a</sup>, Wan-Jing Ho <sup>b</sup>, Ren-Chin Wu <sup>c</sup>, Angel Chao <sup>d, e, \*</sup><sup>a</sup> College of Medicine, Chang Gung University, Taoyuan, Taiwan<sup>b</sup> Department of Cardiology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan<sup>c</sup> Department of Pathology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan<sup>d</sup> Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan<sup>e</sup> Gynecologic Cancer Research Center, Chang Gung Memorial Hospital, Taiwan

## ARTICLE INFO

## Article history:

Accepted 30 September 2017

## Keywords:

Multidisciplinary approach

Renal transplant

Uterine serous carcinoma

## ABSTRACT

**Objective:** Renal transplantation is a risk factor for premalignant and malignant changes of the endometrium. Thus, prompt and aggressive treatment of postoperative complications remains a major issue. We report the case of an asymptomatic postmenopausal woman with a history of renal transplantation who underwent surgery for uterine serous carcinoma (USC).

**Case report:** An asymptomatic 59-year-old woman who had undergone renal transplantation presented with elevated serum CA-125 levels. Cancer screening revealed uterine serous carcinoma, for which she underwent total hysterectomy and bilateral salpingo-oophorectomy. Unfortunately, the postoperative course was complicated by cardiogenic shock and decompensated heart failure. The complexities of the cardiac problems and renal transplantation required a multidisciplinary approach involving different specialists. She was successfully discharged 48 days after the surgery.

**Conclusion:** Gynecologic cancer screening in asymptomatic postmenopausal women after renal transplantation is warranted. If postoperative complications occur in this population, a multidisciplinary approach is recommended.

© 2018 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Compared with the general population, renal transplantation recipients have a higher risk of malignancies [1,2], including endometrial cancer in female recipients [3]. This increased risk is due to 1) chronic immunosuppression post-transplant, 2) the presence of comorbidities (e.g., hypertension, diabetes, and overweight/obesity) that could, in turn, predispose to the malignant transformation of the endometrium, and 3) the high rates of endometrial hyperplasia in women recipients of renal transplantation [4].

While advancements in surgical techniques and perioperative care enable physicians to confidently operate on kidney transplant

recipients with a gynecological cancer, surgery in this clinical population may be complicated by the comorbidities. In this context, prompt and aggressive treatment of postoperative complications remains a major issue.

We report the case of an asymptomatic postmenopausal woman with a history of renal transplantation who underwent surgery for uterine serous carcinoma (USC). Unfortunately, the immediate postoperative course was complicated by cardiogenic shock and decompensated heart failure. The complex nature of the multi-systemic problems required a multidisciplinary approach.

## Case presentation

A 59-year-old G4P4 postmenopausal woman had undergone renal transplantation in 2007. Her comorbidities included obesity (body mass index: 33.9 kg/m<sup>2</sup>), hypertension, and type 2 diabetes mellitus. Additionally, she had a history of two-vessel coronary artery disease, severe mitral regurgitation (MR), and moderate tricuspid regurgitation (TR), for which she had received surgical treatment. She was regularly taking aspirin, candesartan,

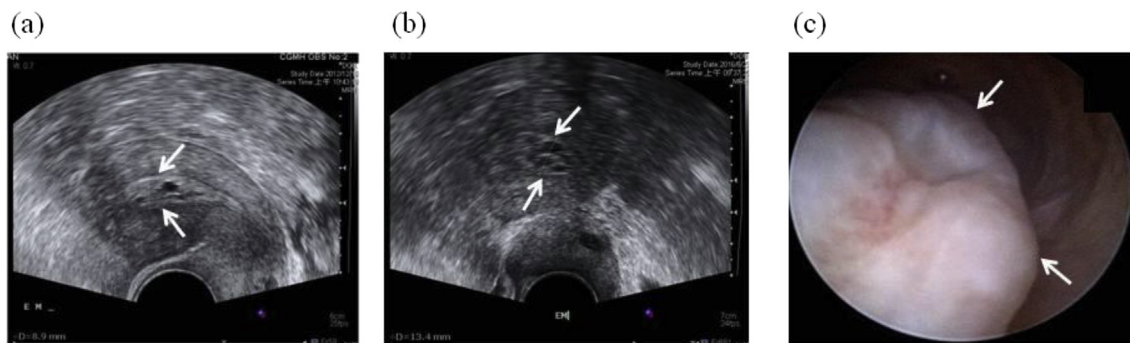
Abbreviations: USC, uterine serous carcinoma; MR, mitral regurgitation; TR, tricuspid regurgitation; LVEF, left ventricular ejection fraction; ICU, intensive care unit; CVP, central venous pressure.

\* Corresponding author. Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan.

E-mail address: [drangiechao@gmail.com](mailto:drangiechao@gmail.com) (A. Chao).

<https://doi.org/10.1016/j.tjog.2018.06.023>

1028-4559/© 2018 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



**Fig. 1.** (a) Preoperative transvaginal ultrasound showing an increased endometrial thickness (arrows), (b) which further progressed by four years (arrows). (c) A hysteroscopic examination revealed an endometrial polyp with both solid and cystic components (arrows).

carvedilol, everolimus (as of 2011), methylprednisolone, cyclosporine, and mycophenolate sodium. Her gynecological history included a thickened endometrium (0.89 cm), which was noted in 2012 (Fig. 1a), but she denied postmenopausal bleeding. During a routine cancer screening in 2016, elevated level of serum CA-125 (258.0 U/mL; reference range:  $\leq 35$  U/mL) was identified, and subsequently confirmed by serial measurements. The endometrial thickness had increased to 1.34 cm (Fig. 1b) and hysteroscopy revealed an endometrial tumor (Fig. 1c), which was successfully removed by transcervical resection. Pathological examination revealed a high-grade USC (Fig. 2a), which was immunologically positive for p53 (Fig. 2b), p16, and estrogen/progesterone receptors.

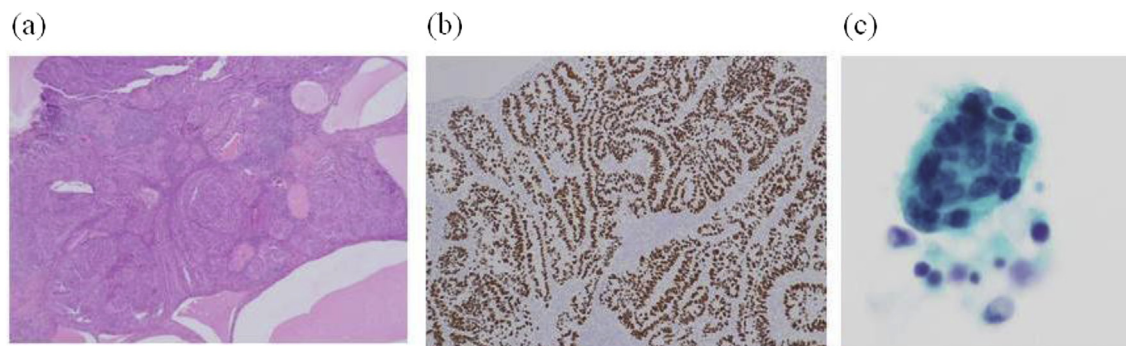
Preoperative echocardiography revealed mild MR and TR, with a left ventricular ejection fraction (LVEF) of 48% (New York Heart Association [NYHA] functional class II; Fig. 3a). Several episodes of transient hypotension (blood pressure: 64/40 mmHg) were observed intraoperatively. Total hysterectomy with bilateral salpingo-oophorectomy was performed. Final pathology revealed no residual tumor. However, cytology of the ascitic fluid revealed clusters of malignant cells (Fig. 2c). *TP53* p.C277F and *BUC1B* p.R550\* were later detected in a genetic test (Comprehensive Cancer Panel, <http://www.actgenomics.com>) with copy number loss of *MRE11A*, *ATM*, *CHEK1*, *BLM*, *TP53*, *FLCN*, and *NF1*.

After the surgery, the patient was transferred to the intensive care unit (ICU), where she developed lethargy, dyspnea with shallow breathing (15–17/min), and oliguria. On the second postoperative day, she was febrile (38.3 °C) and her central venous pressure (CVP) was 26 mmHg. Laboratory analyses showed mild normocytic anemia (hemoglobin: 11.4 g/dL), increased serum creatinine (1.73 mg/dL), hypercapnia, and pyuria. Chest X-ray

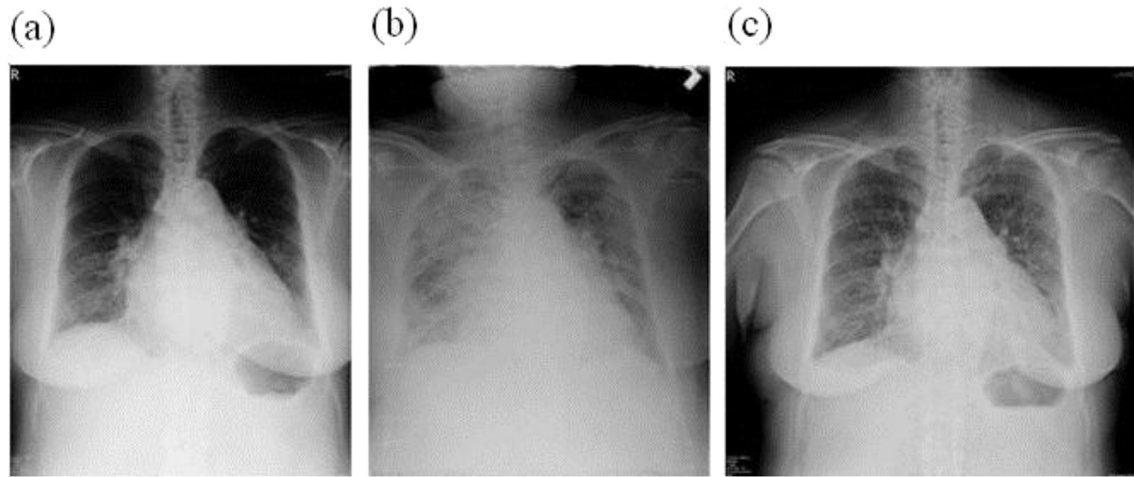
revealed pulmonary edema. Electrocardiogram revealed atrial fibrillation with rapid ventricular response and occasional premature ventricular contractions. Global hypokinesia with LVEF of 41% was evident on echocardiography; the blood pressure dropped to 80/50 mmHg and the patient was diagnosed with cardiogenic shock.

In view of the complex history, a multidisciplinary approach was implemented for her care. The cardiac surgeon prescribed norepinephrine and amiodarone for hypotension and tachycardia. Antibiotic therapy with meropenem and teicoplanin was started according to the nephrologist's suggestion, whereas oliguria and elevated CVP were treated with furosemide (40 mg/day). Bi-level positive airway pressure followed by oxygen via nasal cannula (3 L/min) was used to treat dyspnea. In the following days, the blood pressure improved and norepinephrine was tapered off. Serum creatinine gradually returned to normal values.

After a week, the acute cardiogenic shock had resolved and the patient was transferred to the gynecological ward. During her stay, fluid overload, persistent dyspnea, and pedal edema were observed. A cardiologist was consulted for the decompensated heart failure with pulmonary edema (Fig. 3b). Follow-up echocardiography revealed biventricular systolic failure (LVEF = 31%), moderate MR and TR, and pulmonary hypertension (estimated systolic pulmonary artery pressure = 111 mmHg). Therefore, the dosage of furosemide was increased to 80 mg/day, and candesartan and spironolactone were added. Water and salt restriction was strictly enforced. Thereafter, a favorable response was noted in terms of gradual resolution of pedal edema and dyspnea along with increased urine output. Postoperatively, the patient lost 6 kg in body weight and was discharged 48 days later. Home oxygenation



**Fig. 2.** (a) Photomicrograph (4 × magnification) of hematoxylin and eosin-stained section showing a small focus of serous carcinoma arising in an endometrial polyp with cystically dilated glands. (b) The tumor was characterized by a diffuse and intense p53 immunostaining. (c) Peritoneal washing cytology revealed three-dimensional clusters of tumor cells with severe nuclear pleomorphism.



**Fig. 3.** (a) A preoperative chest X-ray revealed cardiomegaly accompanied by bilateral peribronchial infiltration in the lower lungs. (b) Worsening clinical conditions accompanied by decompensated heart failure and pulmonary edema. (c) Significant improvement of bilateral perihilar opacities two months after surgery.

was required to prevent oxygen desaturation. A follow-up chest X-ray performed a month after she was discharged confirmed improvement of pulmonary edema (Fig. 3b). Based on the genetic tests, everolimus, an immunosuppressant [1], was also used as anticancer therapy for her copy number loss of *FLCN* and *NF1*. Letrozole was prescribed for the positive estrogen and progesterone receptors.

## Discussion

The complex case reported here suggests that 1) women recipients of renal transplantation should be regularly screened for gynecological malignancies, and 2) a multidisciplinary approach is recommended to treat the postoperative complications that may occur in this group of patients following surgical treatment for gynecological malignancies. Specifically, the care for our patient involved gynecologic oncologists, cardiac surgeons, nephrologists, cardiologists, pulmonologists, and ICU specialists [5].

With an increased incidence of endometrial abnormalities in immunosuppressed women after renal transplant, more frequent gynecologic examinations for early diagnosis and treatment of premalignant and malignant transformation of the endometrium is recommended [3]. Asymptomatic patients with suspicious endometrial thickening should alert physicians about the possibility of gynecologic cancer. Additionally, serial measurements of serum CA-125 in postmenopausal women could be useful in identifying occult early-staged cancer [6]. Confirmation of increased concentrations of this tumor marker in this patient without any other known etiology was the clue in diagnosing endometrial cancer.

When a malignancy is diagnosed, careful planning before, during, and after the surgery is crucial for the best clinical outcomes. Owing to the high frequency of cardiovascular complications in renal transplant recipients [7] and unstable intraoperative hemodynamic conditions, bilateral pelvic lymphadenectomy, para-aortic lymphadenectomy, and complete omentectomy were not performed. Despite the best efforts to avoid cardiac complications, they can inevitably occur in high-risk individuals. Notably, our patient had a positive history of coronary artery disease, valvular heart disease, and depressed left ventricular function preoperatively. Unfortunately, but not unexpectedly, she developed cardiogenic shock post-operatively, which required immediate multidisciplinary approach involving the expertise of different medical specialists.

The patient subsequently developed congestive heart failure in the gynecological ward despite resolution of acute cardiogenic shock. An accurate diagnosis and optimized treatment options stemming from the multidisciplinary approach were essential in achieving hemodynamic stabilization. Our main goals were to correct the precipitating factors (i.e., anemia, infection, and pain), as well as strictly enforce optimal drug therapy and sodium restriction [8]. Appropriate medications such as loop diuretics, angiotensin converting enzyme inhibitors/angiotensin II receptor blockers, and aldosterone receptor antagonist are important [7].

## Conclusions

Our case illustrates the importance of screening for gynecological malignancies in female recipients of renal transplantation. Asymptomatic postmenopausal patients with increased CA-125 levels should alert physicians about the possibility of gynecologic cancer. A multidisciplinary approach is required when renal transplant recipients with gynecological malignancies develop post-surgical complications.

## Conflict of interests

All authors declare no competing interests.

## Authors' contributions

IHC, WJH, RCW, AC: preparation of the manuscript; WJH, AC: patient care. All authors have read and approved the final manuscript.

## Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

## Funding

The genomic study of this case was supported by Chang Gung Medical Foundation (CMRPG3E0393).

### Ethics approval

This report was approved by the Institution Review Board of Chang Gung Memorial Hospital (No. 201700204B0).

### Availability of data and material

Not applicable.

### Acknowledgements

The authors are grateful to the members of the ICU and the department of Gynecologic Oncology. We also acknowledge Drs. Anne Chao, Feng-Chun Tsai, and Ping-Chin Lai for their dedication to providing clinical care to the patient.

### References

- [1] Kapoor A. Malignancy in kidney transplant recipients. *Drugs* 2008;68(Suppl 1):11–9.
- [2] Rama I, Grinyo JM. Malignancy after renal transplantation: the role of immunosuppression. *Nat Rev Nephrol* 2010;6:511–9.
- [3] Husslein H, Breitenecker G, Tatra G. Premalignant and malignant uterine changes in immunosuppressed renal transplant recipients. *Acta Obstet Gynecol Scand* 1978;57:73–8.
- [4] Bobrowska K, Kaminski P, Cyganek A, Pietrzak B, Jabiry-Zieniewicz Z, Durlik M, et al. High rate of endometrial hyperplasia in renal transplanted women. *Transplant Proc* 2006;38:177–9.
- [5] Parsons SK, Fineberg IC, Lin M, Singer M, Tang M, Erban JK. Promoting high-quality cancer care and equity through disciplinary diversity in team composition. *J Oncol Pract* 2016;12:1141–7.
- [6] Takami M, Sakamoto H, Ohtani K, Takami T, Satoh K. An evaluation of CA125 levels in 291 normal postmenopausal and 20 endometrial adenocarcinoma-bearing women before and after surgery. *Cancer Lett* 1997;121:69–72.
- [7] Svensson M, Jardine A, Fellstrom B, Holdaas H. Prevention of cardiovascular disease after renal transplantation. *Curr Opin Organ Transplant* 2012;17:393–400.
- [8] Shiralil AC, Bia MJ. Management of cardiovascular disease in renal transplant recipients. *Clin J Am Soc Nephrol* 2008;3:491–504.