Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

An unusual uterine papillary serous carcinoma with post therapy disseminating metastasis presenting as primary renal malignancy: a case report

Kuang-Ting Liu, MT, MS[a,b], Yueh-Ching Chang, MT, MS[a,b], Yu-Chieh Lin, MD[a,d], Junn-Liang Chang, MD, PhD[a,c,d,*]

Introduction: Uterine papillary serous carcinoma (UPSC) is a highly aggressive endometrial carcinoma that often presents as a high-stage disease. UPSC has a high propensity for metastasis and recurrence, even with little or no myometrial invasion. It usually metastasizes to the pelvis, retroperitoneal lymph nodes, upper abdomen, or peritoneum. However, renal metastasis of UPSC is extremely rare.

Case presentation: The authors reported a unique UPSC case in a 75-year-old unmarried woman. Twenty years ago, she had a history of right breast cancer and underwent a modified radical mastectomy. Three years ago, she was diagnosed with endometrial carcinoma, and six courses of chemotherapy and radiotherapy were administered. Computed tomography and retrograde pyelography revealed a right renal pelvic tumor, and a right nephroureterectomy was performed. Renal metastatic UPSC was diagnosed. The patient was administered adjuvant chemotherapy.

Clinical discussion: Metastatic UPSCs initially presenting at distant sites are uncommon manifestations. This tumor should be differentially diagnosed in patients presenting with metastatic high-grade serous papillary carcinoma of unknown primary origin.

Conclusion: Diagnosing metastatic renal UPSC, based on preoperative and imaging examinations, is often challenging. Thus, a review of the past history, histopathology, and immunohistochemical evaluation plays a crucial and valuable role in the definite and differential diagnosis of this tumor type.

Keywords endometrial carcinoma, immunohistochemical, nephroureterectomy, papillary serous carcinoma, pyelography

Introduction

Endometrial cancer is the most common gynecological malignancy and the second leading cause of gynecological cancer-related death[1]. Endometrial cancers are divided into two types. Type I tumors (80–90%), which are primarily endometrioid adenocarcinomas. Endometrioid adenocarcinoma is a morphologically heterogeneous group of tumors. Type II tumors are less common and include clear and serous cell types[1–3]. Uterine papillary serous carcinoma (UPSC) was first described by Hendrickson *et al.*[1] in 1982 as a highly aggressive malignant endometrial cancer. Even with little or no myometrial invasion, UPSC has a high propensity for recurrence and metastasis[4].

Tumor metastasis is a sequential process comprising shedding, adhesion, infiltration, migration, and finally proliferation of primary tumor-derived and circulating malignant cells in competent organs leading to colonization[5]. Renal metastases from gynecological malignancies are uncommon, with only a few reported cases[2,5]. UPSCs usually metastasize to the pericardium, abdominal wall, skin, brain, lung, adrenal glands[1–3,5,6], and pelvic lymph nodes. Metastases to the synchronous right renal and paraaortic lymph nodes[2], as well as to the ureter[5] are rare. Here, we report the case of a 75-year-old unmarried woman with UPSC and highlight the future studies investigating the incidence, histopathology, and outcomes of patients with advanced UPSC renal

HIGHLIGHTS

- Renal metastases from gynecological malignancies are unusually with only a few reported cases.
- Disseminating metastasis of patient with metastatic uterine papillary serous carcinoma (UPSC) is extremely rare in this subtype, and poor prognosis.
- The advanced UPSC renal metastases should be further evaluated and may help optimize the treatment of these patients.
- The final diagnosing metastatic UPSC must be obtained by resection of the tumor and compared with primary neoplasm through the pathologic and immunohistochemical examination.

[a]Department of Pathology and Laboratory Medicine, Taoyuan Armed Forces General Hospital, [b]Hsin Sheng Junior College of Medical Care and Management, [c]Department of Biomedical Engineering, Ming Chuan University, Taoyuaan City and [d]Department of Pathology, Tri-Service General Hospital, National Defense Medical Center, Taipei City, Taiwan

Kuang-Ting Liu and Yueh-Ching Chang contributed equally to this work.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Pathology and Laboratory Medicine, Taoyuan Armed Forces General Hospital, No.168, Zhongxing Rd., Longtan Dist., Taoyuan City 32551, Taiwan. Tel.: +886 34 799 595 extent 325571, fax: 886 34 809 946. E-mail: junn9liang@yahoo.com.tw (J.L. Chang).

Annals of Medicine & Surgery (2024) 86:456–462

Received 28 September 2023; Accepted 21 November 2023

Published online 4 January 2024

http://dx.doi.org/10.1097/MS9.0000000000001574

metastases may help optimize the treatment of these patients. This case report has been reported in accordance with the Surgical CAse REport (SCARE) 2020 criteria[7].

Case presentation

We present the case of a 75-year-old unmarried woman with endometrial cancer, diagnosed after hysterectomy and bilateral salpingectomy with lymph node dissection. Approximately 20 years ago, the patient presented with right breast cancer after a modified radical mastectomy with adjuvant radiotherapy. Three years ago, the patient received six scheduled chemotherapeutic regimens and radiotherapeutic courses. She presented with hematuria for 2 weeks and was admitted for further evaluation.

Upon admission, the patient's vital signs were as follows: body temperature, 37.4°C; pulse rate, 190/min; respiratory rate, 16/min; and blood pressure, 128/80 mmHg. The patient had no family history of cancer. Moreover, there was no relevant family history, including any relevant genetic or psychosocial history. She denied any history of alcoholic beverage consumption or drug abuse. In addition, she did not report drug allergies, adverse reactions, or addictions. The patient did not report any coronavirus disease 2019 (COVID-19) symptoms. In the past 3 months, the patient did not chew betel nut, smoke, work, or travel. The patient had type 2 diabetes mellitus and arrhythmia for several years and was receiving the appropriate medical treatment. She had a history of endometrial endometrioid adenocarcinoma diagnosed after staging surgery. The retroperitoneal fluid cytology results were negative for malignant cells. She had completely received the sixth course of chemotherapy (C/T) and radiotherapy (R/T).

A review of previous MRI of the uterus revealed a heterogenous enhancing lesion (5.1 × 5.1 cm) in the anterior right lateral wall of the endometrium body and fundus, with myometrium invasion extending to greater than 50% (Fig. 1). Therefore, endometrial cancer was suspected. The CT scan revealed a soft-tissue mass in the right renal pelvis. Therefore, urothelial carcinoma of the right renal pelvis was suspected. Both ovaries were unremarkable. The patient underwent a staging laparotomy. The pathological report revealed endometrial UPSC (Fig. 2) with right pelvic, right common iliac, and left para-aortic regional lymph node metastases. The eighth edition of the American Joint Committee on Cancer (AJCC) tumor, node, and metastasis (TNM) staging system was used for the diagnosis of pT1bN2aMx, stage III C2.

Six months postsurgery, the patient had palpable subcutaneous soft-tissue masses over the left supraclavicular and enlarged axillary lymph nodes. She visited our General Surgery Outpatient Division for assistance. The position emission tomography (PET) scan revealed multiple left supraclavicular, left axillary, and right hilar lymphadenopathies with a maximal standardized uptake valve greater than 5.2. Ultrasonography of the thyroid, with fine-needle aspiration cytology, was negative for malignant cells, and multiple goiters were observed. The patient was admitted for further evaluation. A left axillary lymph node excisional biopsy was performed. The final pathological diagnosis was a metastatic papillary serous carcinoma (Fig. 3A). Subsequently, an excisional biopsy of the left supraclavicular subcutaneous mass was performed, and metastatic adenocarcinoma was diagnosed (Fig. 3B).

Upon admission, CT of the abdomen and pelvis revealed a low-attenuation lesion in the right lower pole of the kidney (approximately 2.5 × 2 cm), suggestive of a primary renal neoplasm. We suspected that the right renal lesion was a second primary lesion. Urinalysis and ureteroscopic cytology revealed suspicious malignant cells. Urothelial neoplasm with malignant transformation was considered.

A complete hematological blood count revealed mild leukocytosis with neutrophilia and a normal lymphocyte count: hemoglobin, 10 g/dl (normal 14–18); hematocrit, 32.8% (normal 42–52); white blood cell, 5.29 × 103 μ/l (normal 4.8–10.8); and lymphocytes, 17.2% (normal 19–48). Biochemical analysis revealed a glucose level of 140 mg/dl (normal 70–110) and hemoglobin A1c (HbA1c, or A1C) was 6.5 (normal range, 4.0–6.0%). Urine analysis: red blood cells (RBCs), >20/HPF (high power field, normal reference interval, <2/HPF). The serum biomarker levels were as follows: CA153 (cancer antigen 153) at

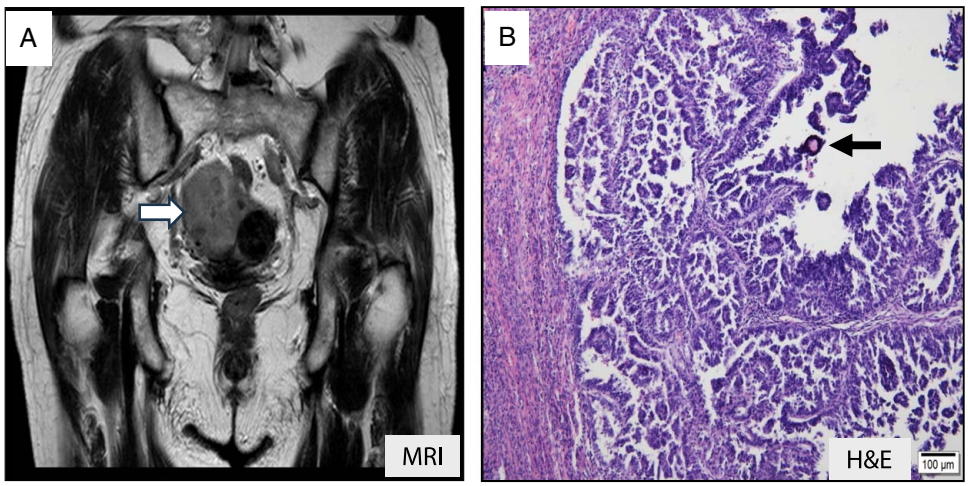

Figure 1. MRI of uterus shows a heterogenous enhancing lesion at anterior right lateral wall of endometrium of body and fundus, with invasion of myometrium (A). (B). Photographs of the uterine papillary serous carcinoma illustrate uterine endometrial papillary serous carcinoma with focal psammoma body (whitish arrow), (H&E, original magnification × 100).

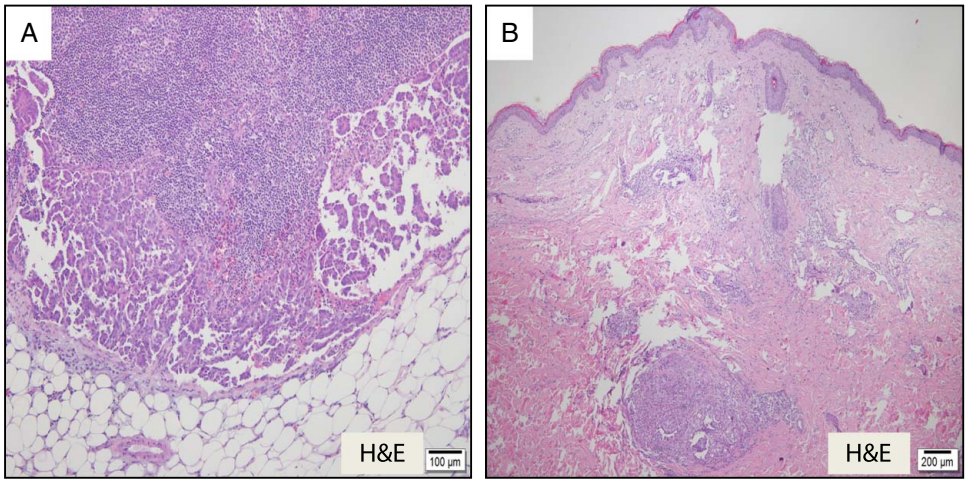

Figure 2. Photographs demonstrate the metastatic uterine papillary serous carcinoma of the left axillary lymph node (A, H&E stain, original magnification × 100), and the left supraclavicular cutaneous (B, H&E stain, original magnification × 40).

74 U/ml (normal <32.4) and CA-125 (cancer antigen 125) at 107 U/ml (normal <35). Serological evaluations for human immunodeficiency virus (HIV, evaluated via enzyme-linked immunosorbent assay or western blotting), hepatitis C virus (evaluated by serologic studies or polymerase chain reaction (PCR)), Epstein–Barr virus (evaluated by PCR), and COVID-19 (evaluated by PCR) were negative. An abdominal CT scan revealed a mass in the right pelvis (Fig. 4). Ureteroscopy with RP revealed a deviation of the right ureter in the M/3 portion. No lesions were observed in the L/3 ureters. The right RP showed a filling defect in the right renal pelvis and medial deviation of the right ureter. Urine cytology, of cells collected from the right-sided ureter, was also positive for malignancy. Subsequently, she underwent a right nephroureterectomy, performed by a senior attending physician in the genitourinary division. The postoperative period was uneventful and there were no complications.

A gross examination of the right kidney nephroureterectomy was performed using a $10 \times 5 \times 5$ cm ureter ($10 \times 0.5 \times 0.5$ cm), weighing 200 g in total. The sections showed a protruding papillary semisolid spongiform mass ($3.5 \times 2 \times 2$ cm) over the upper and renal pelvis with homogeneous light yellow with multifocal hemorrhage and necrosis (Fig. 5). The right ureter was nonremarkable.

Histopathologic and microscopic examination of both portions of the pelvic tumor masses revealed marked papilla infiltration with or without appreciable fibrovascular cores; a micropapillary pattern was observed. Slit-like and gland-like spaces were also observed. Solid growth was also observed in the psammoma (Fig. 6A). The cytoplasm is usually scant but can be abundant in eosinophils. The tumor cells exhibited a discohesive pattern. Nuclei were typically high-grade with pleomorphism, hyperchromasia, prominent nucleoli, and frequent abnormal mitotic figures (Fig. 6B). In addition, the tumor cells invaded the hilum, peripelvic soft-tissue, renal capsule, and focal lympho-

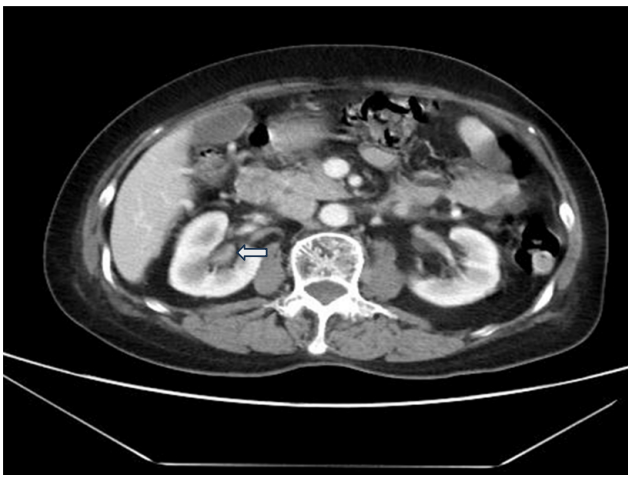

Figure 3. Computed tomography of the abdomen and pelvis displays a soft-tissue mass in the right renal pelvis (whitish arrow).

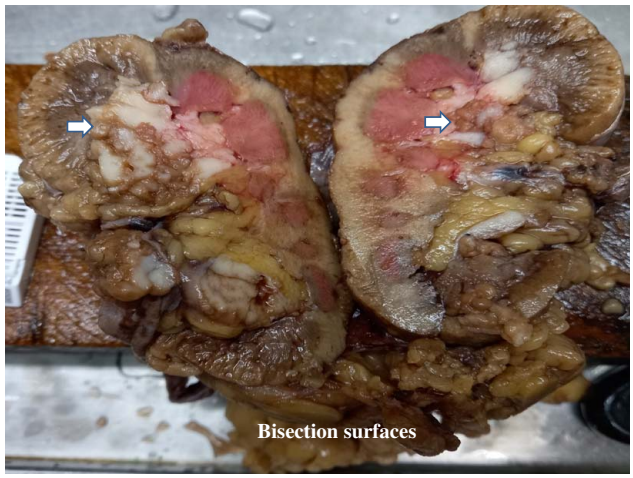

Figure 4. Photograph of bisected right kidney reveals a papillary semisolid spongiform mass (whitish arrows) over the upper portion of the pelvis with homogeneous gray-light to yellowish color with multifocal hemorrhage and necrosis.

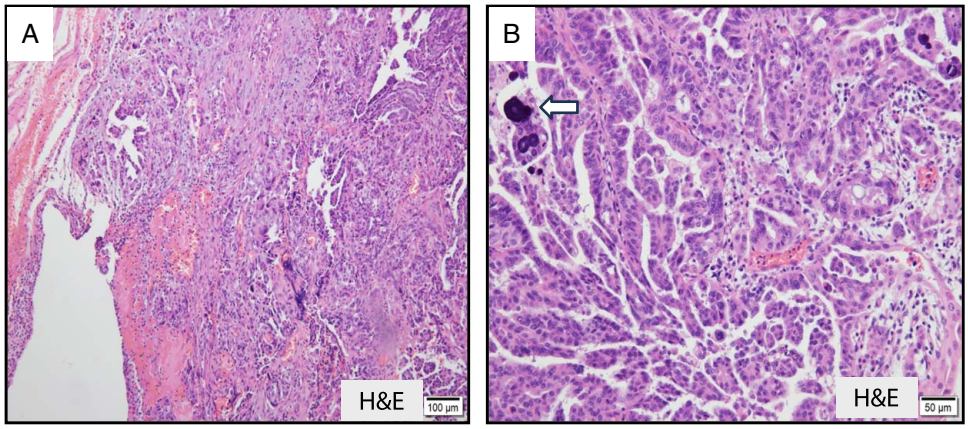

Figure 5. Photographs of metastatic uterine papillary serous carcinoma of the right kidney illustrate the predominance architectures, marked papillary, micropapillary pattern with psammoma bodies (A, H&E stain, original magnification ×100). Nuclei are typically high-grade with pleomorphism, hyperchromatic, prominent nucleoli with focal psammoma body (whitish arrow) (B, H&E, original magnification ×200).

vascular space invasion (LVI), and no evidence of renal parenchymal invasion was found.

Differential diagnoses included invasive papillary urothelial carcinoma, papillary renal cell carcinoma, endometrial endometrioid adenocarcinoma, endometrioid clear cell adenocarcinoma, and mixed carcinoma (endometrioid adenocarcinoma and serous carcinoma).

Subsequent IHC staining analysis demonstrated that neoplastic cells were positive for CK7, PAX8 (strong nuclear staining), CD10 for spindle stromal component (Fig. 6A-C), p16, Her2/neu (DARKO scoring, 2+, equivocal staining), CK18, and focal for CEA. ER and PR expression was downregulated. The Ki-67 labeling index was ~80–90% in affected tumor cells (Fig. 6D). CD31, CD34, and actin expression indicated LVI. In addition, CK20, p53 ('null type' pattern), vimentin, c-Kit (CD117), racemase (AMACR), carbonic anhydrase IX/CA9, GATA-3, TTF1, GCDFP-15, and WT1 immunostaining results were negative in the tumor cells. Microsatellite instability was assessed and MLH1, MSH2, and MSH6 gene expression was stable. Histopathological and IHC examinations suggested advanced

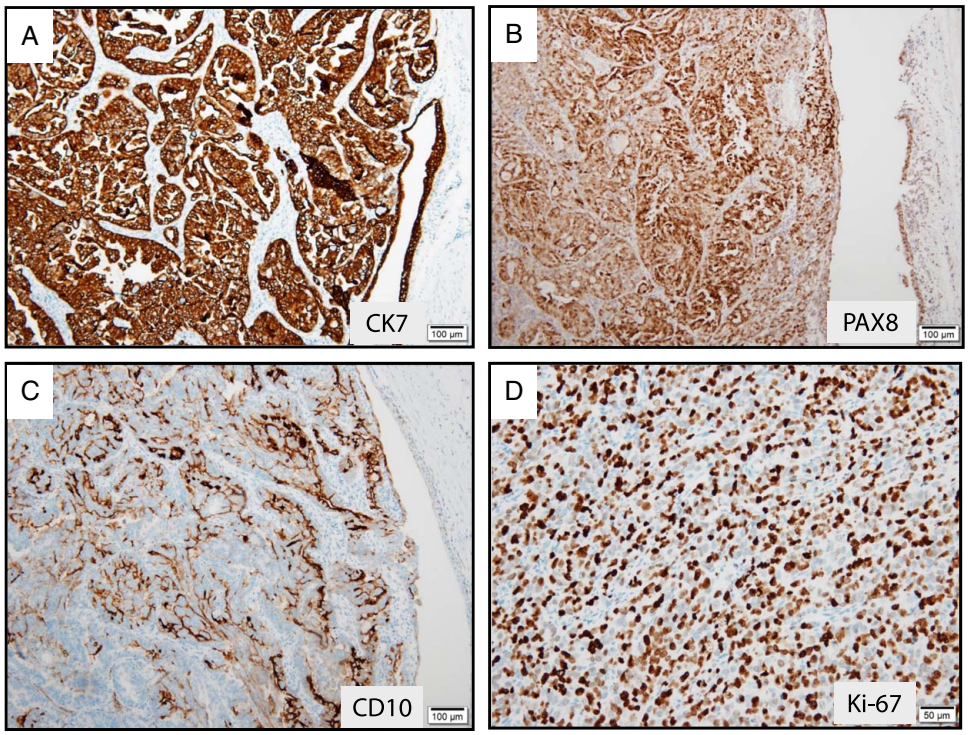

Figure 6. Photographs of immunohistochemical (IHC) analysis of renal metastatic uterine papillary serous carcinoma demonstrate diffusely positive for CK7 (A, IHC, original magnification ×200), strongly nuclear staining for PAX8 (B, IHC, original magnification ×200), CD10 for spindle stromal components (C, IHC, original magnification ×200), and a proliferative Ki-67 labeling index activity in ~80–90% of cancer cells (D, IHC, original magnification ×200).

endometrial UPSC with left axillary lymph node, left supraclavicular cutaneous and right renal metastases. The pathological TNM stage, based on AJCC, was ypT4N2bM1, stage IV, (an additional reference for primary UPSC (pT1bN2a, stage IIIC, reference March 2019)). High-grade papillary serous carcinomas with psammoma bodies that metastasized to the axillary lymph nodes and cutaneous neck was considered. Endometrial sampling confirmed the presence of a primary UPSC.

The patient recovered uneventfully after surgery. She continued to receive further treatment with six courses of adjuvant chemotherapy. Currently, the patient's living conditions are normal. Written informed consent was obtained from the patient. UPSC is an aggressive variant of endometrial cancer that is associated with a high recurrence rate and poor prognosis. Long-term follow-up is required because of the possibility of late metastases[3], as in the present case. The patient completed six courses of chemotherapy following surgery. Unfortunately, multiple metastases to the lungs were found in follow-up imaging. The patient died of multiple organ failure 6 months after surgery.

Discussion

UPSC is a rare uterine endometrial cancer. It tends to occur in postmenopausal women, with a median age of 62 years, which is higher than the reported median age of women with endometrioid carcinoma. UPSC represents ~10% of all uterine cancer cases; however, UPSC accounts for greater than 50% of the relapses and 40% of endometrial cancer deaths[1–6]. UPSC is a highly aggressive malignant endometrial cancer with a high propensity for metastasis and recurrence even when there is minimal or no myometrial invasion[1,3]. Approximately 60–70% of patients with UPSC present with disease outside the uterus[1,3]. However, metastasis into distal axillary lymph nodes, cutaneous, and kidney metastases from UPSC is extremely rare, as in the present case.

Renal metastasis from UPSC has not yet been characterized. Only a limited number of studies have postulated endometrial carcinoma metastasis to the kidney or ureter[2,5]. Upper urinary tract involvement in endometrial cancer is rare and most often manifests as renal parenchymal metastasis. Cochrane *et al.*[5] described a case in which a synchronous renal parenchymal lesion with no ureteral involvement was found simultaneously with primary serous endometrial carcinoma. In addition, a case of recurrent upper urinary tract endometrioid carcinoma, 11 years after hysterectomy for uterine cancer, was reported[2,5].

Previously, the spread of serous endometrial cancer was similar to that of serous ovarian cancer, which most often spread through exfoliative malignant cells via LVI[1,2]. Upper urinary tract tumors, detected by staging or surveillance imaging, are generally considered primary renal malignancies because urinary tract metastases are rare[5]. In the present case, a second primary renal malignancy was diagnosed. This finding is unique because most metastases to the upper urinary tract appear as solitary lesions in the renal parenchyma[1,3,5].

To the best of our knowledge, this is the first report of a known case of UPSC entry into the upper urinary tract and urine cytology of all suspected primary renal malignancies. This case was consistent with previous reports, and the possibility of hematogenous seeding was considered[1,5]. The final diagnosis of Stage III C2 (reference as 8th edited AJCC pT1bN2a), a high-grade papillary serous carcinoma of the endometrium with diagnostic pathology, was consistent with metastatic uterine papillary serous endometrial cancer of the right kidney. The patient has also completed the six C/T and R/T cycles after surgery.

Metastatic UPSC is difficult to distinguish from metastatic ovarian serous carcinomas. In the present case, histopathological findings of the surgically removed ovary specimen were negative. The histopathological findings of metastatic renal lesions demonstrated a pattern similar to that of UPSC. A differential diagnosis was made based on the IHC method or molecular pathology, which suggested that the renal lesion was metastatic UPSC[1]. UPSC typically have a papillary growth pattern with tufted stratification and, on occasion, a hobnail configuration. It also exhibits a high degree of cytological anaplasia[1,2,5,8,9]. Psammoma bodies are found in 60% of UPSC, similar to that observed in the reported patient; however, their absence does not rule out the possibility of UPSC. Tumor necrosis and LVI are common as our case. The pattern of UPSC spread via LVI is prominent[1–3,5].

It was previously suggested that UPSC are characterized by p53 gene mutations, p16 gene inactivation, low E-cadherin expression, and human epidermal growth factor receptor 2 overexpression[1,4]. In addition, HER2 with IHC expression and gene amplification in p53-aberrant high-grade endometrial endometrioid carcinoma suggested that this population may benefit from HER2 testing and targeted therapy[10,11]. The p53 overexpression correlates with decreased survival of patients with UPSC[12]. And p53 mutation staining is strong and diffuse completely absent ('null type' pattern; as observed in the current case) or aberrant (exhibiting distinct abnormal cytoplasmic localization). p16 expression is usually strong and diffuse (not associated with Human Papillomavirus (HPV infection). Cytokeratin AE1/AE3 and CK7 showed strong membrane staining. The developmental transcription factor PAX8 is expressed strongly by nuclear staining in nearly 100% of USPCs. MLH1, MSH1, MSH2, and MSH6 are typically preserved[13–15], as observed in the present case. The tumor marker CA-125 was significantly upregulated in the current case.

After surgery, UPSC is managed with R/T, C/T, or both. To reduce the risk of recurrence and prolong survival, it is recommended that patients with UPSC receive multimodal therapeutic strategies consisting of postoperative adjuvant R/T and C/T[16]. Surgery is the initial step in the treatment of both early-(for comprehensive staging) and advanced-stage disease (as a debulking procedure). As metastases occur even in the absence of myometrial invasion or LVI, patients should undergo comprehensive surgical staging.

Prognostic factors are typically regarded as aggressive subtypes of endometrial cancer. Recent data indicates up to 80% survival of patients with small low-stage tumors[2]. Because stage is the strongest prognostic variable, careful surgical staging is important for predicting UPSC prognosis. CT and 2-deoxy-[fluorine-18] fluoro-D-glucose integrated with computed tomography are widely used for surveillance after surgery[1,2,5,6,17]. The patient in this study underwent hysterectomy with bilateral oophorectomy for UPSC, 3 years ago, and completed the course of chemotherapy. Unfortunately, left axillary lymph node and supraclavicular cutaneous metastases and hematuria developed 2 years later. Unfortunately, the patient died of multiple organ failure 6 months after surgery. This case also highlights the aggressive behavior of this UPSC variant.

Limitations of the study related to this article include that UPSC with renal metastasis is extremely rare and a rather poor prognosis. Diagnosis relies on relevant tumor marker detection and imaging study. The cross-multidisciplinary team for precision medicine therapy must use the pathological tissue morphology of surgical resection to make relevant differential diagnosis, and must also rely on molecular pathology and IHC analysis to make the final diagnosis. This is characteristic of this case report and demonstrates the limitations and complexities of pathological diagnosis and treatment.

Conclusion

Metastatic renal disease caused by UPSC is extremely rare and aggressive variant of endometrial cancer that is associated with a high recurrence rate and poor prognosis. However, despite the rare occurrence of this histopathology, the presence of a renal mass on imaging and possible lymph node involvement requires increased awareness and further investigation. Future studies investigating the incidence and outcomes of patients with advanced UPSC renal metastases may help optimize the treatment of these patients.

Ethical approval

The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee. This study was approved by the Institutional Review Board (IRB) of the Tri-Service General Hospital (TSGH), National Defense Medical Center. The reference number for their IRB approval is TSGHIRB: B202315137.

Informed consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

This study was supported by grants from TYAFGH-A-112011 and TYAFGH-A-112014, Taoyuan Armed Forces General Hospital, Taoyuan, Taiwan.

Author contribution

J.-L.C.: drafting manuscript review, corresponding author, data interpretation, evaluation, information acquisition, and final approval; K.-T.L.: responsible for operating pathological tissue/specimen processing, information acquisition and final approval, concept and design, critical review and final approval; Y.-C.C.: responsible for operating pathological tissue sections, special chemical staining and immunohistochemical staining, information acquisition, critical review, and final approval; Y.-C.L.: responsible for information acquisition and final approval, concept and design, critical review, and final approval.

Conflicts of interest disclosure

The authors have no conflicts of interest to declare.

Research registration unique identifying number (UIN)

This paper is a case report; there was no registration. The datasets in this article are available in the Department of pathology and Laboratory Medicine database, upon request, from the corresponding author.

Guarantor

Junn-Liang Chang.

Data availability statement

Not applicable to this article.

Provenance and peer review

Not commissioned, externally peer reviewed.

Acknowledgements

The authors like to thank Dr Yen-Lin Chen, Department of Radiology, for providing the medical images and explanations of the present case. The authors also like to thank to Dr Zheng-Lia Gao, Department of Surgery, for explaining the intraoperative findings. The authors are also grateful to Mei-Ling Li, medical laboratory technician, for assisting in pathological sectioning and processing IHC and histochemical staining.

References

[1] Hendrickson M, Ross J, Eifel P, *et al*. Uterine papillary serous carcinoma: a highly malignant form of endometrial adenocarcinoma. Am J Surg Pathol 1982;6:93–108.
[2] Cochrane E, Menzies A, Sweeney K, *et al*. Synchronous renal and paraaortic metastasis in a uterine serous carcinoma: a case review and clinical considerations. Gynecol Oncol Rep 2019;28:12–4.
[3] Zhang L, Kwan SY, Wong KK, *et al*. Pathogenesis and clinical management of uterine serous carcinoma. Cancers (Basel) 2020;12:686–707.
[4] Bokhman JV. Two pathogenetic types of endometrial carcinoma. Gynecol Oncol 1983;15:10–7.
[5] Sahl JW, Bachman AG, Nam GH, *et al*. Metastatic serous endometrial carcinoma to the ureter. Urol Case Rep 2021;39:101776–7.
[6] Perna S, Peroni G, Miccono A, *et al*. Multidimensional effects of soy isoflavone by food or supplements in menopause women: a systematic review and bibliometric analysis. Nat Prod Commun 2016;11:1733–40.
[7] Agha RA, Franchi T, Sohrabi C, *et al*. SCARE Group. The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines.. Int J Surg 2020;84:226–30.
[8] Tsurumaki Y, Kume H, Homma Y. Late recurrence of uterine endometrioid carcinoma in the upper urinary tract. Gynecol Obstet 2009;280:631–2.
[9] Cazacu SM, SAndulescu LD, Mitroi G, *et al*. Metastases to the kidney: a case report and review of the literature. Curr Health Sci J 2020;46:80–9.
[10] Naumann RW. Uterine papillary serous carcinoma: state of the state. Curr Oncol Rep 2008;10:505–11.
[11] Mentrikoski MJ, Stoler MH. HER2 immunohistochemistry significantly overestimates HER2 amplification in uterine papillary serous carcinomas. Am J Surg Pathol 2014;38:844–51.
[12] Joehlin-Price AS, Komforti MK, Ladwig NR, *et al*. HER2 IHC expression and gene amplification in p53-aberrant high-grade endometrial

endometrioid carcinoma suggests that this population may benefit from HER2 testing and targeted therapy. Am J Surg Pathol 2023;47:580–8.
[13] King SA, Adas AA, LiVolsi VA, *et al*. Expression and mutation analysis of the p53 gene in uterine papillary serous carcinoma. Cancer 1995;75: 2700–5.
[14] Demopoulos RI, Mesia AF, Mittal K, *et al*. Immunohistochemical comparison of uterine papillary serous and papillary endometrioid carcinoma: clues to pathogenesis. Int J Gynecol Pathol 1999;18: 233–7.
[15] Fares B, Berger L, Bangiev-Girsh E, *et al*. PAX8 plays an essential anti-apoptotic role in uterine serous papillary cancer. Oncogene 2021;40:5275–85.
[16] Murali R, Davidson B, Fadare O, *et al*. High-grade endometrial carcinomas: morphologic and immunohistochemical features, diagnostic challenges and recommendations. Int J Gynecol Pathol 2019;38 Suppl 1 (Suppl 1):S40–63.
[17] Baron M, Hamou L, Laberge S, *et al*. Metastatic spread of gynecological neoplasms to the adrenal gland: case reports with a review of the literature. Eur J Gynaecol Oncol 2008;29:523–6.