Clinical Utility of ^{18}F-FDG PET/CT for Staging and Treatment Planning in Urachal Adenocarcinoma

Jeeban P. Das[1], Hebert A. Vargas[1,2], Soleen Ghafoor[1,2], Alvin C. Goh[3], and Gary A. Ulaner[1,4]

[1]Department of Radiology, Memorial Sloan Kettering Cancer Center, New York, New York; [2]Department of Radiology, Weill Cornell Medical College, New York, New York; [3]Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, New York; and [4]Molecular Imaging and Therapy, Hoag Family Cancer Institute, Newport Beach, California

Our objective was to evaluate the impact of ^{18}F-FDG PET CT on the management of urachal adenocarcinoma (UrC-ADC). **Methods:** A retrospective analysis of patients with UrC-ADC from 2001 to 2019 at Memorial Sloan Kettering was performed. Mayo stage before ^{18}F-FDG PET/CT, rate of detection of the primary malignancy and metastases on ^{18}F-FDG PET/CT, Mayo stage after ^{18}F-FDG PET/CT, and change in patient management were determined. **Results:** Of 21 patients with UrC-ADC before ^{18}F-FDG PET/CT, Mayo staging was I/II in 8, III in 3, and IV in 10. ^{18}F-FDG PET/CT detected previously unidentified metastases in 8 (38%) of 21 patients, resulting in upstaging of disease in 3 (14%) patients and a change in treatment in 4 (19%) patients. **Conclusion:** ^{18}F-FDG PET/CT has clinical utility in patients with UrC-ADC by identifying metastatic disease not appreciated on anatomic imaging, leading to changes in staging and patient management.

Key Words: urachus; urachal adenocarcinoma; ^{18}F-FDG PET/CT; staging

J Nucl Med 2021; 62:643–647
DOI: 10.2967/jnumed.120.251561

Urachal adenocarcinoma (UrC-ADC) is an aggressive nonurothelial tumor of the urachus, a remnant of the embryologic structure connecting the allantois and fetal bladder (*1–4*). Metastatic disease exists on presentation in 20%–50% of UrC-ADC patients (*5–7*). The stage of UrC-ADC is the most important prognostic factor, with 5-y survival rates of 63%, 55%, 19%, and 8% for stages I, II, III, and IV, respectively (*2,6*). Accurate and effective staging is therefore critical in assessing UrC-ADC and guiding treatment (*3,5,8,9*).

Although ^{18}F-FDG PET/CT has demonstrated value in many malignancies (*10–12*), UrC-ADC is often mucinous in histology (*1–4*), and mucinous malignancies may demonstrate low or absent ^{18}F-FDG uptake (*13*). Thus, ^{18}F-FDG PET/CT may not be sensitive for UrC-ADC. Data for ^{18}F-FDG PET/CT in UrC-ADC are limited to brief reports and pictorial essays (*14–17*). The objective of this study was to determine whether ^{18}F-FDG PET/CT impacts systemic staging of UrC-ADC and its clinical management.

Received Jun. 15, 2020; revision accepted Aug. 11, 2020.
For correspondence or reprints contact: Gary A. Ulaner, Molecular Imaging and Therapy, Hoag Family Cancer Institute, Newport Beach, CA 92663.
E-mail: gary.ulaner@hoag.org
Published online Sep. 18, 2020.

MATERIALS AND METHODS

Study Design

This Health Insurance Portability and Accountability Act–compliant, retrospective, single-institution study was performed under Institutional Review Board approval, with the requirement to obtain informed consent being waived by the board. Our hospital information system was screened for patients with pathologically proven cases of UrC-ADC diagnosed between January 2001 and January 2019 who underwent imaging with contrast-enhanced CT or MRI and ^{18}F-FDG PET/CT within 6 wk of each other before systemic or radiation therapy. Patients with the following characteristics were excluded: incomplete clinical or histopathologic records, prior malignancy, nonadenocarcinoma histology of UrC, no ^{18}F-FDG PET/CT imaging, no conventional CT or MRI within 6 wk before the ^{18}F-FDG PET/CT, or administration of chemotherapy or radiation therapy before ^{18}F-FDG PET/CT. For patients included in our analysis, medical records were reviewed to determine age, sex, and pathologic subtype (mucinous or nonmucinous) of the tumor.

Determination of Stage Before ^{18}F-FDG PET/CT

The Mayo staging system for UrC (Table 1) was used to classify the urachal tumors (*5*). Contrast-enhanced CT (or MRI for 1 patient) was used to determine an imaging stage before ^{18}F-FDG PET/CT.

^{18}F-FDG PET/CT Imaging and Interpretation

^{18}F-FDG PET/CT and contrast-enhanced cross-sectional imaging studies were evaluated by a nuclear radiologist who was dually board-certified in nuclear medicine and diagnostic radiology, had 15 y of PET/CT experience, and was masked to the pre-PET/CT stage. A nuclear medicine fellow assisted. SUVs, normalized to body weight, were determined on the GE Healthcare AW suite. According to standard ^{18}F-FDG PET/CT reporting, uptake was considered abnormal when it was focal, was not physiologic or inflammatory, and had an intensity greater than the local background.

Determination of Stage After ^{18}F-FDG PET/CT and Rate of Upstaging

Metastases identified by ^{18}F-FDG PET/CT that had not been detected in prior conventional cross-sectional imaging studies were recorded. ^{18}F-FDG PET/CT results were used to determine disease stage after ^{18}F-FDG PET/CT. The initial clinical stage was compared with the clinical stage after ^{18}F-FDG PET/CT to determine the rate of upstaging. Changes in patient management based on ^{18}F-FDG PET/CT were recorded as determined from medical records. The ^{18}F-FDG PET/CT scan results were confirmed with the histologic data when available. When the histology was not available, imaging follow-up was used.

TABLE 1
Mayo Classification Staging System for Urachal Cancer

Stage	Mayo classification (5)
1	Confinement to urachus or bladder
2	Extension beyond muscular layer of urachus or bladder
3	Involvement of regional lymph nodes
4	Involvement of nonregional lymph nodes or distant metastases

TABLE 2
Demographics for Our Cohort of 21 Patients with UrC-ADC

Demographic	Data
Age (y)	52.7 (range, 32–75)
Sex	
Female	8
Male	13
Histopathology	
Mucinous	14
Nonmucinous	7
Mayo stage (before ^{18}F-FDG PET/CT)	
I/II	8
III	3
IV	10

Characterization of Primary Malignancies

CT or MR images were reviewed to classify the primary UrC-ADC as well defined or ill defined, solid or cystic, enhancing or nonenhancing, and with or without calcifications. On ^{18}F-FDG PET/CT, the primary UrC-ADC was classified as ^{18}F-FDG–avid (above the local background), and if avid, the SUV_{max} was recorded.

RESULTS

Patient Demographics

A Standards for Reporting of Diagnostic Accuracy Studies (STARD) diagram of patients screened and included in our analysis is presented in Figure 1. The demographics of the 21 patients included in the cohort are outlined in Table 2.

Mayo Stage Before ^{18}F-FDG PET/CT

Before ^{18}F-FDG PET/CT, Mayo staging was I/II in 8 (38%), III in 3 (14%), and IV in 10 (48%) patients. All metastatic disease detected on conventional cross-sectional imaging was histopathologically proven from at least 1 site. The most common sites of distant metastases were the peritoneum ($n = 6$), lung ($n = 4$), distant nodes ($n = 2$), liver ($n = 2$), pancreas ($n = 1$), and soft tissue ($n = 1$). Five patients had more than 1 site of metastatic disease.

Additional Metastases Detected by ^{18}F-FDG PET/CT

Twenty-one patients underwent ^{18}F-FDG PET/CT within 6 wk of conventional imaging (Table 3) and before systemic or radiation therapy. In 11 patients, ^{18}F-FDG PET/CT was performed before resection of the primary malignancy, whereas in 10 patients, it was performed afterward. The median number of days from prior cross-sectional imaging to ^{18}F-FDG PET/CT was 17.3 (range, 0–42).

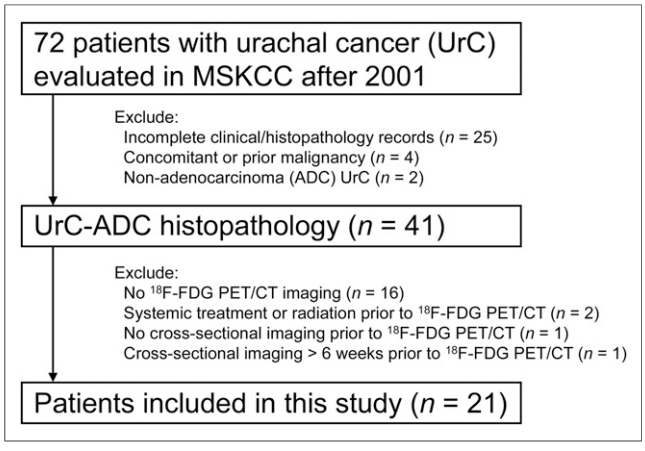

FIGURE 1. STARD diagram for patients screened and included in our analysis.

Previously undetected metastases were identified on ^{18}F-FDG PET/CT in 8 of 21 patients (38%). These included osseous metastases in 4 patients, nodal metastases in 3 patients (pelvic, $n = 2$; thoracic, $n = 1$), pancreatic metastases in 2 patients, and hepatic metastases in 1 patient. Two patients had more than 1 site of newly detected metastatic disease: osseous and nodal in one, and osseous and pancreatic in the other. The SUV_{max} of ^{18}F-FDG–avid metastases ranged from 3.0 to 14.5. Histopathologic confirmation was obtained in 3 patients (pelvic nodal and pancreatic in 1 patient, liver in 1 patient, and pancreatic in 1 patient), whereas in 5 patients newly detected metastases demonstrated an increase in size or ^{18}F-FDG avidity on subsequent imaging studies. Three patients (14%) were upstaged by ^{18}F-FDG PET/CT: two from Mayo stage II to IV and the third from Mayo stage III to IV.

On the basis of the ^{18}F-FDG PET/CT findings, treatment was changed or escalated in 4 of 21 patients (19%). An ^{18}F-FDG–avid pancreatic metastasis that was detected in 1 patient (previously considered a candidate for potentially curative surgical resection of the primary UrC-ADC) resulted in systemic treatment with chemotherapy instead of surgery. An ^{18}F-FDG–avid liver metastasis was detected in 1 patient (Fig. 2), resulting in initiation of systemic chemotherapy. In a third patient, ^{18}F-FDG–avid pancreatic and osseous metastases led to treatment escalation with chemotherapy and radiation to osseous metastases (Fig. 3). A fourth patient (considered Mayo stage IV by CT and thus not upstaged by ^{18}F-FDG PET/CT) being treated with chemotherapy alone was subsequently treated with radiation after detection of additional osseous metastases on ^{18}F-FDG PET/CT.

Characteristics of Primary Urc-ADC Tumors on Contrast-Enhanced CT and ^{18}F-FDG PET/CT

The primary UrC-ADC tumor was imaged with contrast-enhanced CT in 17 patients at the time of their initial clinical presentation. The mean size of the primary tumor in the longest-axis dimension was 4.8 cm (range, 2.2–13.7 cm). Most tumors had well-defined margins (82%), were predominantly cystic or mixed solid–cystic (76%), and demonstrated enhancement (88%). Thirteen (76%) of the primary UrC-ADC tumors contained calcifications.

TABLE 3
Results for 21 Patients with UrC-ADC Undergoing ^{18}F-FDG PET/CT After Conventional CT or MR

Patient no.	Mayo stage before PET/CT	Prior cross-sectional imaging modality	Days from cross-sectional imaging to PET/CT	New metastases detected by PET/CT?	SUV_{max} at sites of detected metastases	Change in stage after PET/CT?	Change in treatment after PET/CT?
1	IV	CT	3	Yes	Nodes (pelvic), 3.0	No	No
2	III	CT	38	Yes	Hepatic, 9.0	Yes (III–IV)	Systemic chemotherapy commenced
3	II	CT	40	No	No metastases	No	No
4	II	CT	27	No	No metastases	No	No
5	II	CT	3	No	No metastases	No	No
6	IV	CT	36	Yes	Osseous, 12–14.5	No	Radiation commenced
7	IV	CT	0	Yes	Osseous, 4.2	No	No
8	III	CT	16	No	No metastases	No	No
9	IV	CT	0	Yes	Osseous, 7.0; nodes (thoracic), 3.0	No	No
10	II	CT	32	No	No metastases	No	No
11	II	CT	26	No	No metastases	No	No
12	IV	CT	4	No	No metastases	No	No
13	IV	CT	7	Yes	Nodes (pelvic), 4.2	No	No
14	II	CT	42	Yes	Pancreatic, 4.0	Yes (II–IV)	Systemic chemotherapy commenced, no longer candidate for curative surgery
15	IV	CT	0	No	No metastases	No	No
16	IV	CT	2	No	No metastases	No	No
17	IV	CT	7	No	No metastases	No	No
18	IV	CT	16	No	No metastases	No	No
19	II	CT	20	No	No metastases	No	No
20	II	CT	40	Yes	Osseous, 5.0–6.8; pancreatic, 7.3	Yes (II–IV)	Systemic chemotherapy and radiation commenced
21	III	CT and MRI	5	No	No metastases	No	No

Six patients had their primary tumor resected before undergoing the contrast-enhanced cross-sectional CT or MRI study that was performed within 6 wk before the ^{18}F-FDG PET/CT imaging study. That left 11 primary urachal tumors imaged on PET/CT. Seven of the 11 (63.6%) primary UrC-ADCs evaluable on PET/CT were ^{18}F-FDG–avid, with a mean SUV_{max} of 13.8 (range, 4.0–27.5), and 4 of the 11 (46%) demonstrated background ^{18}F-FDG uptake. Additional imaging features of primary UrC-ADC on contrast-enhanced CT and ^{18}F-FDG PET/CT are summarized in Supplemental Table 1 (supplemental materials are available at http://jnm.snmjournals.org).

Mucinous Tumors Versus Nonmucinous Tumors and ^{18}F-FDG Avidity

Fourteen UrC-ADCs were mucinous on histopathology. Of these, 10 (71%) had metastatic disease. Seven of the 10 (70%) with metastatic disease demonstrated ^{18}F-FDG–avid metastases. Of the 7 with ^{18}F-FDG–avid metastases, 4 had an evaluable primary tumor, and 3 of the 4 primary tumors were ^{18}F-FDG–avid (SUV_{max}, 4, 1.7, and 24.6).

Seven UrC-ADCs were nonmucinous tumors. Of these, 5 (71%) had metastatic disease. All 5 with metastatic disease (100%) demonstrated ^{18}F-FDG–avid metastases. Of the 5 with ^{18}F-FDG–avid metastases, 3 had an evaluable primary tumor, and all 3 of the primary tumors were ^{18}F-FDG–avid (SUV_{max}, 9, 19.5, and 27).

DISCUSSION

We evaluated the clinical utility of ^{18}F-FDG PET/CT in staging of UrC-ADC. ^{18}F-FDG PET/CT detected additional metastases in nearly 40% of patients and upstaged disease by radiographic criteria in almost 15%, compared with cross-sectional imaging performed within 6 wk beforehand. In addition, ^{18}F-FDG PET/CT resulted in a change in management or treatment plan in almost 20% of patients.

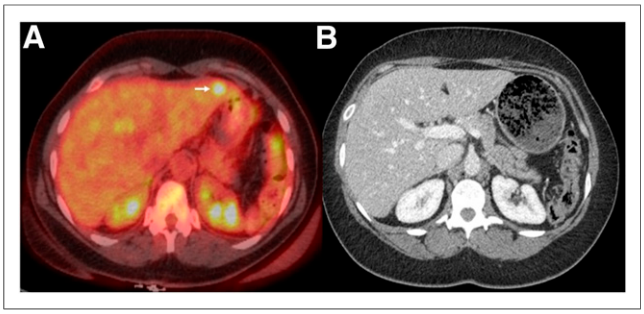

FIGURE 2. A 50-y-old man with UrC-ADC. Axial ^{18}F-FDG PET/CT (A) demonstrates hepatic lesion (arrow) with SUV_{max} of 9.0, which was occult on prior contrast-enhanced CT (B). Lesion was subsequently biopsied under ultrasound guidance and proven to be metastasis.

Because of the rarity of this tumor, the literature pertaining to ^{18}F-FDG PET/CT evaluation of urachal pathology consists primarily of case reports and smaller case series. The positive predictive value of imaging to detect malignancy preoperatively is low when dealing with a urachal mass (*18*), as both benign and malignant urachal pathology can appear similar on contrast-enhanced CT and ^{18}F-FDG PET/CT (*19,20*). Variable ^{18}F-FDG avidity of UrC-ADC has been described in the literature (*21,22*). Guimarães et al. described a primary UrC-ADC demonstrating increased ^{18}F-FDG uptake (without distant metastases), for which ^{18}F-FDG PET/CT provided valuable information for diagnosis and initial staging (*22*). Zeman et al. described a false-negative ^{18}F-FDG PET/CT finding in a mucinous UrC-ADC showing background ^{18}F-FDG uptake without evidence of metastatic disease (*23*). Interestingly, Li et al. described ^{18}F-FDG PET/CT findings in a patient with a primary mucinous UrC-ADC showing low-level ^{18}F-FDG avidity (SUV, 2.4), with ^{18}F-FDG–avid nodal and osseous metastases (SUV, 6.9) (*21*). We noted a similar finding in our series of patients. Of the 4 patients with ^{18}F-FDG–avid metastases and an evaluable mucinous primary UrC-ADC, the primary tumor was nonavid in 1 case.

Mucinous tumors have been shown to demonstrate low or background ^{18}F-FDG uptake due to hypocellularity, potentially limiting the sensitivity of ^{18}F-FDG PET/CT (*13,24*). The mucinous tumor subtype comprised the majority (67%) of our patients with UrC-ADC. Half of these patients (7/14) developed ^{18}F-FDG–avid metastatic disease.

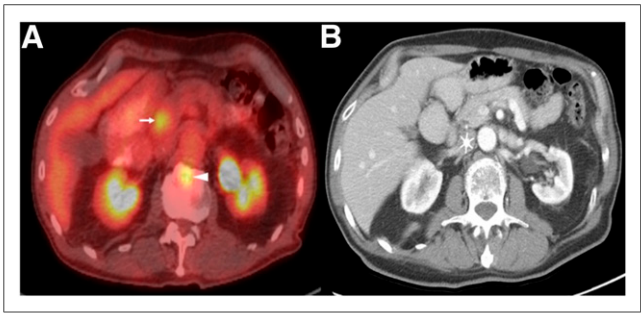

FIGURE 3. A 47-y-old man with UrC-ADC. Axial PET/CT (A) demonstrates ^{18}F-FDG–avid pancreatic lesion (arrow) with SUV_{max} of 14.2, as well as additional osseous metastasis lesion (arrowhead) not detected on prior contrast-enhanced CT of abdomen and pelvis (B). Pancreatic lesion was subsequently sampled by endoscopic ultrasound using fine-needle aspiration and proven to be metastasis.

We are limited by both the small sample size and the retrospective nature of the study. In addition, the absence of data or guidelines for the use of ^{18}F-FDG PET/CT in UrC-ADC may have introduced selection bias in our single-center analysis. However, because of the rarity of UrC-ADC, high-powered prospective studies would be difficult to undertake.

CONCLUSION

Our data suggest that ^{18}F-FDG PET/CT has clinical utility in patients with UrC-ADC by identifying metastatic disease not appreciated on anatomic imaging, leading to changes in staging and patient management.

DISCLOSURE

Funding was received from an NIH/NCI Cancer Center support grant (P30 CA008748). No other potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Does ^{18}F-FDG PET/CT impact the staging and management of UrC-ADC?

PERTINENT FINDINGS: This retrospective analysis of 21 patients with UrC-ADC before chemotherapy or radiation therapy demonstrated that ^{18}F-FDG PET/CT within 6 wk of conventional CT or MRI detected previously unidentified metastases in 8 (38%) patients, resulted in upstaging of disease in 3 (14%) patients and a change in treatment management in 4 (19%) patients.

IMPLICATIONS FOR PATIENT CARE: ^{18}F-FDG PET/CT has clinical utility in patients with UrC-ADC by identifying metastatic disease not appreciated on anatomic imaging, leading to changes in staging and patient management.

REFERENCES

1. Gopalan A, Sharp DS, Fine SW, et al. Urachal carcinoma: a clinicopathologic analysis of 24 cases with outcome correlation. *Am J Surg Pathol.* 2009;33:659–668.
2. Sheldon CA, Clayman RV, Gonzalez R, Williams RD, Fraley EE. Malignant urachal lesions. *J Urol.* 1984;131:1–8.
3. Molina JR, Quevedo JF, Furth AF, Richardson RL, Zincke H, Burch PA. Predictors of survival from urachal cancer: a Mayo Clinic study of 49 cases. *Cancer.* 2007;110:2434–2440.
4. Reis H, Szarvas T. Urachal cancer: current concepts of a rare cancer.*Pathologe.* 2019;40(suppl 1):31–39.
5. Ashley RA, Inman BA, Sebo TJ, et al. Urachal carcinoma: clinicopathologic features and long-term outcomes of an aggressive malignancy. *Cancer.* 2006;107:712–720.
6. Szarvas T, Módos O, Niedworok C, et al. Clinical, prognostic, and therapeutic aspects of urachal carcinoma: a comprehensive review with meta-analysis of 1,010 cases. *Urol Oncol.* 2016;34:388–398.
7. Hamilou Z, North S, Canil C, et al. Management of urachal cancer: a review by the Canadian Urological Association and Genitourinary Medical Oncologists of Canada. *Can Urol Assoc J.* 2020;14:E57–E64.
8. Pinthus JH, Haddad R, Trachtenberg J, et al. Population based survival data on urachal tumors. *J Urol.* 2006;175:2042–2047.
9. Niedworok C, Panitz M, Szarvas T, et al. Urachal carcinoma of the bladder: impact of clinical and immunohistochemical parameters on prognosis. *J Urol.* 2016;195:1690–1696.

10. Macheda ML, Rogers S, Best JD. Molecular and cellular regulation of glucose transporter (GLUT) proteins in cancer. *J Cell Physiol.* 2005;202:654–662.
11. Hillner BE, Siegel BA, Liu D, et al. Impact of positron emission tomography/computed tomography and positron emission tomography (PET) alone on expected management of patients with cancer: initial results from the National Oncologic PET Registry. *J Clin Oncol.* 2008;26:2155–2161.
12. Podoloff DA, Ball DW, Ben-Josef E, et al. NCCN Task Force: clinical utility of PET in a variety of tumor types. *J Natl Compr Cancer Netw.* 2009;7(suppl):S1–S26.
13. Berger KL, Nicholson SA, Dehdashti F, Siegel BA. FDG PET evaluation of mucinous neoplasms: correlation of FDG uptake with histopathologic features. *AJR.* 2000;174:1005–1008.
14. Das JP, Vargas HA, Lee A, et al. The urachus revisited: multimodal imaging of benign & malignant urachal pathology. *Br J Radiol.* 2020;93:20190118.
15. Parada Villavicencio C, Adam SZ, Nikolaidis P, Yaghmai V, Miller FH. Imaging of the urachus: anomalies, complications, and mimics. *Radiographics.* 2016.36: 2049–2063.
16. Yu JS, Kim KW, Lee HJ, Lee YJ, Yoon CS, Kim MJ. Urachal remnant diseases: spectrum of CT and US findings. *Radiographics.* 2001;21:451–461.
17. Das JP, Vargas HA, Ulaner GA. Mucinous urachal adenocarcinoma: a potential non fluorodeoxyglucose-avid pitfall on 18-fluorine-fluorodeoxyglucose positron emission tomography/computed tomography. *World J Nucl Med.* October–December 2020 [Epub ahead of print].
18. Meeks JJ, Herr HW, Bernstein M, Al-Ahmadie HA, Dalbagni G. Preoperative accuracy of diagnostic evaluation of the urachal mass. *J Urol.* 2013;189:1260–1262.
19. Dong A, Zuo C, Wang Y, Lu J, Zhu H. Organized urachal abscess mimicking urachal carcinoma on FDG PET/CT. *Clin Nucl Med.* 2014;39:71–73.
20. Flaus A, Longo MG, Dematons M, Granjon D, Prevot N. ^{18}F-FDG PET/CT in urachal abscess. *Clin Nucl Med.* 2010;44:e349–e350.
21. Li X, Liu S, Yao S, Wang M. A rare case of urachal mucinous adenocarcinoma detected by ^{18}F-FDG PET/CT. *Clin Nucl Med.* 2015;40:282–285.
22. Guimarães MD, Bitencourt AG, Lima EN, Marchiori E. ^{18}FDG PET/CT findings in the unusual urachal adenocarcinoma. *Clin Nucl Med.* 2014;39:831–834.
23. Zeman M, Silver E, Akin E. CT and PET findings for urachal adenocarcinoma: a case report. *Ann Clin Case Rep.* 2017;2:1252.
24. Tanizaki Y, Kobayashi A, Shiro M, et al. Diagnostic value of preoperative SUVmax on FDG-PET/CT for the detection of ovarian cancer. *Int J Gynecol Cancer.* 2014; 24:454–460.