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Late duodenal metastasis from renal cell carcinoma with newly developed malignant lymphoma: A case report

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Abstract. Duodenal metastasis from renal cell carcinoma (RCC) is rare. The current case report presents a very rare case of late duodenal metastasis from RCC with newly developed malignant lymphoma (diffuse large B-cell lymphoma: DLBCL) at the same time. A 64-year-old man with systemic lymph nodes swelling who had undergone left nephrectomy for RCC 25 years previously, was admitted to the present hospital. Inguinal lymph node biopsy was performed, leading to a diagnosis of DLBCL. fluorine-18-fluorodeoxy-glucose (^{18}F-FDG)-positron emission tomography (PET)/computed tomography (CT) revealed multiple lymph nodes, spleen, and ileocecal lesions. CT revealed an obvious hypervascular tumor involving the duodenum/pancreatic head. The tumor was false-negative on ^{18}F-FDG-PET/CT. On esophagogastroduodenoscopy, the tumor was detected in the descending portion of the duodenum and was observed to be consistent with the submucosal tumor with a central ulcer, resembling those of ulcer-forming DLBCL. A biopsy was then performed carefully, and a clear cell RCC-derived metastatic cancer was diagnosed. Ileocolonoscopy revealed mucosal thickening of the terminal ileum, and led to a diagnosis of DLBCL infiltration with biopsy. To the best of the author's knowledge, this is the first case report of the coexistence of metastatic cancer from RCC and malignant lymphoma in the small intestine simultaneously. It was necessary to make a careful differential diagnosis in the imaging studies.

Introduction

Renal cell carcinoma (RCC) is clinically characterized by late recurrence and metastasis, and McNichols *et al* defined late RCC recurrence as occurrence more than 10 years after nephrectomy (1). Duodenal metastasis from RCC is rare (2,3). Herein, we report a very rare case of RCC in a man for whom we performed imaging studies to evaluate the clinical stage of newly developed diffuse large B-cell lymphoma (DLBCL), and were incidentally able to find the ectopic recurrence of RCC in the duodenum/pancreatic head 25 years after its curative resection. Two different malignancies occurred simultaneously in the small intestine (duodenum and ileum), highlighting the need for careful differential diagnosis.

Case report

A 64-year-old Japanese man with systemic lymph nodes swelling who had undergone left nephrectomy for RCC 25 years previously was admitted to our hospital. The patient complained of abdominal pain, night-time fever, anorexia, and weight loss (-7 kg in 2 months), and the performance status was 1. Blood test examinations on admission revealed mild anemia (hemoglobin 12.4: normal range 14.0-18.0 g/dl), decreased total protein (6.2: 6.7-8.3 g/dl) and albumin (3.4: 3.8-5.3 g/dl), and increased lactate dehydrogenase (LDH 798: 120-245 U/l) and C-reactive protein (CRP 4.16: <0.30 mg/dl). The soluble interleukin-2 receptor level had risen to 7,597 (sIL-2R: 121-613 U/ml) and it further increased to 9,300 within 2 weeks. Inguinal lymph nodes biopsy was performed, leading to a diagnosis of DLBCL. The Ki-67 labeling (MIB1) index was approximately 70%.

We performed imaging studies to evaluate the clinical stage. fluorine-18-fluorodeoxy-glucose (^{18}F-FDG)-positron emission tomography (PET)/computed tomography (CT) showed multiple lymph nodes involving the cervical region, an abdominal bulky mass, spleen, and ileocecal lesions. CT revealed an obvious hypervascular tumor involving the duodenum/pancreatic head (Fig. 1A), and small nodules up to 1 cm in diameter were scattered throughout both lung fields, but these tumors demonstrated no uptake on ^{18}F-FDG-PET/CT (Fig. 1B). The right kidney exhibited no abnormalities. On esophagogastroduodenoscopy (EGD), blood refluxed from the duodenum was seen retained in the stomach. The tumor was detected in the descending portion of the duodenum apart from the periampullary region, and was seen consistent with submucosal tumor with central ulcer resembled those of

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Key words: renal cell carcinoma, late metastasis, malignant lymphoma, small intestine, imaging study

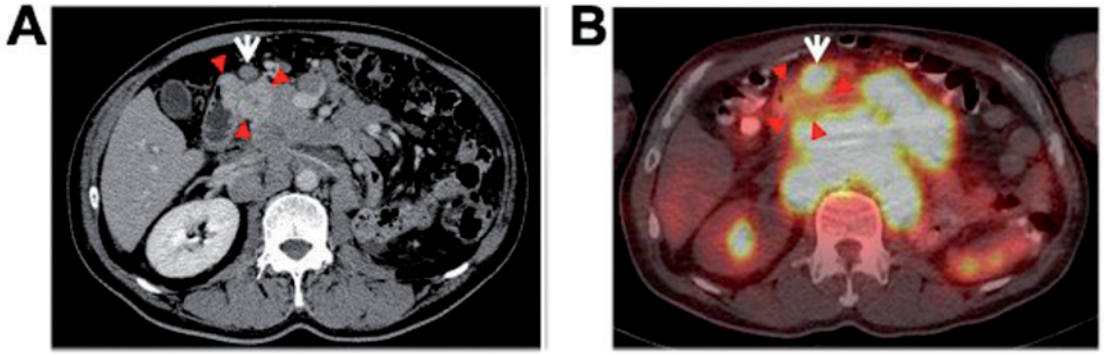

Figure 1. (A) CT imaging. A tumor with hypervascularity compared with the surrounding bulky mass was present in the duodenum/pancreatic head (red arrowhead). On the ventral side of the hypervascular tumor, a lymph node lesion that was enhanced similarly to the bulky mass was present (white arrow). (B) fluorine-18-fluorodeoxy-glucose (^{18}F-FDG)-positron emission tomography (PET)/computed tomography (CT). Marked uptake was noted in the bulky abdominal mass and the lymph nodes lesion described above (white arrow) [maximum standard uptake value (SUV_{max}), 30.6]. In contrast, no uptake was noted in the tumor present in the duodenum/pancreatic head (red arrowhead) (false-negative).

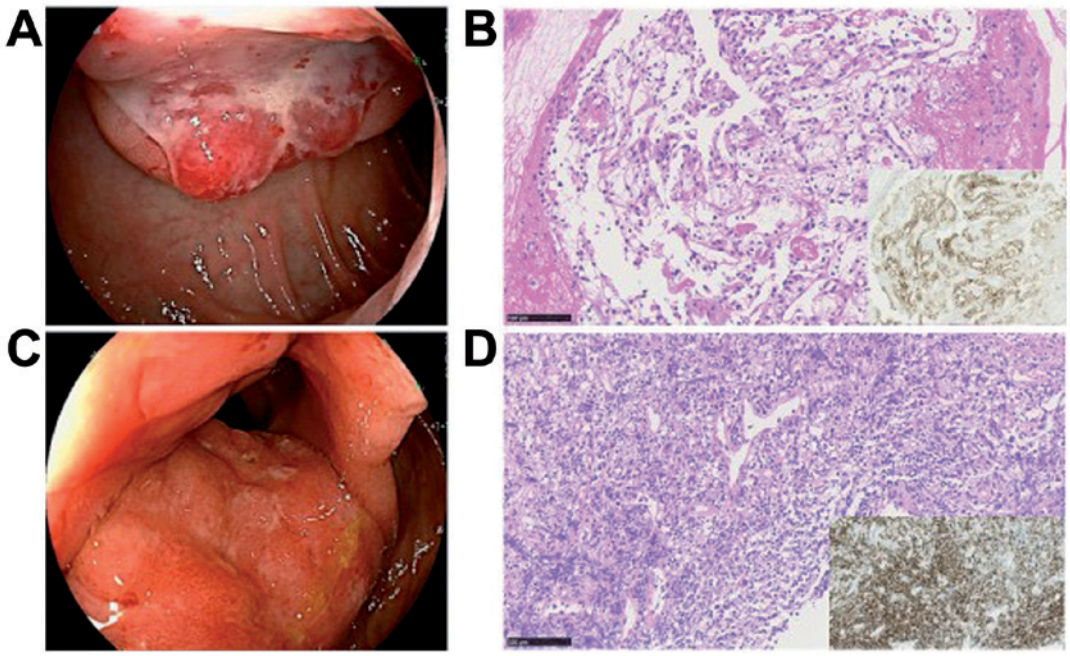

Figure 2. (A) EGD imaging. A submucosal tumor with the ulcer floor covered by white moss like ulcer-forming DLBCL was seen on the descending portion of the duodenum apart from the periampullary region. (B) Histopathologic finding of the duodenal lesion. A biopsy specimen revealed infiltration of cancer cells showing consistent with clear cell renal carcinoma (H&E staining), and these cells were positive for CD10 immunostaining (*inset*). Magnification, x200. (C) Ileocolonoscopy imaging. Mucosal thickening was seen on the ileocecal valve. (D) Histopathologic finding of the ileal lesion. A biopsy specimen revealed large lymphoid cells infiltrating the lamina propria (H&E staining), and these cells were positive for CD20 immunostaining (*inset*). Magnification, x200. EGD, esophagogastroduodenoscopy; DLBCL, diffuse large B-cell lymphoma.

ulcer-forming DLBCL (Fig. 2A). Biopsy was performed carefully, and this tumor was pathologically diagnosed with a clear cell RCC-derived metastatic cancer immunohistochemically positive for CD10 (Fig. 2B). Ileocolonoscopy showed mucosal thickening of the terminal ileum including ileocecal valve (Fig. 2C), and biopsy led to a diagnosis of DLBCL infiltration immunohistochemically positive for CD20 (Fig. 2D).

Based on imaging studies and pathological findings, the patient was diagnosed with coexistence of metastatic duodenal/pancreatic cancer from RCC and DLBCL (Ann Arbor stage IV), and the latter was classified as high-intermediate risk with the international prognostic index (IPI). We then began treatment for DLBCL because of its tumor volume. The patient received five courses of chemotherapy, including rituximab (RTX) + EPOCH regimen (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) and RTX + GDP regimen (gemcitabine, cisplatin, and dexamethasone). As a result, the sIL-2R level decreased to 903 U/ml, and the patient achieved complete remission (assessed by PET). Although the tumor in the duodenum/pancreatic head slightly decreased in size (from 3.6 to 3.0 cm) in the past 4 months, a tumor of about 1 cm in diameter appeared in the pancreatic body, and some of the nodules scattered in both lung fields grew and increased slightly. As these findings suggested that the metastatic cancer from RCC had started to grow mainly in the pancreas and lungs, the patient was transferred to a designated cancer hospital to

receive treatment for these lesions. Subsequent oral pazopanib treatment was successful for this patient, and the treatment is being continued as the outpatient. Written informed consent was obtained from the patient for publication of this case report.

Discussion

RCC has a potential to metastasize to almost any site. The most common sites of metastasis are the lung, liver, and bones (4). Clinically evident gastrointestinal involvement of RCC, especially solitary duodenal metastasis from RCC is rare and most frequently involves the periampullary region or the duodenal bulb (5,6). According to recent report (7), of the 3637 patients diagnosed with RCC, 15 patients (0.4%) with 19 gastrointestinal lesions were identified, and duodenum involvement was 6 lesions.

Because coexistence of two different malignancies, metastatic cancer from RCC and malignant lymphoma (DLBCL), in the small intestine simultaneously is extremely rare, it was necessary to make a differential diagnosis carefully with imaging studies. Metastatic RCC is frequently hypervascular as with primary tumors (8). In gastrointestinal metastasis from RCC, intraluminal polypoid masses (63.2%) with hyperenhancement (78.9%) and heterogeneous enhancement (63.2%) were the most common CT findings (7), especially, than in lymphoma, lymphadenopathy has been reported to be much less prominent, the involved bowel segment shorter, and multi-focality less common (9). RCC (especially clear cell carcinoma) commonly exhibits a low ^{18}F-FDG uptake, and FDG-PET has a high false-negative rate (68.5%) for detecting primary lesions (10). Aide *et al* reported that the sensitivity of FDG-PET for RCC was 47% (11). Comparing the sensitivity and specificity of FDG-PET and CT for primary and metastatic lesions in 66 patients with RCC, Kang *et al* also reported that although the sensitivity of FDG-PET (primary 60%, metastasis 75.0-77.3%) was lower than that of CT (primary 91.7%, metastasis 91.1-93.8%), the specificity of FDG-PET (primary 100%, metastasis 97.1-100%) was higher than that of CT (primary 100%, metastasis 73.1-98.1%) (12). Thus, the role of ^{18}F-FDG-PET in the detection of RCC is limited by low sensitivity (10-12). On the other hand, FDG-PET has emerged as a powerful functional imaging tool for staging, restaging, and is essential for the post-treatment assessment of DLBCL (13). On endoscopy, the metastatic duodenal cancer can be seen as a submucosal mass with ulceration of the tip, multiple nodules of varying sizes or raised plaques (14). Endoscopic findings of ulcer-forming lymphoma are the submucosal tumor with central ulcer (15), and resemble those of metastatic intestinal cancer. In our case, FDG-PET/CT revealed a high uptake in DLBCL lesions, whereas it was false-negative for the metastatic duodenal RCC lesion. In addition, on CT, the metastatic duodenal RCC lesion demonstrated hyper-enhancement more clearly than the DLBCL lesions. These findings led to a differential diagnosis by imaging, and endoscopic biopsy confirmed the diagnosis. CD10 immunostaining is helpful in separating metastatic RCC from other cancers (16).

According to the review of Rustagi *et al* (17), the mean duration post nephrectomy to diagnosis of solitary duodenal metastases was 7.9±4.7 years (median 8 years). RCC can metastasize for a long period of disease latency after nephrectomy, via the lymphatic or hematogenous route, as well as by peritoneal dissemination or direct invasion into adjacent anatomic structures (18). Our case is rare in that 'late'-recurring RCC, so long 25 years after nephrectomy, metastasized to the duodenum/pancreatic head. This tumor was thought to be a slow-growing and direct duodenal invasion from an adjacent recurrent/metastatic lesion of the pancreatic head. On the other hand, DLBCL is considered to progress monthly (19). In our patient, the tumor volume of DLBCL observed on imaging was much greater than that of the metastatic cancer from RCC. IL-2R sharply increased in this patient, revealing that progression was rapid and the current pathology may have been completed within 0.5-1 year after the newly development. As DLBCL was considered to determine the prognosis of this patient, we prioritized its treatment, and the patient achieved CR. However, during the treatment period, the metastatic cancer from RCC spread, mainly to the pancreas and lungs. Generally, an immune cell-inhibiting mechanism is present in the microcirculatory environment of tumors (20). A trace number of cancer cells of RCC were latently present under the control of the immunological surveillance mechanism, but it may have manifested because the DLBCL tumor volume rapidly increased and inhibited immunity, and the subsequent growth of metastatic cancer cells from RCC may have been slightly rapid, unlike the slow growth previously reported (1,6,17).

To the best of our knowledge, this is the first case report of the coexistence of metastatic cancer from RCC and malignant lymphoma in the small intestine simultaneously. It was necessary to make a careful differential diagnosis in the imaging studies.

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