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CASE REPORT

Metastatic Renal Cell Carcinoma of Pancreas without a Detectable Primary Tumor Mimicking Pancreatic Cancer: A Case Report and Review of the Literature

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Distant metastases are common in patients with renal cell carcinoma (RCC). Metastatic neoplasms affecting the pancreas account for <2% of all malignancies in the pancreas and RCC is the most common malignancy among them. Metastatic RCC with the nonidentifiable primary renal tumor is extremely rare. In the present study, we reported the case of a 62-year-old male with metastatic RCC to the pancreas without a primary renal tumor mimicking pancreatic cancer. Accurate pathologic diagnosis with immunohistochemistry staining and proper multidisciplinary treatment with targeted therapy may improve the clinical outcomes of these patients.

Key words: Renal cell carcinoma, carcinoma unknown primary, pancreatic tumor

INTRODUCTION

Renal cell carcinoma (RCC) is the most common kidney cancer.[1] RCC predominantly occurs in men (male-to-female ratio of 1.5:1.0), and the majority of cases are diagnosed in patients aged in the range of 60–70 years.[1] Appropriate histological classification of RCC is important for prognostic and therapeutic strategies. The clear-cell subtype is the most common among all types of RCCs.[2]

RCC is the most common malignancy to metastasize to the pancreas.[3] Moreover, cases of metastatic RCC that present a nonidentifiable kidney mass are rarely reported.[4-7] Herein, we report the case of a 62-year-old male with metastatic RCC of the pancreas who lacked the presence of a primary renal tumor that mimics primary pancreatic cancer.

CASE REPORT

A 62-year-old male with a medical history of hypertension and type 2 diabetes mellitus presented with abdominal fullness, poor appetite, intermittent tarry stool passage, and body weight loss of 5 kg within 1 month. Upon admission, the patient was afebrile and displayed normal vital signs. Physical examination revealed normal conjunctiva and mild tenderness of the upper abdomen. Laboratory studies revealed a white blood cell count of 10,730/μl (normal, 4500–11,000/μl), hemoglobin of 11.6 g/dl (normal, 12–16 g/dl), platelet count of 375 × 10^3/μl (normal, 150–400 × 10^3/μl), aspartate transaminase of 159 U/L (normal <40 U/L), alanine aminotransferase of 293 U/L (normal <40 U/L), total bilirubin of 0.4 mg/dL (normal <1.2 mg/dL), carcinoembryonic antigen of 1.48 ng/ml (normal, 0–5.0 ng/ml), and carbohydrate antigen of 19-9 (CA199) 55.89 ng/ml (normal: 0–37.0 ng/ml). Panendoscopy (PES) exposed the presence of one gastric tumor in the mid-body region, and pathological examination of the limited specimen showed poorly differentiated carcinoma. Contrast-enhanced computed tomography (CT) of the abdomen revealed a well-defined heterogeneous enhancing mass in the

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pancreatic tail, several contrast-enhanced nodules in the liver, and peritoneal carcinomatosis [Figure 1a and b], and no kidney lesions were noted [Figure 1c]. The patient refused a pancreatic tail tumor biopsy. Upon diagnosis of pancreatic tail cancer with multiple metastases to the liver and stomach, the patient received palliative concurrent chemoradiotherapy (CCRT) with weekly gemcitabine treatment.

His tarry stool condition improved after completion of CCRT. However, the patient presented coffee ground vomitus and tarry stool passage 4 months later. The repeated PES revealed the presence of an actively bleeding ulcerative gastric tumor. Histopathologic examination of the gastric cancer biopsy revealed clear-cell neoplasm. Microscopically, the tumor was characterized by neoplastic solid nests with nuclear hyperchromatism and abundant cytoplasm [Figure 2a]. Immunohistochemistry (IHC) showed positive cytokeratin (CK) 18, vimentin, PAX2, PAX8, and focal CD10 staining [Figure 2b-d] and negative staining for CK 7, CK 20, CD56, synaptophysin, and chromogranin A. The morphological appearances and IHC profiles were suggestive of metastatic renal cell carcinoma. The patient also underwent liver biopsy. The histopathologic and IHC examinations had similar findings.

We treated the patient with sunitinib (12.5 mg) three times per day, from March 2013, and his symptoms improved significantly. The follow-up abdominal CT scan, 3 months later, showed decreased size of hepatic and pancreatic tail lesions. Stable disease was noted during follow-up, until August 2014, when the patient developed progressive jaundice, hepatic encephalopathy, and cachexia, due to progression of liver tumors. Palliative radiotherapy was performed for pain relief, and the patient succumbed in August 2014 because of hepatic failure.

DISCUSSION

Metastatic RCC without known primary renal tumor is rare, and only a few cases have been reported in the literature.[4-7] It remains unclear why primary RCC lesions are occult, but we hypothesize that this may be due to its small size and resolution limits of detection by current imaging techniques. Spontaneous regression of the primary RCC lesion or ectopic RCC development in the kidneys with distant metastases has been reported.[8]

Fine-needle aspiration and core needle biopsies are common procedures used for histological diagnosis of carcinoma with unknown patient origins; however, the amount of specimen is often limited. IHC staining is important for diagnosis and treatment, and IHC markers commonly used for the diagnosis of primary RCC are PAX2, PAX8, RCC marker, CD10, and a combination of vimentin and CK.[9] However, the correct diagnosis of metastatic RCC remains challenging because the morphology of metastatic RCC differs from that of primary RCC. Furthermore, the currently available biomarkers are also used to diagnose other neoplasms.[9] For example, CD10 and PAX8 are helpful for the diagnosis of metastatic RCC, but they are also expressed in many other cancers.

The clear-cell morphology; positive staining for CD10, vimentin, PAX2, and PAX8; and negative staining for CK7 have contributed to the successful diagnosis of clear-cell subtype RCC in previous reports as well as in our case [Table 1]. Shen *et al*. suggest that the IHC panel for metastatic RCC should include PAX2 or PAX8 and RCC marker or CD10, with auxiliary markers for differential diagnoses.[9] In our case, the aforementioned subdiagnoses

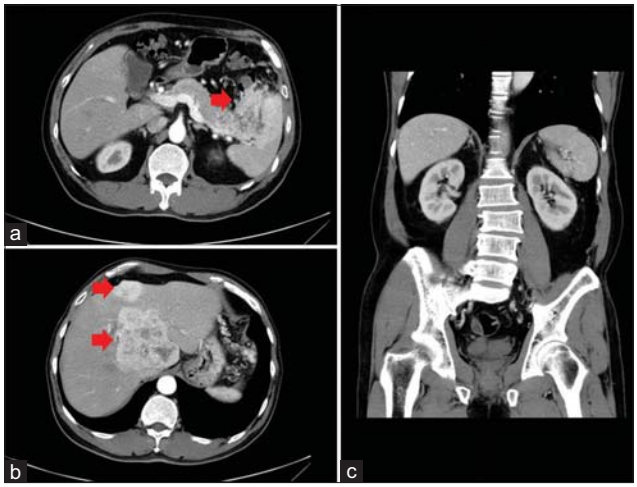

Figure 1: Abdominal computed tomography showing (a) one pancreatic tail tumor (red arrow) (b) hepatic tumors (red arrows) with contrast enhancement, and (c) normal kidneys

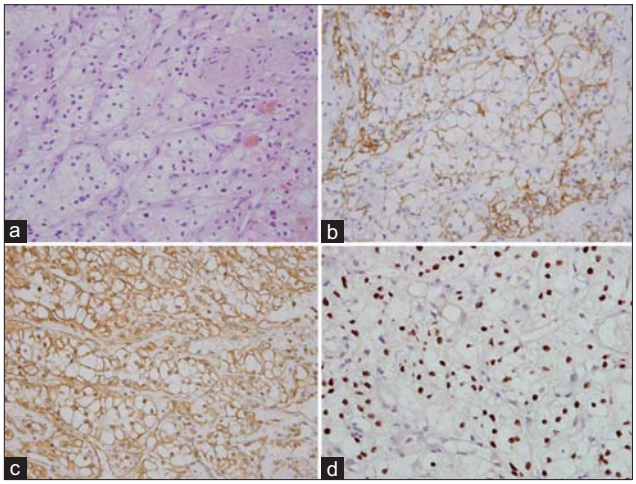

Figure 2: (a) Tumor cell nests with nuclear hyperchromatism and clear cytoplasm, intermixed with vascular network (H and E stain; ×400). Cells were immunoreactive for (b) cytokeratin 18, (c) vimentin, (d) PAX8 (×400)

Table 1: Literature review of metastatic renal cell carcinoma with no primary renal lesions

	Sex	Age	Clinical presentation	Pathology and IHC staining	Treatment	Survival	References
1	Male	70	Lung and bone metastases with hypercalcemia	Clear-cell carcinoma, CK CAM5.2(+), vimentin(+), CD10(+)	Sunitinib	A, 18+ months	9
2	Female	69	Right knee and lung metastases	Renal cell carcinoma, EMA(+), vimentin(+), CD10(+)	Radiotherapy, sunitinib	D, 8 months	9
3	Male	68	Bilateral adrenal metastases	Clear-cell carcinoma, panCK(+), RCC(+), PAX2(+), PAX8(+)	Bilateral adrenalectomy, subsequent sunitinib, radiotherapy	A, 16+ months	10
4	Male	71	Left adrenal metastasis	Clear-cell carcinoma, AE1/3 (+), EMA(+), vimentin(+), CD10(+), PAX2(+), PAX8 (+), RCC(+), carbonic anhydrase IX(+)	Left adrenalectomy	A, 36+ months	11
5	Male	54	T-spine epidural mass	Renal cell carcinoma, AE1/3(+), EMA(+), vimentin(+), CD10(+), PAX8 (+), RCC(+)	Tumor removal	D, 12 months	12
#	Male	62	Liver, pancreas, stomach, and peritoneal metastases	Clear-cell carcinoma, CK 18(+), vimentin(+), CD10(+), PAX2(+), PAX8(+)	Radiotherapy, sunitinib	D, 17 months	

IHC=Immunohistochemistry; CK=Cytokeratin; EMA=Epithelial membrane antigen; Survival=Time from presentation; A=Alive; D=Dead; #=Our case; RCC=Renal cell carcinoma; CAM=Cerium ammonium molybdate

were excluded by IHC staining, as we observed negative staining for chromogranin and synaptophysin and positive staining for CD10 and PAX8.

Antiangiogenic drugs that target the vascular endothelial growth factor (VEGF) pathway, such as sunitinib, have markedly improved the clinical outcomes of patients with metastatic RCC, and sunitinib is considered the first-line treatment option for this disease.[10] Multidisciplinary management is important in advanced RCC, and metastasectomy may be considered in medically fit patients with oligometastatic cancer and long disease-to-recurrence time.[11] Palliative radiotherapy can be used to control bone and brain metastases,[12] and the combination of anti-VEGF tyrosine kinase inhibitors (TKIs) and radiotherapy can enhance disease control and long-term survival.[8,13] By means of multidisciplinary treatment with sunitinib, our case and previously reported cases [Table 1] have achieved patient survival similar to those reported in clinical trials.[10]

We reported a rare case of multiple metastatic RCC without a known primary renal lesion. We suggest that clear-cell carcinoma RCC should be included as a distinct tumor diagnosis, as the phenotype presents clear-cell morphology without evidence of a primary kidney tumor. IHC staining is essential for an accurate diagnosis, to guide the appropriate targeted therapy. Multidisciplinary treatment, in combination with anti-VEGF TKIs, can improve the clinical outcomes and quality of life of patients diagnosed with this metastatic disease.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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