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CASE REPORT

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A case of hypervascular tumors in the liver and pancreas: synchronous hepatocellular carcinoma and pancreatic metastasis from renal cell carcinoma 36 years after nephrectomy

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Abstract

It is sometimes difficult to distinguish between multiple cancers and metastases using only diagnostic imaging, particularly when multiple hypervascular tumors are found in multiple organs. We present a case in which the preoperative histological evaluation was essential to determine the management of a hypervascular pancreatic tumor and liver tumor.

KEYWORDS

EUS-FNA, Hepatocellular carcinoma, Metastatic pancreatic carcinoma, Renal cell carcinoma

1 | INTRODUCTION

Assessing tumor vascularity via diagnostic imaging can provide substantial information for a differential diagnosis. Typical hypervascular tumors include hepatocellular carcinoma (HCC), renal cell carcinoma (RCC), and neuroendocrine tumors (NETs).[1–3] Since the vascularity of the metastatic lesion reflects the primary tumor, it can be difficult to distinguish between multiple cancers and metastases, particularly when multiple hypervascular tumors are found in multiple organs. In such cases, histological evaluation was necessary to make a diagnosis and determine the management of tumors.

In this report, we preoperatively diagnosed and appropriately treated two hypervascular tumors: pancreatic metastasis from RCC (36 years post-nephrectomy) and HCC.

2 | CASE REPORT

A 76-year-old man who had previously undergone left nephrectomy due to the presence of a renal tumor 36 years ago, and total cystectomy for bladder cancer 4 years ago, was referred to our department due to the identification of a pancreatic tumor and liver tumor by regular follow-up computed tomography (CT). The pancreatic tumor was located in the head of the pancreas; it was 10 mm in size and showed strong early enhancement in the arterial phase. The contrast of the pancreatic tumor gradually diminished through the portal phase and delayed phase (Figure 1A-C), which is not a typical pattern of pancreatic ductal cancer. The liver tumor was located in segment 7 and was 22 mm in size. This tumor showed early enhancement in the arterial phase, and the contrast medium was washed out in the portal and delayed phase (Figure 1D-F). The liver tumor also showed early enhancement, followed by washout, in gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging (Figure 2A-C). This tumor showed hypointensity in the hepatobiliary phase (Figure 2 D) and restriction (hyperintensity) on the diffusion-weighted image (b value = 800 s/mm^2) (Figure 2E).

In the abdominal ultrasound scan, the hyperechoic tumor was located in segment 7 of the liver (Figure 3A). Conversely, the pancreatic tumor was recognized as a hypoechoic mass by endoscopic ultrasonography (Figure 3B). These findings revealed that echo levels of these tumors were different. Contrast-enhanced ultrasonography of the liver tumor showed both an early enhancement in the vascular phase (Figure 3C) and a perfusion defect in the post-vascular (Kupffer) phase (Figure 3D). Laboratory tests showed no evidence of hepatitis B or C virus infection. Protein induced by vitamin K absence/antagonist-II (PIVKA-II) level was high, 72 mAU/mL, but alpha-fetoprotein level was within the normal range of 3.3 ng/mL (Table 1). There was no evidence of liver cirrhosis on laboratory or imaging tests. Furthermore, he had no history of alcohol intake.

As these two tumors seemed to be different according to imaging analysis, we concluded that histological evaluation was essential to diagnose these tumors. We performed endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for the pancreatic tumor and percutaneous ultrasound-guided biopsy for the liver tumor. Histologically, the pancreatic tumor was diagnosed as clear cell RCC, with positive staining for CD10 and vimentin, and negative staining

Key Clinical Message

In this report, we preoperatively diagnosed and appropriately treated two hypervascular tumors: pancreatic metastasis from renal cell carcinoma (36 years post-nephrectomy) and hepatocellular carcinoma. In some cases, preoperative histological evaluation may be essential for determining the management of tumors.

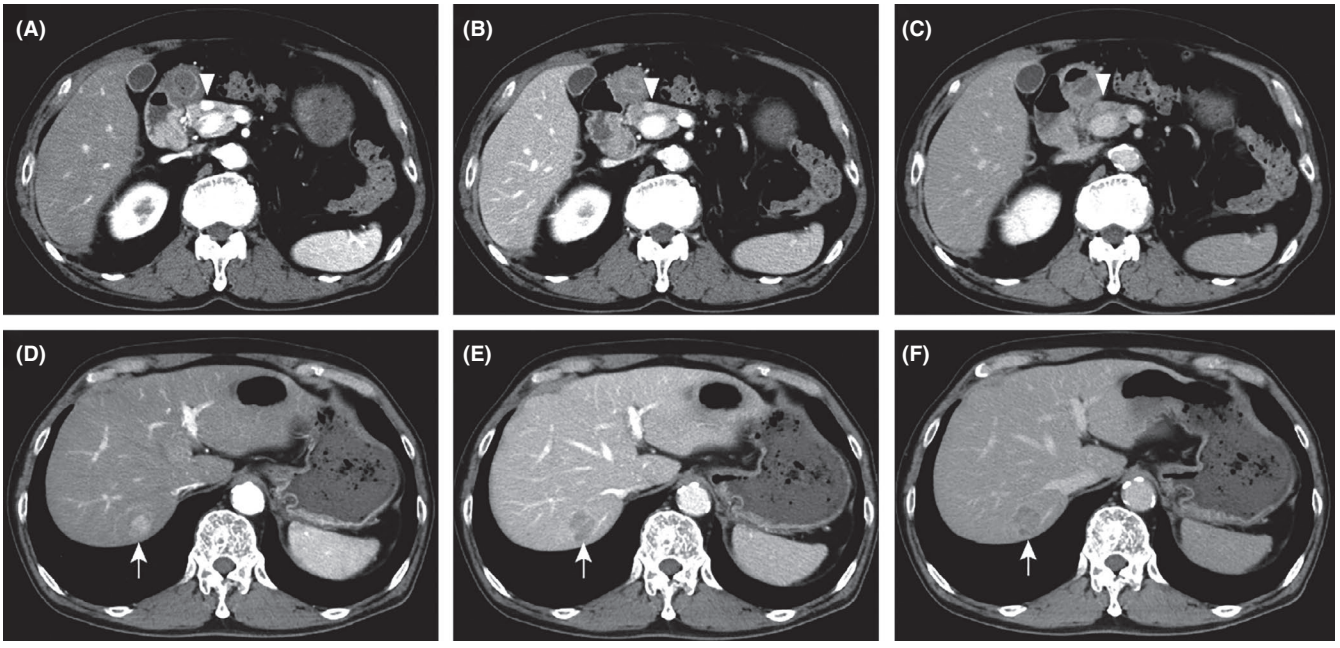

FIGURE 1 Computed tomography (CT) images. The pancreatic tumor (arrowhead) was located in the head of the pancreas and showed strong early enhancement in the arterial phase (A). The contrast medium was gradually diminished in the portal phase (B) and delayed phase (C). The liver tumor (arrow) was located in segment 7, with early enhancement in the arterial phase (D). The contrast medium was washed out in the portal phase (E) and delayed phase (F).

for synaptophysin and chromogranin A (Figure 4A-E). The liver tumor was diagnosed as moderately differentiated HCC (Figure 4F). Except for these two tumors, there was no additional evidence of malignancy. Middle pancreatectomy for the pancreatic tumor and partial liver resection for the liver tumor were therefore conducted as curative therapies. The final pathological diagnosis was identical to the preoperative diagnosis. No significant fibrosis or inflammation was observed in the resected liver. This patient was discharged from our institute 38 days post-surgery, and within the next seven months, there were no reports of complications or recurrence.

3 | DISCUSSION

In the case presented here, both the pancreatic tumor and liver tumor demonstrated a hypervascular pattern. Initially, we assessed these tumors to be pancreatic NETs with liver metastasis. However, CT revealed that the liver tumor had typical contrast patterns of HCC, and the PIVKA-II level was high enough to suspect HCC. Furthermore, we also considered the recurrence of RCC, which was resected 36 years ago. RCC can relapse even decades after primary diagnosis, and the pancreas is a known site for late-relapsing disease. Patients with recurrence in the pancreas tend to survive longer than those with recurrence at other sites.[4] For these reasons, we concluded that histological evaluation was necessary to make a diagnosis of these tumors prior to surgery.

EUS-FNA has been recognized as a useful and safe technique in diagnosing pancreatic ductal adenocarcinoma.[5,6] We used this technique to successfully diagnose pancreatic metastasis from RCC. Several studies have reported that EUS-FNA provides a highly specific diagnosis of metastatic pancreatic tumors (PMETs).[7–9] Krishna et al.[8] showed that the sensitivity, specificity, positive predictive value, and accuracy of EUS-FNA for diagnosis of PMETs were 84.9%, 100%, 100%, and 98.8%, respectively. In a study conducted by El Hajj et al.,[9] all patients with pancreatic metastasis from RCC (n = 21) were successfully diagnosed by EUS-FNA cytology.

In the case presented here, the pancreatic tumor was diagnosed by EUS-FNA as a metastatic RCC. Taking this pancreatic diagnosis into consideration, along with the radiological findings, there was not sufficient evidence to rule out either liver metastasis from the RCC, or HCC, as a diagnosis of the hypervascular liver tumor. Percutaneous ultrasound-guided biopsy of the liver tumor was therefore conducted, leading to a final diagnosis of HCC. Current guidelines [European Association for the Study of the Liver (EASL),[10] the American Association for the Study of Liver Diseases (AASLD),[11] and Japan Society of Hepatology (JSH)][12] propose surgery for cases of HCC, and we therefore selected partial liver resection as the treatment method.

The management of metastatic RCC has recently been revolutionized by the advancement of tyrosine kinase inhibitors (TKIs),[13,14] with six molecular targeted agents being approved in Japan in 2017.[15] While TKIs are a widely accepted treatment option in the patients with multiple metastases and palliative setting, the aforementioned studies suggest that resection of pancreatic metastases from RCC may still be indicated in select patients with low surgical risk and limited metastasis. Santoni et al.[16] suggested that the Memorial

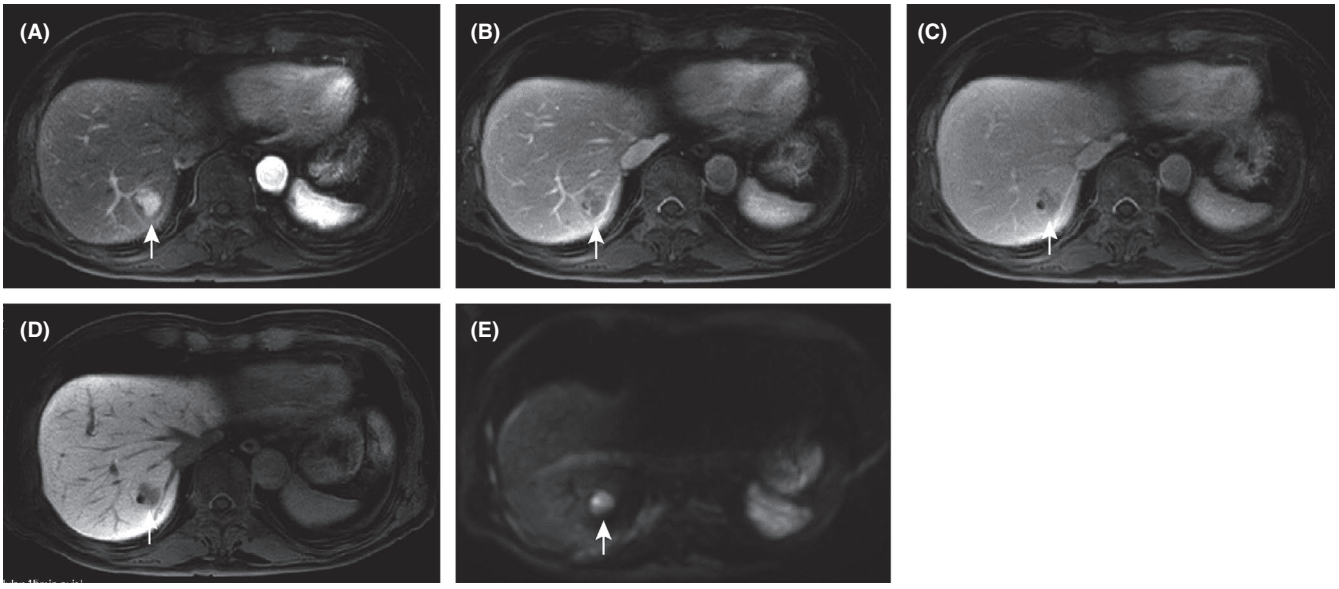

FIGURE 2 Gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid-enhanced magnetic resonance images. The liver tumor (arrow) showed hypervascularity in the arterial phase (A). The contrast medium was washed out in the portal phase (B) and delayed phase (C). This tumor showed hypointensity in the hepatobiliary phase (D) and restriction (hyperintensity) on the diffusion-weighted image (b value= 800 s/mm^2; E).

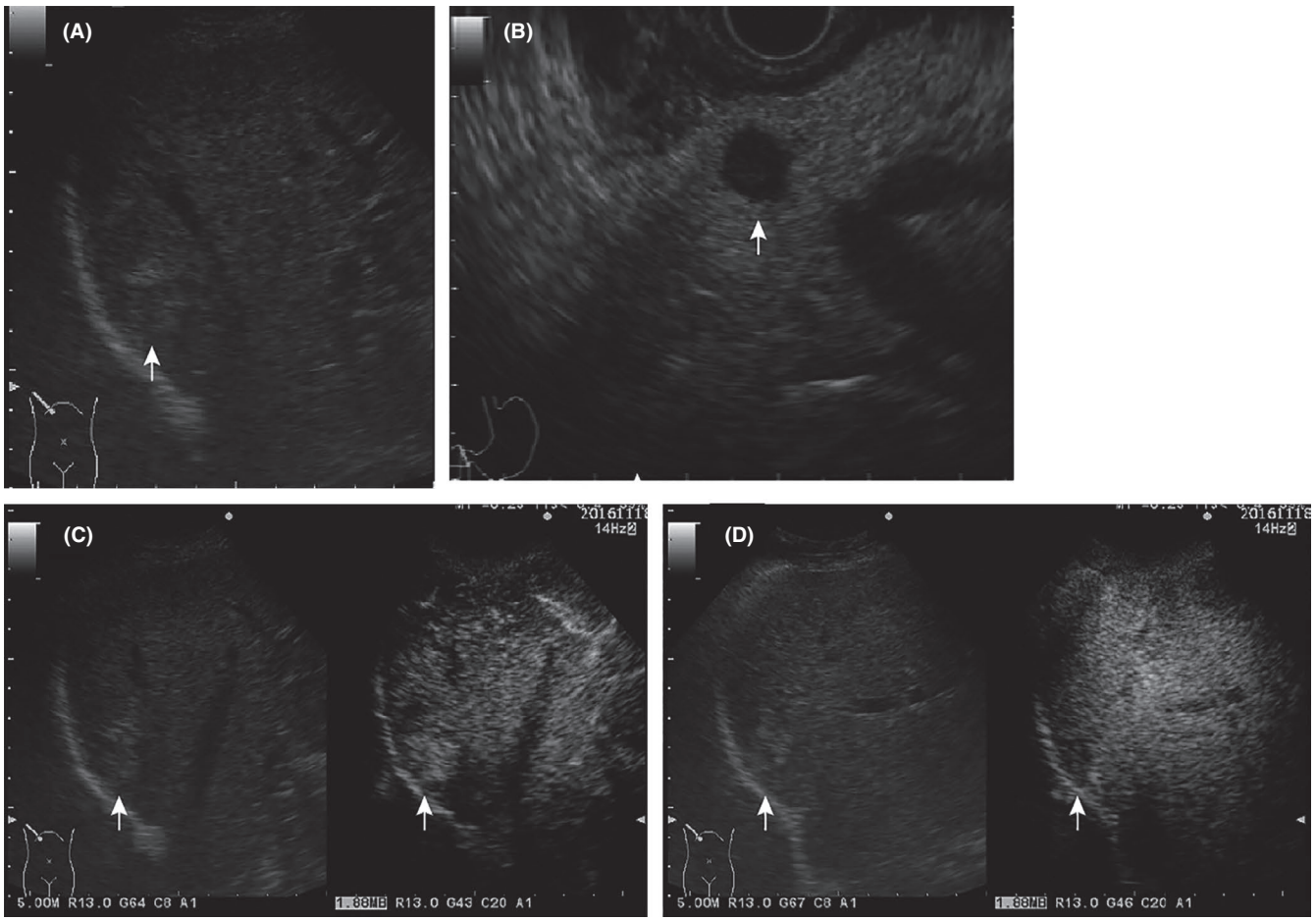

FIGURE 3 Ultrasound images. In the abdominal ultrasound examination, the hyperechoic tumor was located in segment 7 of the liver (A). Conversely, the pancreatic tumor was hypoechoic when viewed by endoscopic ultrasonography (B). Contrast-enhanced ultrasonography images are shown in C and D. Early enhancement of the liver tumor was observed in the vascular phase (C), and a perfusion defect was observed in the post-vascular (Kupffer) phase (D).

TABLE 1 Laboratory data on admission

<Peripheral blood>			<Blood chemistry>			<Tumor markers>		
WBC	8100	/μL	TP	7.6	g/dL	AFP	3.3	ng/mL
Neutro	60	%	Alb	4.5	g/dL	PIVKA-II	72	mAU/mL
Lymph	13	%	T-bil	0.4	mg/dL	CEA	1.7	ng/mL
Mono	26	%	D-bil	0.1	mg/dL	CA19-9	4.8	ng/mL
Eosino	1	%	AST	22	IU/L			
Baso	0	%	ALT	32	IU/L	<Serological test>		
RBC	420×10^4	/μL	LDH	169	IU/L	HBs Ag	(−)	
Hb	13.0	g/dL	γ-GTP	137	IU/L	HBs Ab	(−)	
Ht	39.0	%	ALP	256	IU/L	HBe Ag	(−)	
Plt	13.8×10^4	/μL	BUN	15	mg/dL	HBe Ab	(−)	
			Cr	1.05	mg/dL	HBc Ab	(−)	
<Coagulation test>			Na	145	mEq/L	HCV Ab	(−)	
PT	89.0	%	K	4.4	mEq/L	RPR	(−)	
APTT	33.9	sec	Cl	107	mEq/L	TPHA	(−)	
FBG	324	mg/dL	Ca	9.4	mEq/L			
FDP	4.6	μg/mL	CRP	0.44	mg/dL			
AT-III	117	%						

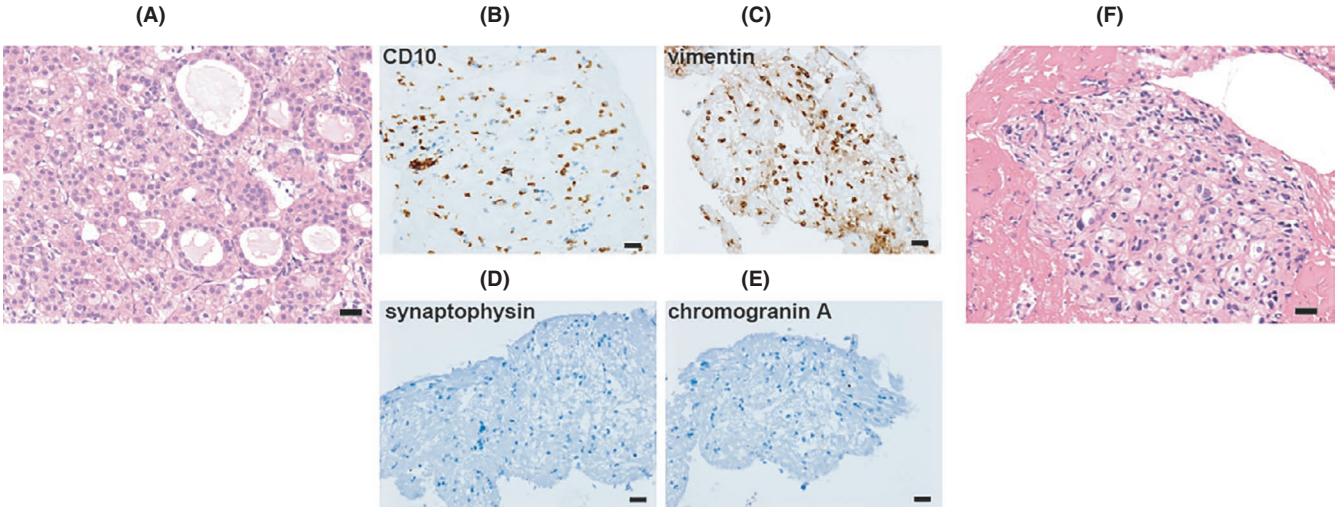

FIGURE 4 Histopathological images. They were obtained during endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for the pancreatic tumor (A-E) and percutaneous ultrasound-guided biopsy for the liver tumor. The pancreatic biopsy sample was stained with hematoxylin and eosin (HE). The tumor cells had clear cytoplasm and were arranged in nests (A). The pancreatic tumor cells were positive for CD10 (B) and vimentin (C) and negative for synaptophysin (D) and chromogranin A (E). The liver biopsy sample was stained with HE. It showed moderately differentiated hepatocellular carcinoma growing in a pseudoglandular pattern (F). Scale bar = 200 μm.

Sloan Kettering Cancer Center (MSKCC) prognostic criteria for advanced RCC[17] are an independent predictor of survival in patients with PMETs of RCC and could be a useful indicator for patient selection. In the case presented here, the patient had the solitary metastatic site (pancreas) and no risk factors of the MSKCC prognostic criteria. Median survival time was reported to be just 19.9 months in this group,[17] and we expected long-term survival following surgical treatment in this case.

The median interval between nephrectomy and pancreatic recurrence of RCC has been reported to be 104 months (range 0–348 months).[18] Late recurrence is one of the common clinical features of pancreatic metastasis from RCC. However, the patient in this study had a history of left nephrectomy 36 years earlier, and this particularly long duration between nephrectomy and recurrence is extremely rare. The mechanism of pancreatic metastasis from RCC remains controversial and has not been fully clarified.[19] According to Ballarin et al.,[20] the most likely explanation for late recurrence lies in the specific biology of the tumor. Tumor cells appear to have high affinity for the parenchyma of the pancreas, and only there do they have the conditions necessary to mature and become metastatic.

In conclusion, we encountered a rare case in which a patient was diagnosed with two hypervascular tumors: pancreatic metastasis from RCC (36 years post-nephrectomy) and HCC. In the case presented here, histological evaluation was essential in making an accurate diagnosis prior to surgery, since CT revealed that both tumors presented similar enhanced patterns. Surgical resection of both tumors contributed to longer survival. However, treatment strategies may differ from case to case. Such cases should be discussed in multidisciplinary teams to improve patient outcomes.

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CONFLICT OF INTEREST

The authors state that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

HN and ST: drafted the manuscript. KM, YK, TO, KI, MY, HO, KM, KT, HY, MN, and YK: were involved in the patient's care. IT and JK: supervised the study.

ETHICAL APPROVAL

This study does not require any ethical committee approval.

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