Cholangiolocellular Carcinoma of the Liver Exhibiting High F-18 FDG Uptake

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Cholangiolocellular carcinoma (CoCC) is a rare primary liver cancer. It is considered to originate from hepatic progenitor or stem cells. We report a rare case of a 74-year-old male with CoCC of the liver and duodenal gastrointestinal stromal tumor (GIST). Both tumors manifested tracer uptakes on F-18 fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT); however, the uptake in hepatic tumor was extremely higher than that in the duodenal tumor. This finding was helpful to exclude the metastasis of GIST.

Key words: cholangiolocellular carcinoma, duodenal gastrointestinal stromal tumor, F-18 fluorodeoxyglucose positron emission tomography/computed tomography

INTRODUCTION

Cholangiolocellular carcinoma (CoCC) is a rare malignant liver tumor accounting for 1% of all primary liver cancers which was first reported by Steiner and Higginson [1]. They described the distinct pathological characteristics of CoCC which derives from the cholangioles or the smallest and most peripheral branches of the biliary tree (canals of Hering). CoCC is categorized as a subtype of intrahepatic cholangiocarcinoma (ICC) on the basis of World Health Organization (WHO) [2] and the 4th edition of the General Rules for the Clinical and Pathological Study of Primary Liver Cancer in Japan [3]. However, recent advancements in the study and knowledge of hepatic progenitor cells (HPCs) [4], which exist in canals of Hering, have suggested that CoCC originates from HPC. Thus, the new classification in the 6th edition of the General Rules for the Clinical and Pathological Study of Primary Liver Cancer in Japan, published in 2015 [5], proposes that CoCC is independent from ICC.

CoCC sometimes contain a hepatocellular carcinoma (HCC) or ICC component within a tumor because the origin might be HPC. It sometimes confuses a diagnosis of CoCC by images such as compused tomography (CT), magnetic resonance imaging (MRI).

We report a case report that the F-18 FDG PET/CT was helpful to diagnosis the liver tumor with duodenal gastrointestinal stromal tumor (GIST) to CoCC in distinction from the liver metastasis of the duodenal GIST.

CASE REPORT

A 74-year-old male was incidentally diagnosed with a hepatic tumor by abdominal ultrasonography. Almost serum biochemistry and tumor markers, such as AFP, PIVCA-II, and Carcinomenbyonic antigen were within normal range, but Aspartate 2-oxogulutarate aminotransferase (80 U/l),Aalanine aminotransferase (62 U/l) and Carbohydrate antigen 19−9 (at 176 U/ml) were elevated. Hepatitis B surface antigen and hepatitis C virus antibody were negative.

Abdominal contrast-enhanced CT images showed two hypervascular tumors (Fig. 1). One was in the right lobe of liver and the other in the third part of duodenum, with diameters of 3.5 cm and 4 cm, respectively. The hepatic artery and portal vein passed through the hepatic tumor on early and portal phases. The tumor kept heterogenerous enhancement on delayed phases without washing out. The margin of the tumor was clear. A duodenal hypervascular tumor had central low density area, suspected to be cystic change or necrosis.

On MRIs, The hepatic tumor was low intensity on T1-weighted image, whereas, an area of high intensity was observed at the periphery of the tumor on T2-weighted image. The diffusion-weighted imaging showed high intensity. The tumor showed low uptake on hepatocellular phase on Gd-EOB-DTPA enhanced MRI (Fig. 2).

F-18 FDG PET/CT images showed tracer uptakes on both tumors and the maximum standardized uptake value (SUVmax) of hepatic and duodenal tumors was 25.2 and 3.12, respectively (Fig. 3). The uptake in

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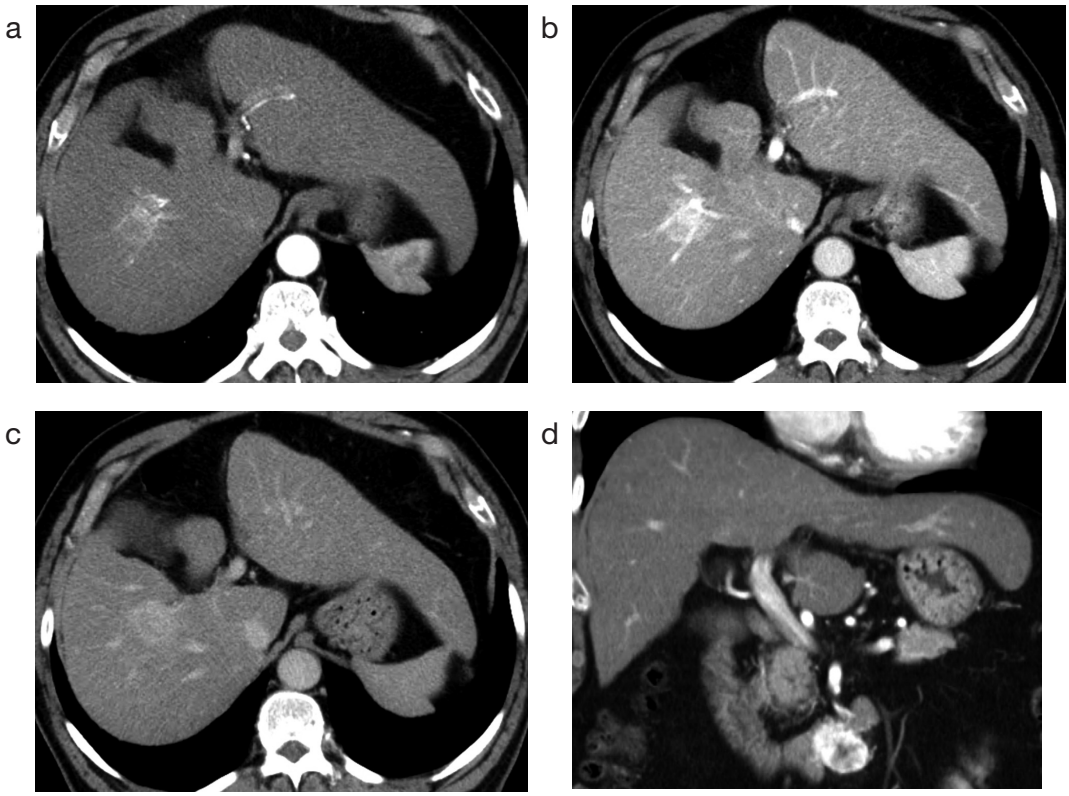

Fig. 1 Contrast-enhanced CT images
(a) An early-phase image shows a hypervascular tumor in the right lobe of liver with diameters of 3.5 cm. A portal-phase (b) and a delayed-phase (c) images show a hetrogeneous hyper attenuating tumor without washing out. The hepatic artery and portal vein passed through the hepatic tumor on early- and portal-phases. (d) A coronal reformatted image of early-phase shows a duodenal hypervascular tumor in the third part of duodenum with diameters of 4 cm. A duodenal tumor has central low density area, suspected to be cystic change or necrosis.

hepatic tumor was significantly higher than that in the duodenal tumor (Fig. 3: arrow).

Right anterior segmentectomy of the liver and partial duodenectomy were performed.

Photomicrography of the resected hepatic tumor showed that small oval tumor cells arranged in anastomosing tubular pattern were increased (Fig. 4). Final pathological diagnosis was CoCC of the liver.

While, final pathological diagnosis of duodenal tumor was benign duodenal GIST because photomicrography of the resected duodenal tumor showed that fascicles of slender spindle cells without mitosis and the tumor cells were positive for C-Kit and DOG-1(Fig. 5).

DISCUSSION

CoCC is a rare malignant liver tumor accounting for 1% of all primary liver cancers.

Thus, there have been a small number of reports revealed the imaging findings of CoCC.

Motosugi *et al.* [6] reported that CoCC occasionally exhibited HCC-like uniform and complete early enhancement or ICC-like peripheral ringlike enhancement. A delayed washout pattern and capsulelike enhancement, such as that found in HCC, however, was not observed in CoCC. This was true even in the case of CoCCs that showed HCC-like early enhancement because of abundant fibrosis among tumor nests (abundant fibrosis is not usually observed in HCC). The combination of early enhancement and delayed retaining enhancement is considered a characteristic imaging finding of CoCC; however, this is also observed in combined HCC-CC. Additionally, CoCC with dense central fibrosis exhibits imaging features that are quite similar to those of ICC, such as peripheral rimlike enhancement, central delayed enhancement.According to the summarized report of nine cases of CoCC by Kanamoto *et al.* [7], MRIs were performed in 4 of the 9 cases and shows hypointensity on T1-weighted images and hyperintensity on T2-weighted images in all cases. Motosugi *et al.* [6] reported that T2-weighted images showed heterogeneously high intensity of the entire tumor in 2 lesions (2/5 40%) and predominantly peripheral high intensity in 3 lesions (3/5, 60%). The area of high intensity on T2-weighted images of CoCC might reflect edematous fibrosis stroma.

CoCC also tends to show that the vascular such as portal vein passed through the tumor without invasion on dynamic study because of the replacement growth pattern [8, 9].

In recent reports [4, 10, 11], CoCC is considered to originate from hepatic progenitor or stem cells. That might be why that CoCC cells often proliferate heterogeneously and presents ICC-like and HCC-like areas within the tumor. Because of this complexed pathology, it is often difficult that CoCC is differentiated from other tumors such as combined HCC-CC, ICC, liver metastasis, and liver hemangioma etc. by imagings. These imaging findings have over raps, respectively.

In our case, the liver tumor was hypervascular

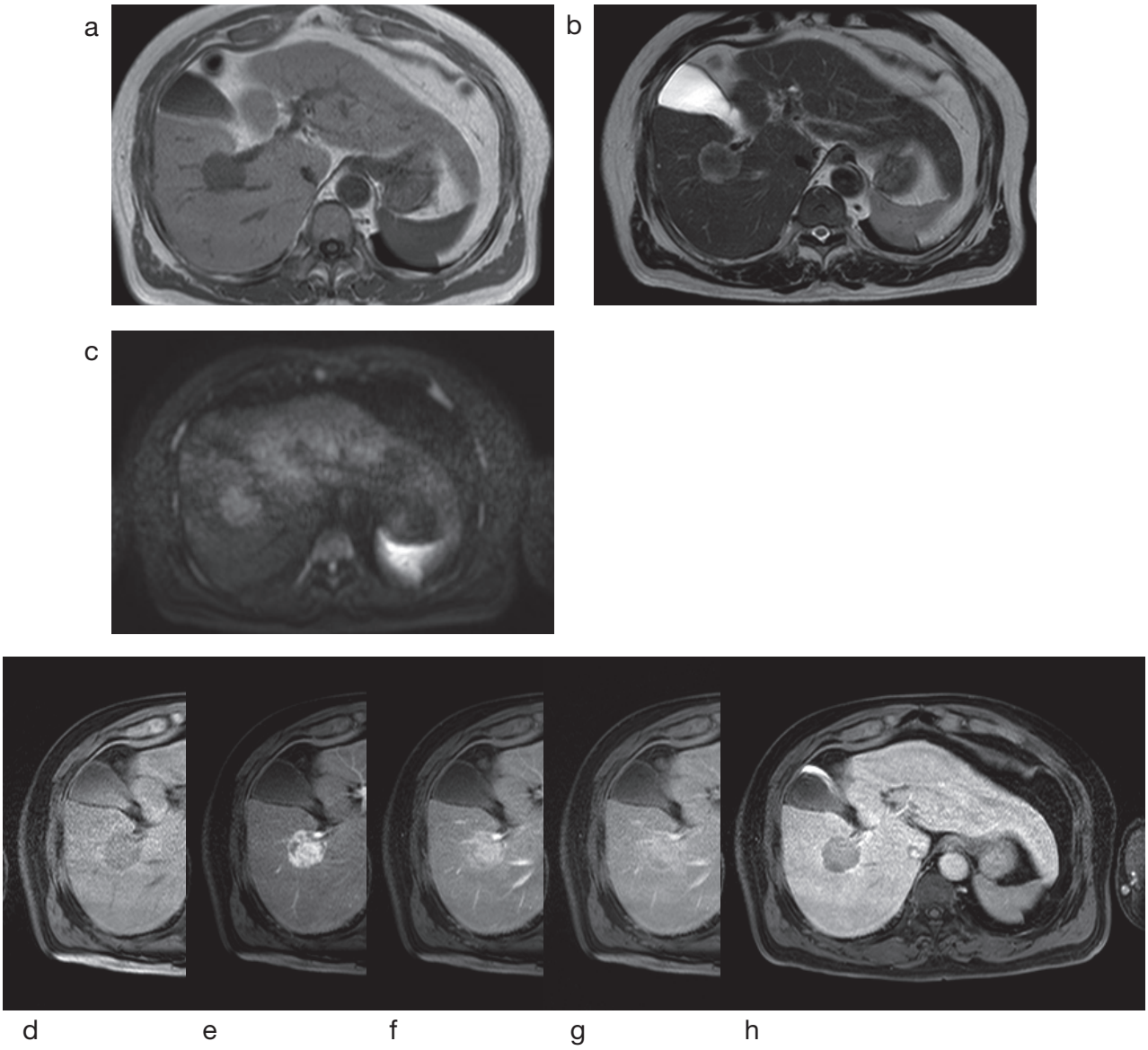

Fig. 2 Magnetic resonance images
(a) On T1-weighted image, the hepatic tumor is low intensity. (b) T2-weighted image shows an area of high intensity at the periphery of the tumor, and most of the lesion appeared isointense. (c) The diffusion-weighted image shows high intensity. (d) A Fat Sat. T1-weighted image shows low intensity. (e) An early-, (f) a portal- and (g) a delayed-phase on Gd-EOB-DTPA enhanced images show same dynamic enhanced pattern as contrast-enhanced CT. (h) A hepatocellular-phase on Gd-EOB-DTPA enhanced shows low uptake.

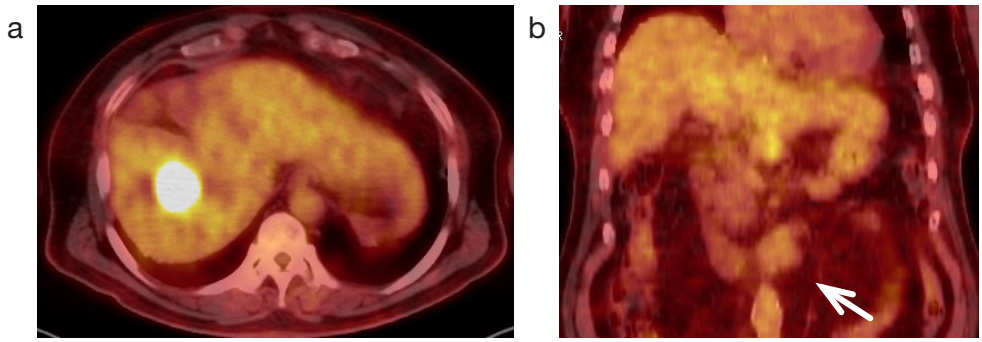

Fig. 3 F-18 FDG PET/CT images
F-18 FDG PET/CT images show tracer uptakes on both tumors and the maximum standardized uptake value (SUVmax) of hepatic and duodenal tumors was 25.2 (a) and 3.12 (b), respectively. The uptake in hepatic tumor is significantly higher than that in the duodenal tumor (b: arrow).

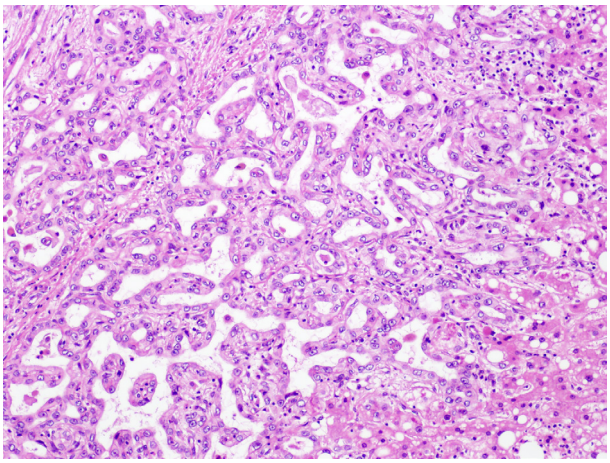

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Fig. 4 Photomicrography of the resected hepatic tumor shows that small oval tumor cells arranged in anastomosing tubular pattern are increased. HE: hematoxylin and eosin stain

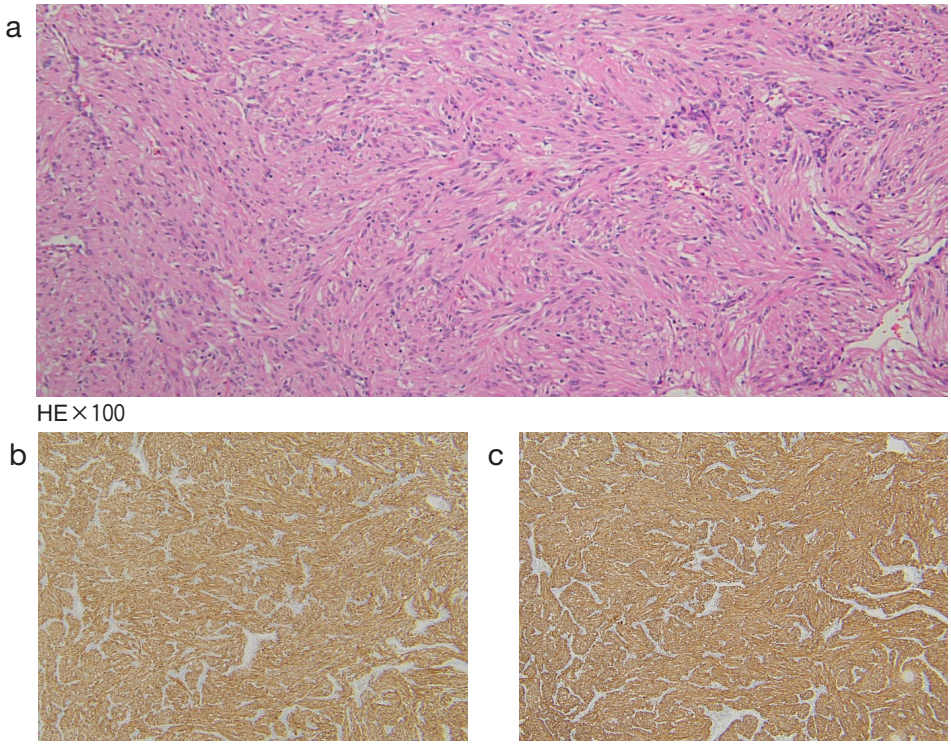

Fig. 5 Photomicrography of the resected duodenal tumor shows that fascicles of slender spindle cells without mitosis and the tumor cells (a) are positive for C-Kit (b) and DOG-1(c). HE: hematoxylin and eosin stain

without delayed washing out and the vascular passed through the tumor without invasion. These findings were more suspected CoCC than ICC, classical HCC and liver metastatasis.

The other side, GIST is also a hypervascular submucosal gastrointestinal tumor. The possibility of malignancy is associated with large size (> 5–6 cm) and associated ulceration and necrotic lesion [12, 13]. Thus, in our case, the tumor could not be ruled out liver metastasis of the duodenal GIST.

In our case, the CoCC had an extremely higher uptake than that of the duodenal GIST on F-18 FDG PET/CT. Sometimes an uptake in metastatic lesion is higher than that in the primary lesion on F-18 FDG PET/CT [14]. Through it is said so, in our case, the gap of the uptake between them was extremely big. Additionally, the duodenal GIST showed the SUVmax of under 5 on F-18 FDG PET/CT while GIST with an SUVmax of over 5 on F-18 FDG PET/CT may be malignant [15]. In result, it was suspected that the liver tumor was not metastasis of duodenal GIST but CoCC.

It is suggested that malignant CoCC cells develop significant alterations in metabolism during the process of transformation from normal cells. Different uptakes of two tumors on F-18 FDG PET/CT might be caused by malignant potential and tumor characteristics.

The sensitivity of FDG-PET for HCC is low, approx-

imately 50%. There appears to be some association between the histological differentiation of HCC and FDG uptake, with poorly differentiated tumors showing higher intensity on FDG-PET, which may be explained by the enzymology of HCC [16]. Thus, only using F-18 FDG PET/CT, CoCC could not be distinguished from poorly differentiated hepatocellular carcinoma and high-volume ICC etc. because both of them also present high FDG uptake [16].

It is expected that F-18 FDG PET/CT could be one of the helpful modality about diagnosis of CoCC in addition to CT and MRI like our case.

In conclusion, CoCC is one of malignant hepatic tumors with high uptake on F-18 FDG PET/CT.

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