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Case Report

Ectopic hepatocellular carcinoma, an unexpected diagnosis of a retroperitoneal mass: A case report and literature review ☆

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ABSTRACT

Ectopic hepatocellular carcinoma (HCC) is defined as HCC arising from hepatic parenchyma located in an extrahepatic organ or tissue without any communication with the mother liver. It is very rare and difficult to diagnose by imaging alone. We report a case of a rare ectopic HCC mimicking a right para-aortic retroperitoneal mass and present a review of the literature. It is about a 79-year-old female patient, who presented with a progressive enlarged right paraaortic retroperitoneal mass, thought first to be leiomyosarcoma of vena cava on imaging. Subsequently, high alpha-fetoprotein (AFP) level and biopsy allowed the diagnosis of primary extrahepatic hepatocellular carcinoma.

Introduction

Ectopic hepatocellular carcinoma (HCC) is defined as HCC arising from hepatic parenchyma located in an extrahepatic organ or tissue without any communication with the mother liver [1]. Ectopic liver tissue by itself is very rare with incidence ranging between 0.27% to 0.7% of the general population [2]. Thus, ectopic HCC is exceptional. It can occur anywhere near the liver; for example, gallbladder, hepatic ligaments, omentum, retroperitoneum, and thorax [3]. HCC is usually associated with elevated alpha-fetoprotein (AFP) levels [4]. Here, we report a case of extrahepatic HCC located in the retroperitoneum near the inferior vena cava (IVC), not arising from any other solid organ, mimicking a right para-aortic lymphadenopathy, with elevated AFP levels. To our knowl-

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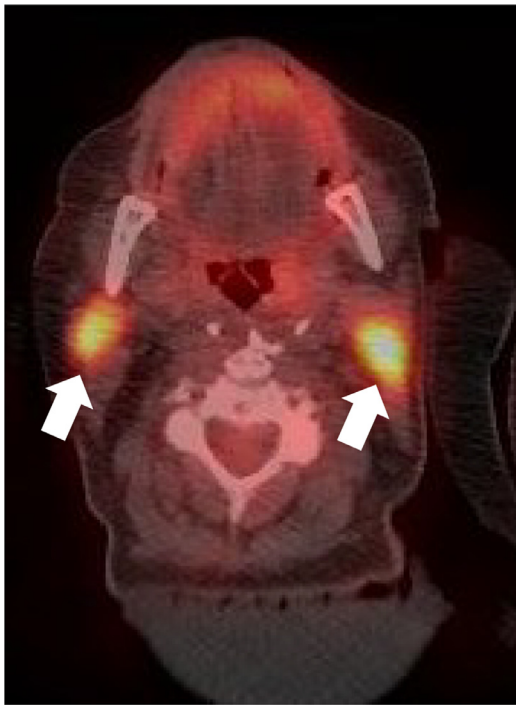

Fig. 1 – First PET-Scan showing FDG avid bilateral enlarged cervical lymph nodes (arrows).

edge, it is the most recent reported case in this location since 2014 [5].

Case report

A 79-year-old female patient presented to our radiology department for evaluation of a retroperitoneal mass. Her past medical history is significant for breast cancer in remission since 2010.

History started 16 months ago, when she noticed enlarged palpable lymph nodes in her neck, for which she sought medical advice. A PET-Scan was ordered as part of the workup. It showed FDG avid enlarged cervical lymph nodes (Fig. 1) and an enlarged FDG avid nodule, right-sided, anterior to the IVC, measuring 26 mm in short axis with a max SUV of 17.6 (Fig. 2). One of the enlarged cervical lymph nodes was biopsied, and histopathology showed Warthin tumor without evidence of malignancy. After that, the patient was lost to follow up for financial problems.

About 10 months later, she presented to the emergency room for abdominal pain. Abdominal CT-Scan showed an increase in size of the previously described retroperitoneal nodule, reaching 4 cm in diameter (Fig. 3). About 2 months later, a follow up MRI showed a further increase in the diameter of this nodule reaching 5.9 cm. The nodule exhibited restricted diffusion on DWI and progressive enhancement after gadolinium injection; however, the characteristic wash-in and washout usually encountered in hepatic hepatocellular carcinoma were not seen. No hepatic lesion was identified (Fig. 4).

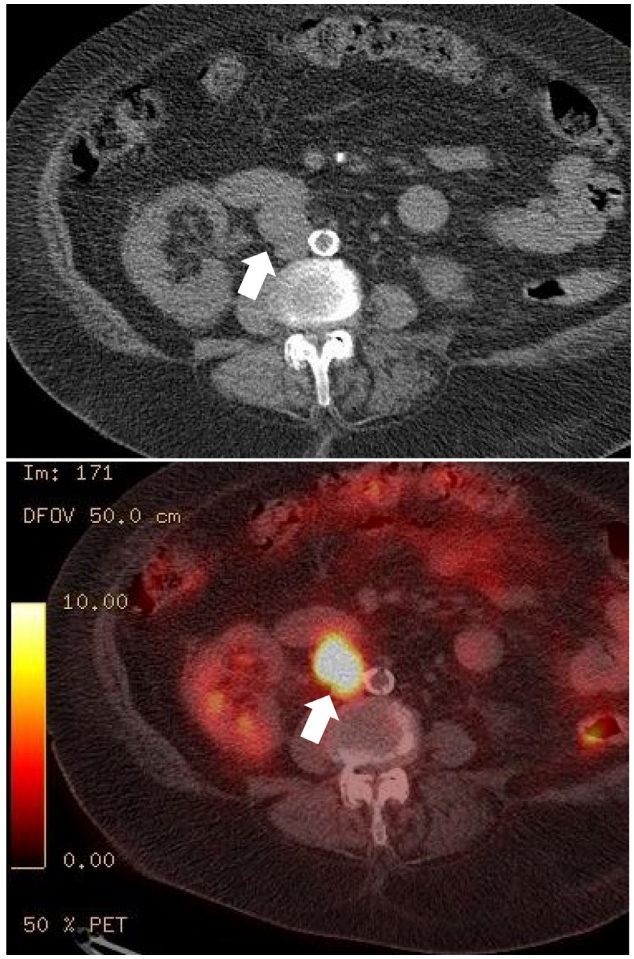

Fig. 2 – First PET-Scan showing enlarged FDG avid right-sided nodule anterior to the IVC measuring 26 mm in short axis with an SUV max of 17.6 (arrows).

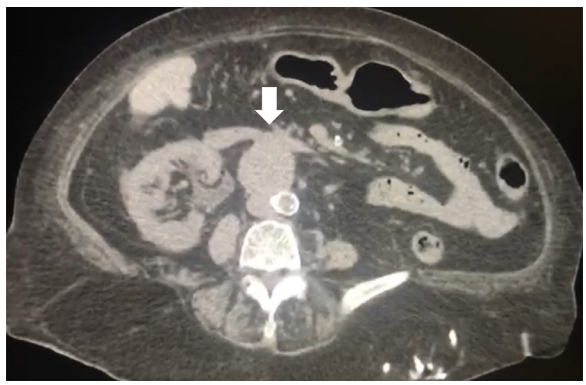

Fig. 3 – CT-Scan showing progression of the retroperitoneal nodule, anterior to the IVC, reaching 4 cm in diameter (arrow).

A percutaneous biopsy of the retroperitoneal nodule was performed. Histopathology showed a poorly differentiated carcinomatous tissue. Immunostains with adequate controls

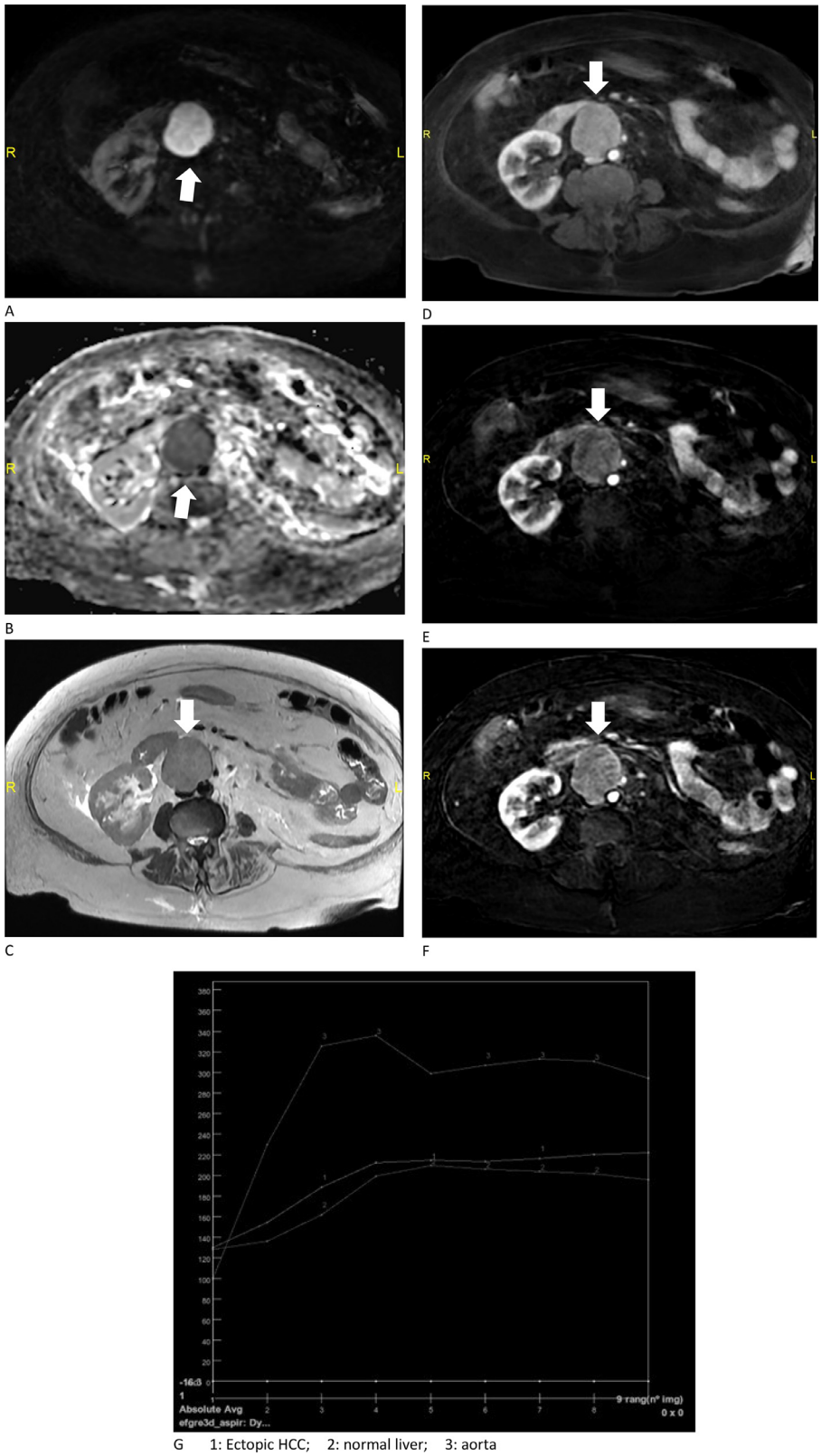

Fig. 4 – MRI showing progression of the retroperitoneal mass (arrows) reaching 5.9 cm in diameter with restricted diffusion on DWI (A), corresponding ADC map (B), and intermediate signal on T2-weighed imaging (C). Dynamic gadolinium injection series (D, with subtraction: E and F, injection kinetic curve: G) showed progressive enhancement. However, the characteristic wash-in and wash-out typical of hepatic hepatocellular carcinoma was not seen.

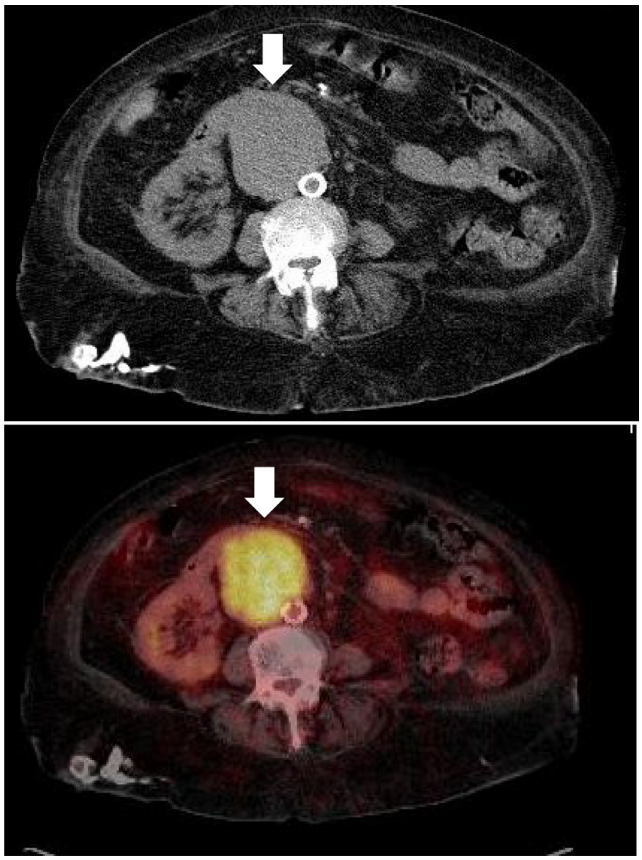

Fig. 5 – Follow-up PET-Scan 16 months after the first one shows interval progression of the pericaval retroperitoneal mass (arrows) measuring up to 7.5 cm with SUV max of 10, with no evidence of metastatic adenopathy, liver or bone disease.

were positive for CK AE1/AE3, extensively positive for Hep Per-1, multifocally with Glypican 3, with cytoplasmic positivity for TTF-1, and negative for ER, GATA3, HER-2/Neu, CK20, CDX2, PAX 8, Inhibin, CD117 and DOG 1. These findings were in favor of a hepatocellular carcinoma. PET-Scan was repeated 1 month later showing interval progression of the pericaval retroperitoneal mass measuring up to 7.5 cm with SUV max of 10, with no evidence of metastatic adenopathy, liver, or bone disease (Fig. 5). Assay of serum tumor markers showed a carcinoembryonic antigen (CEA) of 6.5 ng/mL, a CA-15-3 of 18.9 u/mL and an AFP of 4655 ng/mL. The biopsy results with elevated AFP serum marker and the absence of a liver lesion were compatible with the diagnosis of an ectopic retroperitoneal hepatocellular carcinoma.

Discussion

The ectopic liver is a tissue similar to liver tissue regarding morphology and histology; however it has an abnormal location without a linking structure to the mother liver [6]. Embryology may provide a possible basis for the presence of ectopic hepatic tissue. Liver development starts in the middle of the third week of embryonic life. The hepatic diverticulum (liver bud) is formed from the foregut and becomes a hepatocellular cord. Subsequently, a bile duct, a gallbladder and a gallbladder duct develop from a connection part between the hepatic diverticulum and the foregut [3]. According to congenital theory, any variation in hepatic diverticulum development would lead to liver ectopy. Therefore, the gallbladder is the most frequent place for ectopic liver tissue based on its closest position to the original liver in the embryonic development period. Ectopic liver tissue can also be found in the adrenals, diaphragm, pancreas, spleen, stomach, jejunum, peritoneum, thorax, and retroperitoneum. (Table 1) summarizes the previous reported ectopic hepatocellular carcinoma [6,7].

Ectopic HCC is an HCC arising from ectopic liver tissue. It is one of the rare carcinomas, usually discovered incidentally during autopsy or laparoscopy [8].

A survey of the literature showed that a significant proportion of patients with ectopic liver tissue were found to have ectopic HCC, which may indicate that ectopic liver tissue is more prone to develop HCC. The basis behind this hypothesis may be a histopathology difference such as an abnormality of vascular supply or biliary drainage [6].

Ectopic HCC is often asymptomatic, however a variety of clinical presentations were described, including abdominal pain, poor appetite, nausea and asymptomatic palpable mass [6]. In the case of our patient, ectopic HCC was initially an incidental finding. Later on, the patient developed abdominal pain.

The diagnosis of ectopic HCC is difficult without obtaining histopathology. Indeed, the clinical presentation is nonspecific, and laboratory testing and imaging rarely lead to confirmation of the diagnosis.

Serum AFP can be a useful marker when suspecting ectopic HCC. In healthy adults, serum AFP level typically measures 5 to 10 ng/mL. An elevated AFP serum level is frequently associated with HCC or other liver diseases. Studies have shown that an AFP level above 400 ng/mL can generally be considered as diagnostic for HCC [9]. A review of the literature showed that an elevated AFP >20 ng/ml is encountered in 54% to 62% of cases of ectopic HCC [6].

Immunohistochemistry plays a crucial role in the diagnosis of ectopic HCC. The tissue markers currently used to histologically diagnose HCC are hepatocyte paraffin 1 (HepPar-1), Glypican-3 (GPC3), arginase-1, CD10, polyclonal carcinoembryonic antigen (pCEA), and bile salt export pump (BSEP) [10].

Hepatocyte paraffin 1 is an antibody to carbamoyl phosphate synthetase 1, a urea cycle enzyme of mitochondria, predominantly expressed in the liver and also in other organs. It is usually strongly expressed in normal liver, hepatoblastoma, and HCC cells. HepPar-1 is considered a marker of all tumors with hepatoid features. HepPar-1 has 70%–84% overall sensitivity for the diagnosis of HCC [10]. Similarly, ectopic HCC was reported to be frequently positive for hepatocyte or hepatocyte-paraffin-1. Therefore, HepPar 1 is considered as an essential clue for ectopic HCC diagnosis. [6].

Glypican-3 (GPC3) is a membrane-anchored heparin sulfate proteoglycan normally expressed in fetal liver and placenta,

Table 1 – Updated summary table of the previous reported cases with their location and size [6,7].

Case	Study	Location	Size – greater diameter (cm)
1	Our Case (2024)	Right paraaortic retroperitoneal	7.5
2	Park et al. [11]	Stomach	7.2
3	Yang et al. (2022)	Right adrenal	11.8
4	Liu et al.	Tail of pancreas	1.8
5	Bravo-Taxa et al. [12]	Stomach	17.0
6	Wei et al.	Right adrenal	9.1
7	Adachi et al.	Head of pancreas	6.0
8	Ko et al.	Peritoneum	5.5
9	Rorris et al.	Right adrenal	3.2
10	Li et al.	Near the pancreas	5.0
11	Jin et al.	Abdominal	30.0
12	George et al.	Choledochal cyst	N/A
13	Cheng et al.	Bile duct and gallbladder	N/A
14	Cui et al.	Thoracic and abdominal cavities	N/A
15	Lee et al.	Left subphrenic region	3.8
16	Aarås et al.	Diaphragm	3.5
17	Segura-Sanchez et al.	Gallbladder	12.0
18	Miyake et al.	Abdominal cavity	1.0
19	Nishikawa et al.	Left diaphragm	N/A
20	Nenekidis et al.	Chest wall and skull	7.0
21	Singh et al.	Left suprarenal region	8.0
22	Matsuyama et al.	Spleen	6.0
23	Kanzaki et al.	Left diaphragm	2.0
24	Schmelzle et al.	Extrahepatic bile duct	N/A
25	Seo et al.	Left subphrenic space	4.5
26	Kubota et al.	Tail of pancreas	6.3
27	Huang et al.	Diaphragm	16.0
28	Shigemori et al.	Lower abdomen	14.0
29	Tsushimi et al.	Bile duct	2.7
30	Kim et al.	Between spleen and diaphragm	10.0
31	Asselah et al.	Left chest wall	17.0
32	Takayasu et al.	Left diaphragm	5.0

but not in normal adult liver. It was reported that GPC3 was significantly expressed in HCC rather than normal liver and nonmalignant liver lesions. GPC3 has an overall specificity for HCC of 86%, however the use of GPC3 alone to establish the exact histogenesis of a liver tumor should be evaluated carefully [10].

We searched " retroperitoneal ectopic hepatocellular carcinoma case report " in PubMed, and 4 case reports were found. Only 1 case of retroperitoneal tumor not arising from any other solid organ, mimicking a left paraaortic lymphadenopathy, was identified, dated in 2014 [5]. Our case is the most recent similar reported case to our knowledge since 2014 and has the feature of presenting its aspect in different imaging modalities (Figs. 2-5). In the absence of liver lesions, our imaging findings with positive Hepatocyte paraffin 1 and Glypican-3 on biopsy and elevated serum AFP (> 400 ng/mL) were diagnostic for primary ectopic hepatocellular carcinoma.

We still lack precise information regarding the evolution and prognosis of ectopic HCC and the efficiency of available treatments.

In a literature review of 27 patients with ectopic HCC, 26 patients underwent surgical operation, and the majority recovered well [6]. Therefore, ectopic HCC seems to have an excellent outcome with complete resection. This makes surgery the first choice for patients with ectopic HCC who are surgical candidates.

On the other hand, around one-quarter of the patients who underwent radical surgery had recurrence [6].

Although tumor resection is being performed in the majority of ectopic HCC, the clinical benefit of tumor resection is still controversial with potential excellent therapeutic outcome, since the carcinogenetic potential of these tumors is usually limited to the ectopic liver only, and requires long-term follow up [3,11].

Metastatic ectopic HCC was reported in 5 patients.

Other treatment options include chemotherapy, transarterial chemoembolization, and Sorafenib. The review showed an overall survival rate at 1 and 3 years of 92.6% and 85.2% respectively [6]. These numbers are comparable to the survival rate in patients with HCC, based on a study showing the 1- and 3-year overall survival rate to be 96.6% and 88.8% respectively [13].

In our patient, the tumor has tripled in size in approximately 16 months (between the 2 PET-CTs) with no evidence of locoregional invasion or metastasis.

Conclusion

Ectopic liver tissue is generally more prone to develop HCC. The diagnosis of ectopic HCC is often challenging. The cornerstone is elevated AFP serum marker along with immunohistochemical staining (Hepatocyte paraffin 1 and Glypican-3). Concerning therapeutic options, tumor resection seems to have acceptable results.

Patient consent

The authors confirm that a written informed consent was obtained from the patient for the publication of this case report and accompanying images.

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