Clinical Journal of Gastroenterology (2019) 12:336–340
https://doi.org/10.1007/s12328-019-00934-6

CASE REPORT

Recurrence of hepatocellular carcinoma at the porta-hepatis following liver transplantation diagnosed on EUS-FNA

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Received: 9 November 2018 / Accepted: 7 January 2019 / Published online: 17 January 2019

Abstract
Hepatocellular carcinoma (HCC) is a potentially fatal complication of chronic liver disease. Liver transplantation is now the preferred treatment due to good outcomes. We present a unique case of recurrence of HCC at the porta hepatis four years after orthotopic liver transplantation diagnosed via endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). Our report also highlights that intrahepatic recurrence of HCC can be surgically treated. However, further studies are needed to develop treatment algorithms for intra-hepatic recurrence of HCC post liver transplantation.

Keywords HCC (hepatic cellular carcinoma) · Liver transplant · EUS (endoscopic ultrasound)

Introduction

Hepatocellular carcinoma (HCC) is a potentially fatal complication of chronic liver disease. Several treatment options including radiological therapies, resection, and liver transplantation are available both pre and post-liver transplantation. Liver transplantation is the preferred treatment due to positive long-term outcomes, however, no definite treatment guidelines exist for treatment of HCC recurrence post-orthotopic liver transplantation (OLT). The most common sites of HCC recurrence post-OLT are extrahepatic, including the lung, bone, abdominal lymph nodes, adrenal glands, and peritoneum [1–4]. We present a unique case of recurrence of HCC at the porta hepatis 4 years after OLT which was diagnosed using endoscopic ultrasound-guided fine needle aspiration (EUS-FNA).

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Case report

A 57-year-old male with a past history of OLT four years prior due to decompensated cirrhosis and HCC presented after a lesion was found at the porta hepatis during routine post-OLT screening for HCC. The patient had a long-standing history of hepatitis C virus (HCV) infection. Six years prior to his current presentation, he was found to have a hypoechoic lesion in the left lobe of the liver on ultrasound of his liver performed for HCC screening. Subsequently, a computed tomography (CT) scan of the liver showed a 2.1 cm ill-defined lesion in the left hepatic lobe. A liver biopsy was performed which showed mildly enlarged nuclei, absence of significant pleomorphism, focal loss of reticulin, several pseudoacinar formations, mild nuclear enlargement, and increased nuclear to cytoplasmic ratios which were consistent with HCC. After a multi-disciplinary discussion, the decision was made to perform radiofrequency ablation (RFA). The patient did well post procedure.

In the interim, the patient was evaluated and listed for OLT after he received MELD exception points due to his HCC which increased his MELD score to 25. During this time the patient underwent transjugular intrahepatic portosystemic shunt (TIPS) placement for bleeding gastric varices. Despite this, the patient continued to decompensate and his MELD score increased to 29. Fortunately, a donor liver became available and the patient successfully underwent OLT. The patient's initial post-OLT course was complicated by acute cellular rejection which was successfully

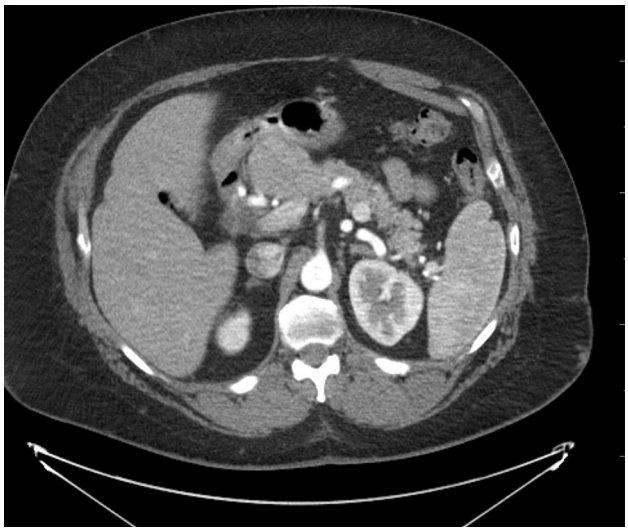

Fig. 1 CT scan of the liver showing a well-circumscribed enhancing mass in the porta hepatis measuring 4.6 × 5.6 × 6.4 cm

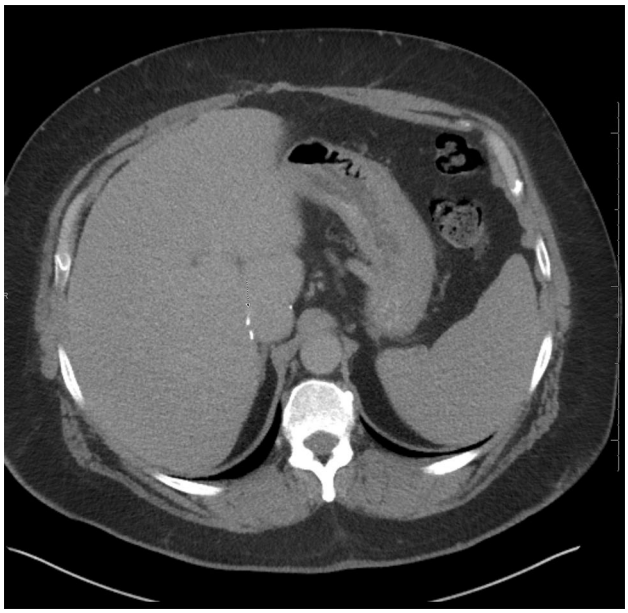

Fig. 2 CT scan of the liver post liver transplantation showing post-surgical changes

treated with steroids and immunosuppression. The patient was maintained on tacrolimus and mycophenolate acid.

The patient was lost to follow-up for 1.5 years and presented again to the hepatology clinic. Four years after his OLT, a surveillance CT scan of the liver showed a well-circumscribed enhancing mass in the porta hepatis measuring 4.6 × 5.6 × 6.4 cm [Fig. 1]. His previous CT scan two years ago was unremarkable, except for post-surgical changes [Fig. 2]. Endoscopic Ultrasound was performed which showed a 6.9 × 4.1 cm heterogeneously hypoechoic lesion at the porta hepatis. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) was performed using a 19 gauge needle without suction by slow withdrawal of the stylet. Histopathological examination showed neoplastic cells in loose clusters with low nuclear to cytoplasmic ratio, round nuclei, focal endothelial cell wrapping, transgressing vessels, as well as mild increased nuclear density and focal pseudoglandular pattern of cells with loss of normal reticulin framework which was indicative of well-differentiated HCC [Fig. 3].

CT scan of the chest and positron emission tomography (PET-CT) scan were performed for staging purposes and showed no evidence of metastatic disease. The patient underwent resection of HCC and lymphadenectomy. Surgical pathology revealed a large, ovoid, nodular, red mass (7.7 × 4.8 × 4.3 cm, 90 g) with a smooth intact surface and minimal attached fibroadipose tissue that was consistent with well differentiated HCC and focal necrosis with areas of hemorrhage and fibrosis (Fig. 4).

The patient tolerated the procedure well and continues to follow-up with hepatology. A CT scan of the liver performed 3 months post resection is unremarkable except several liver imaging reporting and data system (LI-RADS) 3 lesions (Fig. 5).

Discussion

HCC is the third leading cause of cancer-related deaths worldwide and the fifth most common cancer [5]. Common risk factors include alcoholic liver disease, nonalcoholic fatty liver disease, and hepatitis B and C virus infections [1]. OLT provides excellent long-term outcomes in patients with HCC and has become the preferred treatment modality [6]. The recurrence rate of HCC post-OLT can be up to 25% with majority of the cases within the first two years post-OLT, while the median recurrence time is reported to be 12.8 months [1, 2, 7–9]. The most common sites of recurrence are extrahepatic, including the lung, bone, abdominal lymph nodes, adrenal glands, and peritoneum [1–4].

The American Association for the Study of Liver Diseases (AASLD) recommends an initial ultrasound of the abdomen and/or serum alpha fetoprotein level for screening of HCC, followed by magnetic resonance imaging (MRI) or a triple-phase CT Scan of the abdomen [10]. The Li-RADS criterion are usually used for reporting liver lesions on advanced imaging [11, 12]. Previously, Fuijii-Lau et al. have described diagnostic ultrasound criteria to evaluate benign versus malignant lesions with a positive predictive value of 88% [13]. Percutaneous liver biopsy was initially used in 1923 until the transjugular approach was proposed in 1973 [14]. Currently, EUS-FNA can evaluate the left lobe and proximal right lobe of the liver, as

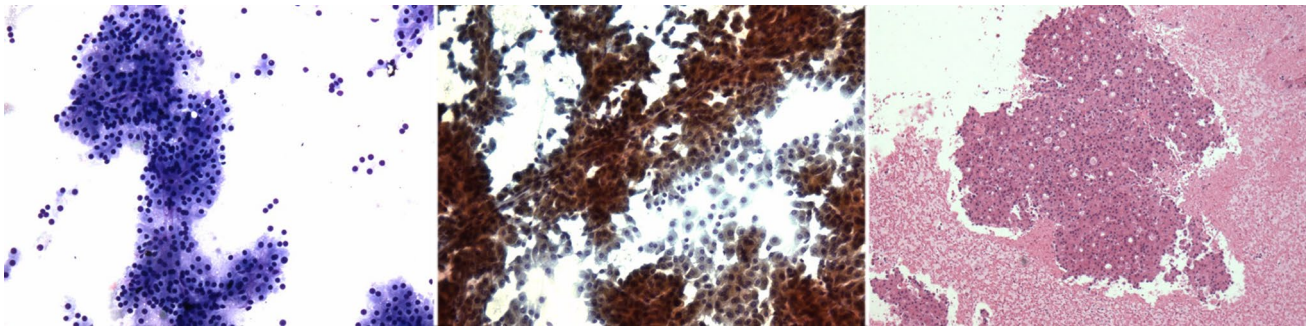

Fig. 3 Fine needle aspiration cytology of the porta-hepatis mass. Left: (40 × magnification, Romanowsky stain) showing malignant cells in clusters and lying singly; Middle: (40 × magnification, Papanicolaou stain) showing clusters of malignant cells with transgressing vessels; Right: (40 × magnification, cell block with H&E stain) showing pseudoglandular pattern

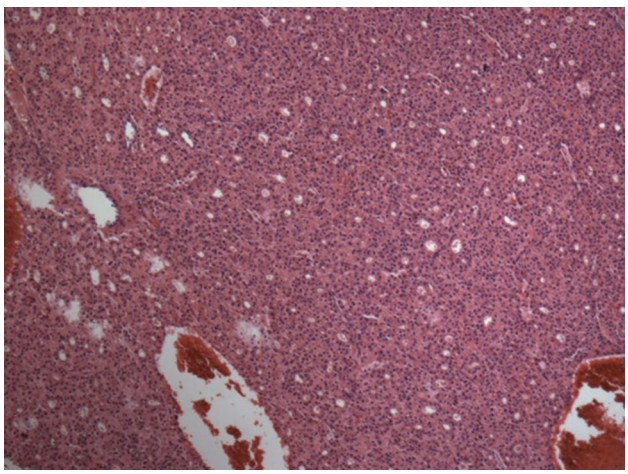

Fig. 4 40 × magnification, H&E Stain: Resection of the porta-hepatis mass showing well-differentiated hepatocellular carcinoma

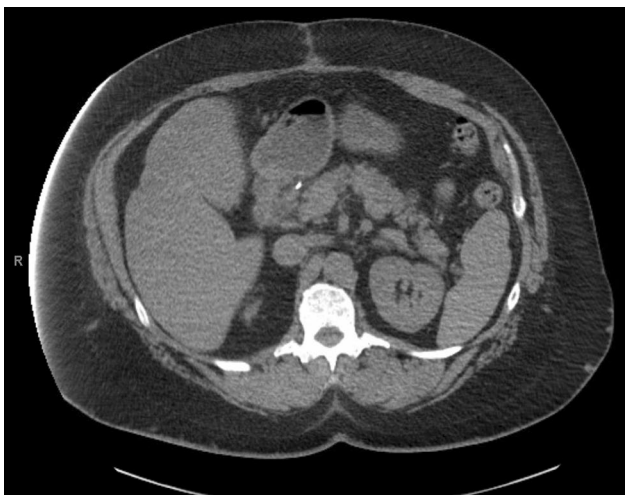

Fig. 5 CT scan of the liver after surgical resection of HCC

well as the hilum and part of the intrahepatic biliary tract [15]. Studies have shown that EUS-FNA is a safe and reliable modality for diagnosis of liver lesions, and is gaining popularity [16, 17]. EUS-FNA can be especially useful in patients with underlying liver disease who have ascites or coagulopathy, however, complications including bleeding, pain, fever and hemoperitoneum should be discussed in detail with the patient [18, 19].

No current recommendations are available for treatments options for recurrence of HCC post-OLT. Therefore, the treatment modalities used for HCC prior to OLT are also used post-transplantation. These include surgical resection, trans-arterial chemoembolization (TACE), radio-frequency ablation (RFA), radiation therapy, immunosuppression, mTor inhibitors (sirolimus), and multi-targeted tyrosine kinase inhibitors (sorafenib) [1, 2]. The ideal treatment for each patient should be determined by a multidisciplinary team including hepatology, surgery, oncology, and radiology.

Pre-transplant HCC can be treated with surgical resection or other modalities. RFA has shown comparable success to that of surgical intervention, but no studies have compared the post-transplant population [20]. Two cases of successful treatment of recurrent HCC post-transplant have been reported for intra-arterial infusion of yttrium-90 microspheres and stereotactic body radiation therapy [21, 22]. Although TACE is a difficult endeavor post-transplant due altered vasculature, it has also been described [23, 24]. Prior reports have also shown the use of sorafenib, but in the majority of cases, it was discontinued due to side effects including fatigue, gastrointestinal symptoms, hypertension, and hand–foot–skin reactions [25]. Despite the fact that the first case of recurrence of HCC post-OLT was reported in 1995, there continues to be paucity of the literature on approaches to the treatment of HCC recurrence post-OLT [26]. One systematic review addressing

this subject suggested the following: (1) decreasing overall immunosuppression or using an mTor inhibitor; (2) applying surgical resection; (3) using other treatment modalities; and (4) applying systemic treatments, such as sorafenib, for unresectable multifocal disease and HCC re-recurrence [27]. In spite of these guidelines, the treatment of HCC post-OLT varies on a case-by-case basis.

Our case is unique in several ways. Recurrence of HCC post OLT is mostly extra-hepatic and our patient developed recurrence of HCC at the porta-hepatis. In addition, the diagnosis of HCC is exceedingly rare with the use of EUS-FNA. Our patient had classic features of HCC on FNA-cytology obtained during EUS. Our report also highlights that intra-hepatic recurrence of HCC can be surgically treated. However, further studies are needed to develop treatment algorithms for intra-hepatic recurrence of HCC post liver transplantation.

Author contributions RS, MB, RN prepared the manuscript. SM, SP and PG edited the manuscript and provided expert opinion. SP, PG, SM and RN were involved in the care of this case.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest related to this manuscript and no financial declaration.

Informed consent Informed consent was obtained.

Human rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from all patients for being included in the study.

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