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Clinical Case Panel: Treatment Alternatives for Inoperable Hepatocellular Carcinoma

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Surgical resection or liver transplantation offers the best chance of cure for patients with hepatocellular carcinoma (HCC). Unfortunately, most patients are not good candidates for liver resection due to locally advanced disease or compromised liver function. Moreover, liver transplantation waiting lists are long. For those cases not amenable for resection, a variety of local treatment modalities are available, such as image-guided ablative procedures, transarterial chemoembolization, and radioembolization, as well as external beam radiation. HCC presentation can vary considerably in size, number, and location of lesions. The management of inoperable HCC is, therefore, quite complex, and there is a lack of consensus on the best local treatment modality for each type tumor presentation. Here, we present 4 clinical case scenarios representative of commonly seen cases in the clinical setting, with different therapeutic perspectives from institutions with high expertise in the management of HCC.
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Introduction

The most common primary liver cancer, hepatocellular carcinoma (HCC), is currently the third leading cause of cancer-related death worldwide, and its incidence is predicted to increase in the near future.[1] Commonly associated with chronic liver inflammation caused by excessive alcohol consumption, hepatitis B and hepatitis C virus infection,[2,3] more evidence has suggested the association of HCC development with nonalcoholic steatohepatitis.[4,5] With the increasing prevalence of nonalcoholic steatohepatitis, HCC is becoming the fastest growing cause of cancer death in developed Western countries.[6]

The management of HCC is dictated by the prognostic assessment of the disease. Prognosis is influenced by many factors such as age, performance status (PS), tumor size, location, number of lesions, presence of major vascular invasion, and extrahepatic spread, as well as degree of liver function impairment. All these features need to be taken into consideration in order to properly define the best treatment strategy. Different prognostic classifications have been proposed to help stratify patients and aid in treatment decision-making. The ideal approach for each disease stage is still controversial, especially for cases with unresectable localized disease and compromised liver function.[7]

Many local treatment modalities for HCC have emerged in the last decades such as image-guided ablative procedures, transarterial chemoembolization (TACE), transarterial radioembolization (TARE), and stereotactic body radiotherapy (SBRT), all with distinct advantages and disadvantages depending on tumor characteristics. Also, treatment modality is highly influenced by each institution's expertise. The aim of this review is to present 4 representative cases of HCC seen in the clinical setting and offer different therapeutic

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perspectives by institutions with large expertise in the management of HCC.

Clinical Case Scenarios

Case 1: Peripheral Single Lesion and Child-Pugh Class B

A 64-year-old Asian male with a history of untreated chronic hepatitis C presents with a 3 × 2.5 cm mass seen in peripheral segment 6 of the liver. A triphasic computed tomography (CT) scan shows that the mass has arterial enhancement on early phase with washout seen on delayed imaging phases, consistent with HCC. Complete physical exam and radiologic staging demonstrate no evidence of ascites, hepatic encephalopathy, or extrahepatic spread, but signs of portal hypertension were identified on abdominal CT imaging. Laboratory values at the time of diagnosis are the following: alpha-fetoprotein level of 35 ng/mL [28.9 IU/mL]; an albumin of 3 g/dL [30 g/L]; a serum total bilirubin of 1.9 mg/dL [32.5 μmol/L]; INR of 1.7; serum sodium of 134 mEq/L [134 mmol/L]; serum creatinine of 1.1 mg/dL [97.2 μmol/L]; platelets of 95 10^3/mm^3 [95 10^9/L]; elevated transaminases 2 times the reference values; anti-HCV positive; and HCV viral load of 400.000 UI/L. Beyond hepatitis C infection, his past medical history includes only hypertension. His performance status is ECOG 0. His Child-Pugh (CP) score is 7, his MELD score is 18 and MELD-Na score 19 (Fig. 1).

[] = Laboratorial values in International System of Units.

- What is your treatment recommendation?
- If the patient were not a surgical candidate, what treatment option would you recommend?
- If this patient were treated with radiation therapy, what dose, fractionation, and liver dose constraints would you use?

Expert Opinion No. 1—Stanford Cancer Institute

Despite presenting with a good PS and a small, peripheral lesion, tumor resection for a patient with CP score of 7 (Class B), a MELD-Na score of 19 (without exception points under the 6-month delay period after diagnosis) and portal hypertension has been associated with high postoperative morbidity and mortality.[8-10] Orthotopic liver transplantation should be considered an appropriate option in accordance with the United Network for Organ Sharing (UNOS) eligibility criteria,[11] with expected 5-year survival rates above 70%.[12,13] However, median waiting-list time may approach 2 years in the United States,[14] and thus, the patient will require bridge therapy. Radiofrequency ablation (RFA), TARE with yttrium-90 glass microspheres and TACE have all shown low dropout and post-transplant recurrence rates,[15-17] with our institutional preference being TACE.

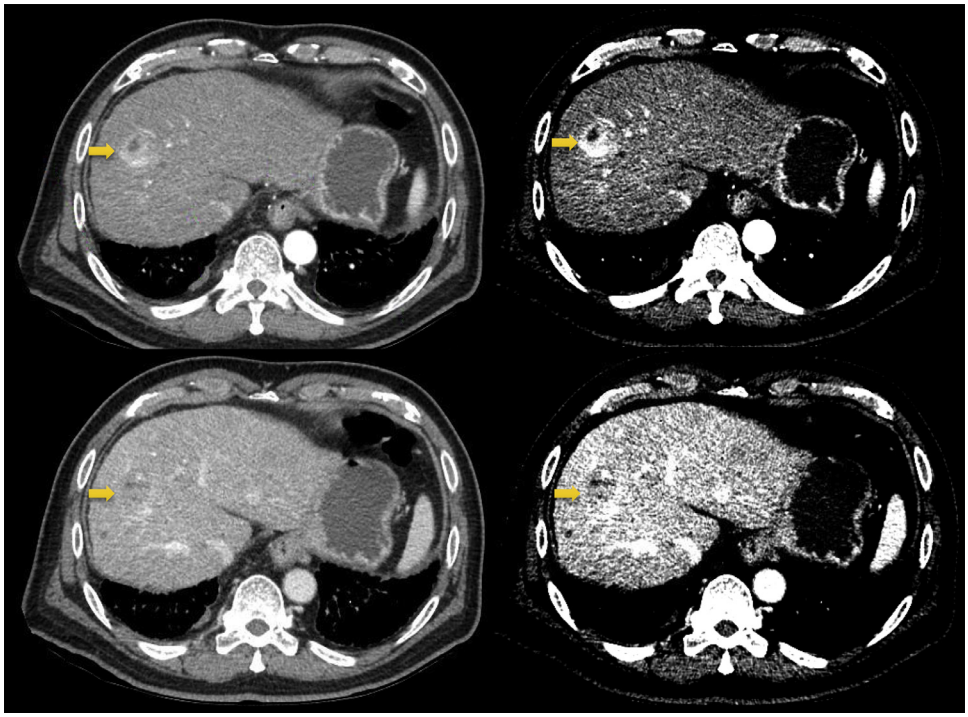

Figure 1 Dynamic computed tomography axial images of the abdomen from a patient diagnosed with hepatocellular carcinoma demonstrating a 3 × 2.5 cm lesion (*yellow arrow*) on segment 6 of the liver. (Color version of figure is available online.)