Immune Checkpoint Inhibitors for Downstaging Unresectable Hepatocellular Carcinoma for Liver Transplantation and Liver Resection.

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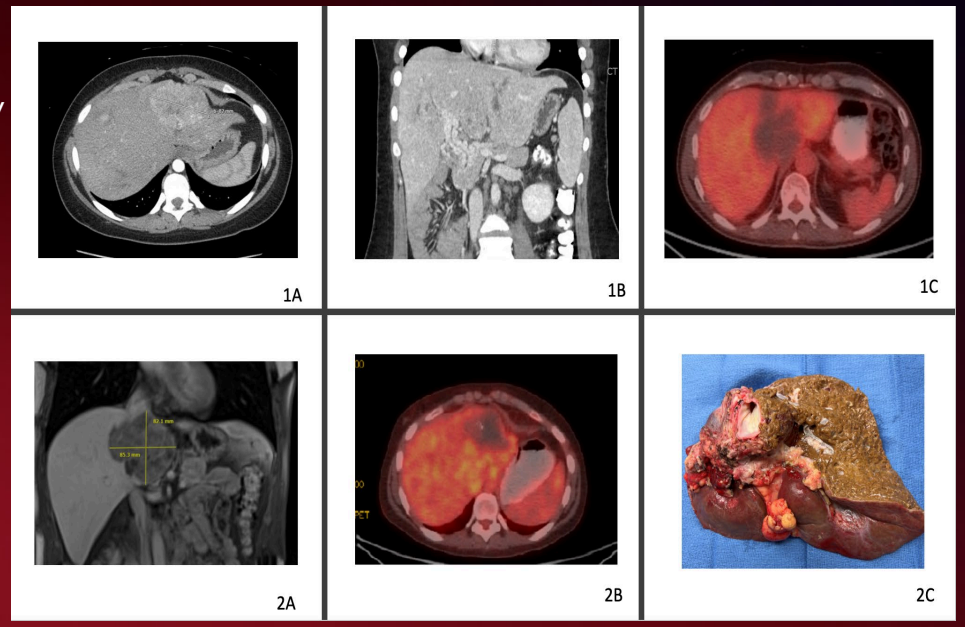
Introduction:

Hepatocellular Carcinoma (HCC) usually presents in an unresectable stage without ideal treatment options, and current management modalities do not suffice in successfully downstaging patients to definitive surgical intervention. Recently, the use of Immune Checkpoint Inhibitors (ICI) has shown to have a potential benefit for some patients with unresectable HCC.

Methods:

We present two patients with unresectable HCC treated with ICI (nivolumab) in combination with tyrosine kinase inhibitors (TKI), chemotherapy and Y-90 embolization for downstaging for liver transplantation and liver resection.



Patient 1. **1A** Axial CT scan: 8.4 x 5.2 cm rounded mass with central calcifications. **1B.** Coronal CT scan showing portal vein thrombosis. **1C.** Post neoadjuvant images without evidence of residual, recurrent, or metastatic disease.
Pa**tient 2. 2A.** Coronal CT scan showing a 14x10x7.8 cm vascular heterogeneous mass. **2B.** Post neoadjuvant images without evidence of residual, recurrent, or metastatic disease. **2C.** Left trisegmentectomy including inferior IVC resection.

Results:

Case 1:

- 17 y.o female with an 8.4 x 5.2 cm Fibrolamellar HCC (Figure 1A) associated with portal vein thrombus (Figure1B).
- Treated with 5-Fluorouracil and interferon-alpha (18 cycles) with poor response.
- Subsequently received Nivolumab (14 cycles) and Y-90 embolization (x3) with excellent results (Figure 1C).
- Underwent living donor liver transplantation four weeks after ICI discontinuation to prevent ICI-induced cellular rejection.
- Pathology demonstrated a 7.5 cm HCC with >95% necrosis (1.2 cm viable tumor) without lymphovascular invasion. After ten months, the patient is asymptomatic without evidence of recurrence.

Case 2:

- 52 y.o male with a 14 x 10 x 7.8 cm HCC that invaded the inferior vena cava (IVC), middle and left hepatic veins (Figure 2A).
- Received a combination of Carbozantinib (TKI) - Nivolumab (7 cycles) and Y90 embolization (x3). FDG PET-CT post-therapy showed no evidence of tumoral activity (Figure 2B).
- The patient did not have access to liver transplantation, so he underwent a left trisegmentectomy and IVC resection (Figure 2C).
- Pathology showed an HCC with >95% necrosis and 9 mm of focal residual tumor. A biliary leak complicated his postoperative course. No evidence of recurrence has been observed after five months.

Conclusions: ICI in combination with locoregional therapies and systemic agents seems to be an effective strategy treating and downstaging unresectable HCC. Despite extensive HCC necrosis post-therapy, the presence of viable focal tumor in the explant pathology warrants liver transplantation or extensive resection to assure control of residual cancer.