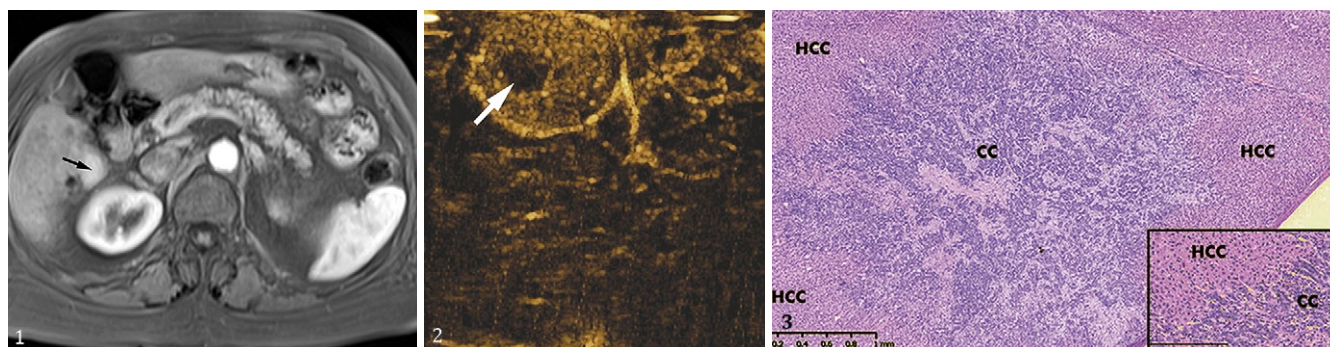


Nodule-in-nodule Hepatocellular Carcinoma: A Surprise Lesion

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A 79-year-old woman with compensated Child-Pugh A5 cirrhosis (Model for End-Stage Liver Disease score of 11) secondary to hepatitis B virus infection was admitted for a lesion with a marked enhancement on arterial phase (Fig. 1) with washout on portal venous and delayed phase images on abdominal contrast-enhanced magnetic resonance imaging, which was most likely consistent with hepatocellular carcinoma (HCC). Laboratory findings revealed normal serum alpha-fetoprotein (3.3 ng/mL). Therefore, the patient had a laparoscopic wedge resection under a diagnosis of hepatocellular carcinoma (HCC). Intra-operatively, a 25-mm solitary tumor was identified on the inferior surface of segment 5 and it became more distinguishable under fluorescence [intravenous indocyanine green (ICG) at a dosage of 0.3 mg/kg was administered 3 days before surgery]. Laparoscopic ultrasound with contrast agent (Sonovue, Bracco SpA, Milan, Italy) (CEUS) confirmed the presence of a lesion with an arterial phase hyperenhancement followed by late (>60 s) washout, with a well-demarcated hypoechoic nodule inside, which did not show any enhancement for each phase (Fig. 2).

Histological analysis confirmed the presence of a 23-mm well-differentiated HCC (G1 according to Edmondson-Steiner) with clear resection margins (more than 8 mm). A 3 mm-sized focal cholangiocellular differentiation was also detected and was separated by a clear band within the primary nodule (Fig. 3, H&E staining).

The combined type of HCC plus cholangiocarcinoma (CC) is relatively rare, representing <1% of all primary hepatic malignancies [1]. Generally, the most common form of HCC-CC is the classical type: it contains areas of typical appearing HCC intermixed with CC and identifiable transition zones, where the two components merge and show tumor cells with intermediate morphology [2]. Nodule-in-nodule architecture of HCC is suggestive of clonal expansion of more dedifferentiated cells along the hepatocarcinogenesis process compared to the outer nodule [3]. In this case, however, HCC-CC had a nodule-in-nodule aspect without a transition zone, also well visualized by the laparoscopic CEUS. This technique, already used in open surgery

[4], should be considered as complementary to the intraoperative ultrasound: it provides new findings that are based on the pattern of enhancement due to the tumor vascularity. Laparoscopic CEUS is also useful for an immediate evaluation after radiofrequency ablation and permits adjunctive ablations, reducing the risk of local recurrences [5].

HCC-CC clearly represents a distinct subtype of hepatic carcinoma: preoperative clinical diagnosis is currently exceptionally difficult and the detection of a nodule-in-nodule architecture at the imaging requires great attention.

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Conflicts of interest: None to declare.

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