

From small nodule to overt HCC: a multistep process of carcinogenesis as seen during surveillance

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Abstract. – BACKGROUND: Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related death in the world. Despite many diagnostic and therapeutic tools are now available to improve survival and reduce its recurrence, prognosis is closely conditioned by the time of diagnosis. Surveillance and early diagnosis are crucial for a successful therapy.

We report a clinical case from the HCC archive of the Hepatocatt meetings held in Gemelli Hospital (Catholic University of Rome). The case describes a tumor progression in a multistep process from a small liver nodule to overt HCC and its management by a multidisciplinary team.

Key Words:

Hepatocellular Carcinoma, Early HCC, Nodule in nodule, Overt HCC, Multidisciplinary team.

Background

Hepatocellular carcinoma (HCC) is a major health problem, the third most common cancer-related death in the world. It arises generally on the setting of chronic liver disease. Many efforts have been made to respond to this arising challenge; however treatment options are hardly conditioned by the stage of the tumor and of the underlying liver disease¹.

Barcelona Clinic Liver Cancer (BCLC) is actually the more endorsed scoring system for staging and treatment. Patients are divided into four stages, from 0/A to D based on liver function, performance status, number and size of nodules, extraepatic spread and associated diseases. A specific treatment and estimated survival are associated with each stage².

One of the most common diagnostic knot for the hepatologist is to decide about a small nodule

(defined as < 2 cm in diameter) in liver cirrhosis, as most of them are regenerative nodules (RNs). However among these nodules there could be present dysplastic lesions such Low Grade Dysplastic Nodules (LGDN) and High Grade Dysplastic Nodules (HGDN). In a multistep process of hepatocarcinogenesis they may lead to “early HCC” and then overt HCC³. “Early HCC” is an histopathological definition for a small (< 2 cm), well differentiated and vaguely nodular HCC. It has a better prognosis than progressed HCC, because it infiltrates stroma but not the hepatic vessels⁴.

Unfortunately, early HCC nodules show “hypovascular pattern” on the modern imaging techniques (Magnetic Resonance – MR, Computerized Tomography – CT, Contrast Enhanced Ultra Sound – CEUS) due to a lack of arterial supply in the early phases of carcinogenesis, so they are hardly distinguishable from previous lesions. In these cases biopsy is indicated^{2,5}.

In the forward steps of liver carcinogenesis intranodular arterial supply increases with the grade of malignancy. The shifting to a “hypervascular pattern” due to neoangiogenesis may occur diffusely throughout the lesion on in a restricted subnodular area. This area shows the characteristic image of “nodule in nodule” and is the first radiological sign of a malignant transformation in a small liver nodule. The identification of this hemodynamic shift by imaging techniques allows the physician to diagnose “small” (or “progressed”) HCC without biopsy and start a potentially curative treatment.

Case Report

On November 2010 a 56-year-old man with HBV-related cirrhosis in therapy with entecavir, presented to our Department for a mild ascites. Clinical examination and laboratory data showed

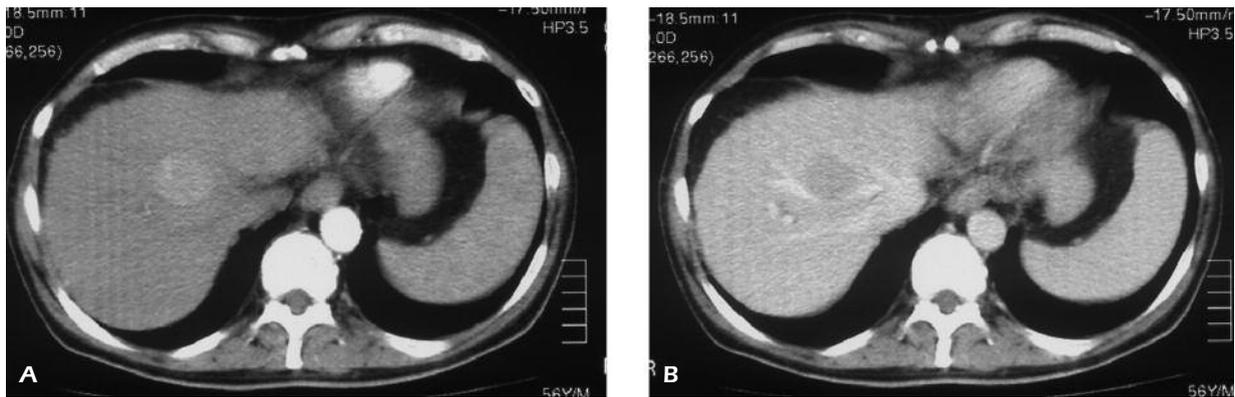


Figure 1. A, B, Contrast enhancement pattern typical for HCC in segment IV (arterial hypervascularity and venous phase washout) (October 2010).

that he was in fairly good clinical conditions (Child Pugh stage A6, MELD score 11). The patient underwent an abdominal CT that showed a 4 cm nodule at VIIIth liver segment with a contrast enhancement pattern typical for HCC (arterial hypervascularity and venous phase washout) (Figure 1), and another small lesion in segment VII (1.5 cm) only evident as hypodense in the delayed phase (Figure 2). The case was presented to our multidisciplinary team during the weekly meeting on liver primitive lesions. The team decided to treat the large nodule with a balloon-occluded radio-frequency thermal ablation (RFA) followed by transcatheter arterial chemoembolization (TACE), (a new combined single-step therapy performed in our Center) and strictly follow the smaller nodule: biopsy was not performed because of its deep position and lack of visibility on US. On January 2011, a month after the treatment, the patient underwent to a Gadolinium-based MR that showed a complete

necrosis of the large nodule on segment VIII (Figure 3). On the other hand the small nodule, unchanged in size, had a higher signal intensity on T1-weighted images, with a subnodular partial spot showing arterial contrast enhancement and late phases washout. This feature now appeared specific for malignant transformation, so we decided to treat also this nodule as a “progressed HCC”. On February 2011 a RFA was performed. No complications occurred. Unfortunately the needle’s tip did not hit the target lesion, making a necrosis only nearby. The next MR and CEUS imaging performed on March 2011 confirmed the “nodule in nodule” pattern, in a lesion unchanged in size. The patient was proposed for an Orthotopic Liver Transplantation (OLTx) in order to cure both HCC and liver disease. We decide to make a strict follow up of the lesion. A CT scan on June 2011 recorded a complete typical vascular pattern for HCC, in an unchanged in size lesion.

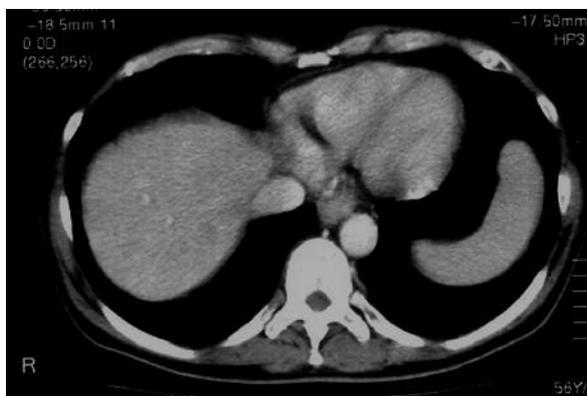


Figure 2. Small lesion (1.5 cm) evident as hypodense in the delayed phase in segment VII (October 2010).



Figure 3. Gadolinium based RM shows complete necrosis of the large nodule in segment VIII (January 2011).

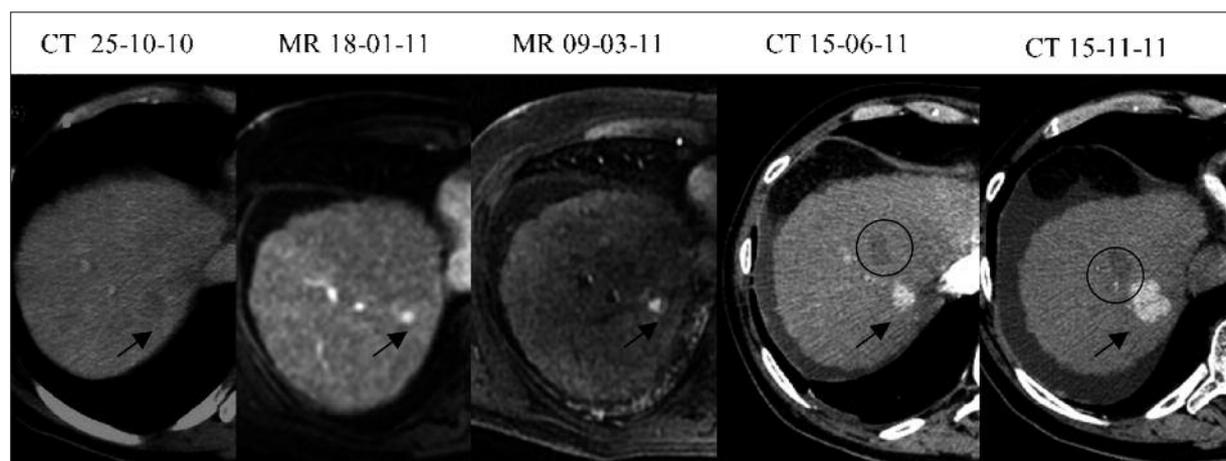


Figure 4. Evolution of the small liver nodule of segment VII (arrow): from small nodule to overt HCC. Inside the black circle the necrosis area nearby the lesion caused by the failed RF attempt.

On November 2011, just one year after the first detection, the lesion was enlarged (3 cm vs 1.4 cm). The multidisciplinary team proposed a new combined TACE plus RFA treatment for downstaging in OLTx waiting list for overt HCC. On this time the needle hit the nodule, thanks to the larger diameter and the relative contrast enhancement during chemoembolization.

The patient is now waiting for a liver transplantation.

Conclusions

We reported a case of multistep process from a small liver nodule to overt HCC. This experience may teach to consider as potentially malignant and to strictly control every liver nodule on cirrhosis larger more than 1 cm, also if it has not a typical vascular pattern for HCC: when biopsy is not easy to perform, strict imaging surveillance enables hepatologist to detect early signs of transformation.

Nowadays, HCC clinical management needs the employ of modern diagnostic and therapeutic tools, whose choice is entrusted to a panel of expert in a multidisciplinary team. Surveillance,

early diagnosis and choice of treatment are the key points to offer a better prognosis to patient and improve survival.

References

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