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Surveillance of Hepatocellular Carcinoma Post Intervention with Primovist Enhanced MRI: Comparison with MDCT: A Case Presentation

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Abstract
Surveillance of hepatocellular carcinoma has significantly increased life expectancy inpatient already diagnosed with hepatocellular carcinoma (HCC) with the addition of new hepato-specific contrast along with powerful magnetic resonance imaging (MRI). This combination has significantly improved the detection of the new, recurrent and residual lesion. This is a case report of a 40-year-old Chinese female with primary liver cancer treated with liver resection. Space occupying lesions of the liver was detected for which she also underwent trans-catheter arterial chemoembolization (TACE) at The People's Liberation Army No. 81 Hospital, Nanjing, China. In our case report, the surveillance was possible through the use of 3T MRI with Primovist™, which revealed a new HCC lesion and the patient, was later planned for TACE.
Keywords: Hepatocellular carcinoma (HCC), MRI, trans-catheter arterial chemoembolization, surveillance.

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Introduction

Hepatocellular carcinoma is the most common kind of primary liver carcinoma. According to the World Health Organization, it is the third leading source of cancer associated deaths all across the globe [1, 2]. Patients with a pre-existing liver disease such as liver cirrhosis, hepatitis B, and C infections are most susceptible to developing HCC, however, risk factors vary from country to country. Hepatitis B is the most important cause of HCC in China due to high endemic prevalence. Previously, HCC was usually diagnosed in the advanced stages when patients presented with symptoms such as weight loss, yellow skin, distended abdomen and other signs of decompensated liver disease[3]. The advancement in imaging modalities along with the new hepatospecific contrast medium has markedly increased diagnosis of small hepatocellular carcinoma. Imaging modality plays a key part in the therapeutic treatment of liver lesions [4].

Primovist is a gadolinium paramagnetic contrast agent to be used in combination with magnetic resonance imaging. The enhancing effect of primitivist is facilitated by gad oxetane disodium, an ionic molecule consisting of gadolinium ethoxybenzyl diethylenetriamine Penta acetic acid[5]. Primovist is eliminated through renal and hepatobiliary in equal amounts in patients with normal functioning liver and Kidney. Therefore, primovist can produce dynamic phase imaging in the liver and can aid in characterization and detection of focal liver lesions [5]. We can choose either to treat the lesion or monitor it on the basis of information provided by the imaging modality.

This case report elucidates the importance of MRI using Primovist as an essential tool in the differential diagnosis between regenerative liver nodules, dysplastic hepatic nodules, and early hepatocellular carcinoma. The objective of surveillance is to achieve a decrement in mortality due to HCC. This can be accomplishing through a timely diagnosis that will boost the application of curative treatment. Surveillance of hepatocellular carcinoma in identifiable target population can reduce the disease burden and mortality [2].

Case Report

A 40-year old Chinese male presented to the hospital with abdominal discomfort. She suffered from hepatic cirrhosis due to chronic hepatitis B along with hepatocellular carcinoma and had undergone resection one year ago. The clinical examination showed abdominal tenderness and dyspnea. The patient also complained of severe fatigue. Laboratory examination showed raised levels of AFP < 5605 µg/l and HBV DNA < 500/ml.

The 1st imaging technique performed was pre-contrast and post-contrast CT. Early arterial phase, hepatic or late portal phase and delayed phase was performed after contrast administration with bolus tracking. Completed accumulation of lipiodol in lesions treated with TACE was seen on the dynamic phase of Computed Tomography (CT) (**Figure 1**). MRI was performed with 3-tesla MRI system with

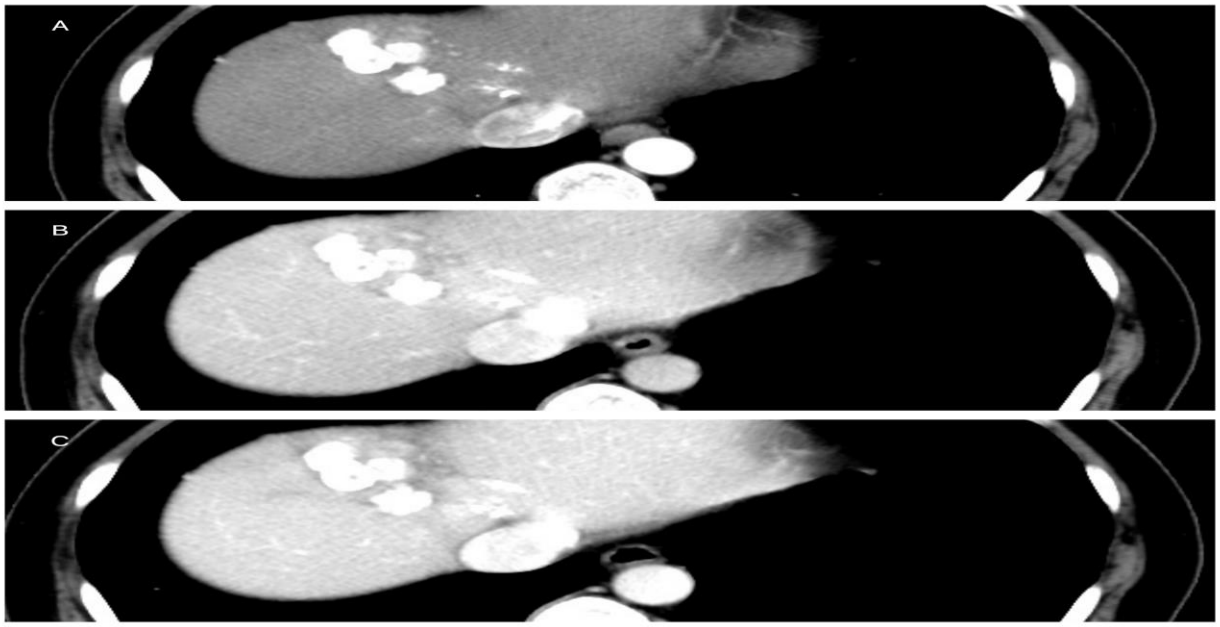

Figure 1: Dynamic computed tomography: shows a high-density center indicating lipiodol deposition in treated Hepatocellular Carcinoma lesion in (A) Arterial phase (B) Portal Phase (C). Delayed phase. No residual or new lesion was detected.

3 mm thickness. The MRI sequence included pre-contrast T2-weighted images (T2WI), pre-contrast T1-weighted images (T1WI) dynamic contrast-enhanced T1WI with hepatospecific contrast agent primovist and diffusion-weighted images (DWI). This imaging technique revealed a 3.0×2.0cm hypervascular lesion in the Vth liver segment on the T2 weighted sequence (**Figure 2A**). The lesion demonstrated washout pattern in venous phase (**Figure 2B**), suggestive of new HCC lesion. T1WI sequence had low signal.

DWI and ADC showed mild enhancement, which was lower than the normal parenchyma. In the post contrast phase, the lesion was more enhanced in the arterial phase at 20 seconds. At 20 min hepatobiliary after the contrast uptake, the lesion showed complete washout.

Discussion

According to the current guidelines for diagnosis of hepatic cancer from The European Society for the Study of Liver (EASL) and the American Association for the Study of Liver Disease (AASLD), the noninvasive diagnosis of liver cancer necessitates the presentation of arterial hyper enhancement followed by washout in the venous phase by dynamic imaging. This pattern is deemed to be the radiological hallmark of liver cancer in a patient with cirrhosis [6, 7]. Accurate pathological diagnosis, especially in early stages, is difficult even for an expert pathologist [8, 9].

Surveillance Tests

CE-US (contrast enhanced ultrasound) use is described as controversial in the latest EASL guideline, principally due to the contrast agents used in CE-US investigations, which are limited to blood vessels. The echographic contrast agent (SonoVue) is comprised of small gas-filled microbubbles; these micro-bubbles flow in the capillaries and generate a map of the intratumoral vascularization (angiogenesis)[6, 15]. CEUS provides low specificity when compared to other imaging techniques and is not recommended in current guidelines [6, 10]. Cholangiocarcinoma can also display contrast uptake at ultra-sonogram contrast followed by washout, i.e. the classical hallmark of HCC [7, 11]. At our institute routine use of CE-US for surveillance of HCC is not performed.

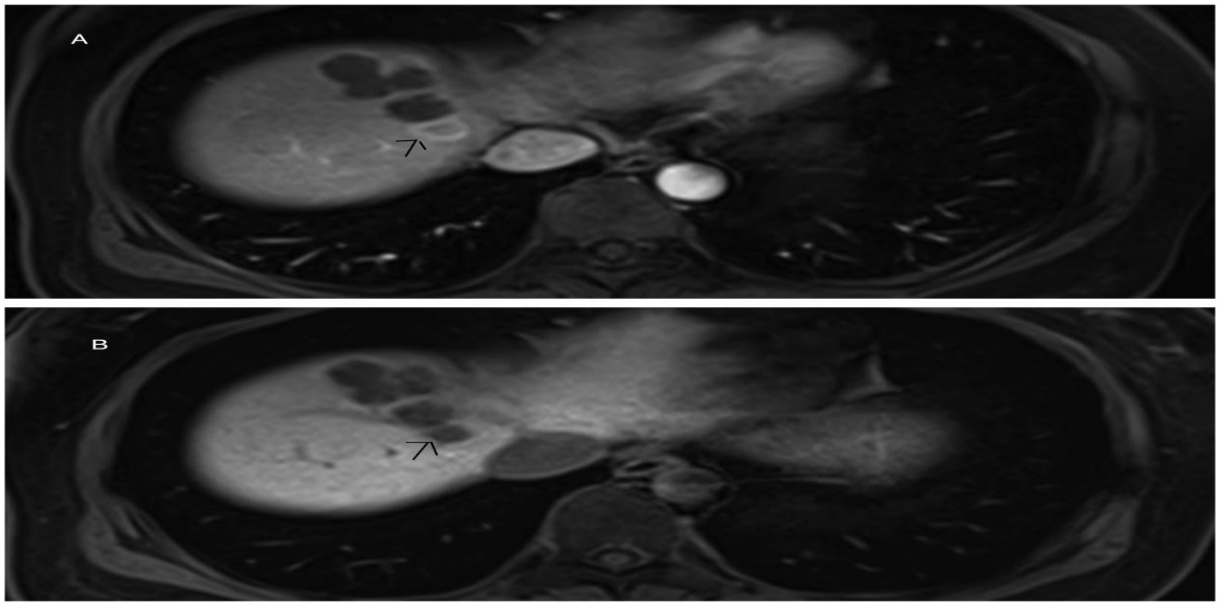

Figure 2: Primovist enhanced MRI technique shows 3.0×2.0cm. (A) In Hepatic arterial phase the lesion is seen hypervascular and **(B)** in Delayed phase the lesion had low signal.

A standard biopsy is mostly limited due to local disadvantage like neoplastic needle-track seeding and bleeding [12-14]. Thus, the state-of-the-art imaging modalities following the stated protocols are advocated for noninvasive diagnosis of liver carcinoma [15].

In clinical practice, CT scan is the most frequently used imaging procedure to diagnose HCC. Quadruple-phase multidetector computed tomography, which includes the unenhanced phase, arterial, venous and delayed phase is obtained for more accurate characterization of the Hepatic lesion [16, 17]. There are studies that have documented that the earliest detectable nodules in HCC seldom display typical radiological changes due to decrease in blood flow to the nodule from the portal vein, while arterial hypervascularization might not have yet entirely advanced and a decline in the portal flow might not be detectable [18, 19] Even with ideal arterial phase imaging, a large number of small (<1.5 cm) HCCs remain iso-dense compared with adjacent liver parenchyma and go undetected on CT [6].

Optimal acquisition timing, in combination with thinner collimation, may improve lesion detection and also probably improve characterization of lesions[20]. Peak enhancement of hypervascular lesion is usually seen in late arterial phase, which may provide better characterization of the small hypervascular lesion [21]. The computer tomography examination didn't reveal new lesion in our case Gadoxetic acid commonly known by the tradenames Primovist™ and has 50% biliary excretion, it is considered as the best option for analyzing small hepatic lesions [22, 23]. Primovist produces liver-specific hepatobiliary and dynamic MRI images, consequently showing very distinct patterns of the hepatocyte and the vascular uptakes [24].

With the use Gadoxetic acid we can assess with the highest sensitivity rate and certain features present only in early HCC, such as hypointensity in the portal/venous plus hepatobiliary phases. Dysplastic nodules are usually isointense but may also appear hypointense during the portal phase [25].

The combination of hypointensity in portal and hepatobiliary phase is an upcoming standard for diagnosis of early hypovascular HCC [24]. A hypervascular lesion exhibiting arterial enhancement is probably HCC with a high degree of certainty regardless of tumor size,[24]. There is also an open discussion regarding the nodule in nodule pattern, which apparently is suggestive of dysplastic nodule comprising smaller early HCC [26]. The accuracy level is reduced by 40-50% for tumors less than 1 cm, in particular, if the liver has a dysmorphic architecture with multiple regenerative and DN, lacking normal tissue as a basis for comparison [26]

3T MRI with Primovist™ has been suggested in order to ensure a more accurate characterization of liver nodules, especially for those of small sizes

[27]. Several studies have suggested that hyperintensity on diffusion-weighted MRI (DW-MRI) can be proposed as an added criterion for nodule characterization in order to discriminate between DN and early HCC with benefits for long-term prognosis. A

A Recent study supports the idea that the diagnosis of early hepatocellular carcinoma small hypovascular lesions with hypointensity in hepatobiliary phase on Primovist enhanced MRI and hyperintensity on DW-MRI has a high accuracy, sensibility and specificity ranging between 90% and 98%, respectively [28]. In our case the surveillance was possible through the use of 3T MRI with Primovist^{TM}, which revealed a new HCC lesion and the patient, was later, planned for TACE.

Conclusion

In our case study, a new focal hepatic HCC lesion was detected on surveillance through the use of hepatospecific contrast Primovist along with high-field 3T MRI in perfect accord with EASL and AASLD guidelines. The same lesion was not detected by MDCT. Gadoxetic acid (primovist) along with high field strength 3T MRI may improve the diagnosis of the noninvasive small HCC nodules in patients with cirrhosis on surveillance. This case study demonstrates that MRI using Primovist is a better imaging modality compared to MDCT and can thus serve as an essential tool in the differentiating the diagnosis of regenerative nodules, dysplastic nodules, and well-differentiated HCC. This can be explained by the fact that evaluation of CT images can be difficult sometimes due to beam hardening artifacts produced by iodized oil [29].

Declaration

All authors have disclosed no conflicts of interest.

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