Portal vein thrombosis with contrast-enhanced ultrasound in a patient with hepatocellular carcinoma: a case study

Abstract
Portal vein thrombosis (PVT) is the presence of thrombus in the portal vein that causes partial or complete occlusion. It is prevalent in hepatocellular carcinoma (HCC), where it can be either bland or malignant depending on the presence of invasion. Recent studies have identified contrast-enhanced ultrasound (CEUS) as the most reliable method of imaging to make this distinction. The arterial neovascularisation that is evident in a neoplastic thrombus can be visualised on CEUS with enhancement and pulsation, witnessed in real-time. This case study describes the use of contrast-enhanced ultrasound used as a non-invasive method to define the bland and malignant components of portal vein thrombosis in a 76-year-old male with hepatocellular carcinoma and cirrhosis.

Keywords: contrast-enhanced ultrasound, hepatocellular carcinoma, portal vein thrombosis.

Case
A 76-year-old male with known hepatocellular carcinoma (HCC) and cirrhosis was admitted to hospital after the presence of portal vein thrombosis (PVT) was identified on helical computed tomography (CT). In order to rule out tumour infiltrate of the portal vein, the use of real-time contrast-enhanced ultrasound (CEUS) was suggested.

Informed consent was obtained from the patient.

Figure 1: B-mode image (a) demonstrating echogenic material within the lumen of the anterior and posterior right portal veins. Colour Doppler image (b) demonstrating poor colour fill in the same areas. Ultrasound appearances are consistent with thrombus in the portal vein.
patient and a venous cannula inserted. A GE LOGIQ E9 ultrasound unit with contrast mode capabilities was utilised for the study. Initially, B-mode and colour Doppler imaging was obtained, and demonstrated thrombus in the main portal vein and anterior and posterior branches of the right portal vein (Figures 1a and 1b).

Contrast mode was selected, allowing the utilisation of a low mechanical index (MI) technique. The GE ultrasound machine allows the use of a split-screen, one with the B-mode image, the other displaying contrast signals. A third generation contrast agent, Definity®, produced by Bristol-Myers Squibb Medical Imaging Inc. (New York, New York, USA), was used. This consists of perflutren with a lipid shell. Before use it is agitated for 45 seconds after which a 1.3 mL vial is made up to 10 mL with saline.

Contrast was injected, at which time the contrast clock was started on the ultrasound machine. In the early arterial phase (15s), the anterior right portal vein enhanced avidly, prior to enhancement of the liver parenchyma (Figure 2a). There was also early anterior mural enhancement of the posterior branch of the right portal vein and a thin connecting channel of enhancement within the right and main portal veins (Figure 2b).

As Doppler spectral analysis demonstrated arterial flow in the areas of contrast enhancement, these areas were thought to correlate with invasive tumour (Figure 3).

Therefore, the enhancement indicated partial malignant thrombus of the main portal vein and right portal vein. This was superimposed with bland thrombus completely obstructing the main portal vein and anterior and posterior branches of the right portal vein.

Discussion
Portal vein thrombosis is defined as the “complete or partial obstruction of blood flow in the portal vein due to the presence of thrombus in the vessel lumen.” It may develop as a result of a number of local or systemic factors with liver cirrhosis being a significant predisposing factor, up to 16% of affected patients developing thrombus.

Risk of thrombus increases in those with HCC, with 35%-40% developing PVT. HCC is the most common primary malignant cancer of the liver and more easily invades adjacent vasculature.
when compared to other liver tumours.\(^1\) Lesions in the disease are hypervascular, demonstrating disorganised arterial flow, a characteristic demonstrated on imaging.\(^2,6,7\) Tumour invasion into the portal vein is a sign of an advanced disease state\(^2\) and can be shown on imaging, if characteristics similar to the malignant lesions are evident.\(^2,5,8,9\) Potential interventions for PVT include surgical resection, liver transplantation and percutaneous ablation.\(^2,4,5,8,9\) As tumour reoccurrence for malignant PVT is almost 100%,\(^9\) it is important to differentiate between bland and malignant PVT as the presence of malignant PVT may be a contraindication for intervention.\(^2,6,9\)

Ultrasound with colour Doppler (CD) has previously been identified as the imaging modality of choice in the diagnosis of PVT.\(^7\) For differentiating between bland and malignant PVT Power Doppler (PD) has shown to have a higher sensitivity and specificity than CD.\(^5,10\) Both these methods have also been compared with CEUS, which was found to be the superior method. In one study, CEUS was able to accurately differentiate between malignant and bland lesions in 55 patients.\(^7\) Another study of 54 patients reported a sensitivity of 88% and a specificity of 100% for CEUS in detecting malignant PVT.\(^2\)

CEUS has also been compared to contrast CT in the characterisation of PVT in cases of patients with HCC. In a study conducted by Rossi, et al. (2008),\(^4\) detection and characterisation of PVT was evaluated in 50 patients with known cirrhosis, HCC lesions and PVT. CEUS resulted in a higher sensitivity (98% vs 67%) and specificity (100% v 60%) than contrast CT in this study. The superior performance of CEUS in the above studies is as a result of its ability to detect and demonstrate very tiny vessels in tissue.\(^5,8,9\) The ultrasound contrast agent (UCA) acts as a blood pool tracer and there is enhancement of echogenicity with areas of high blood flow,\(^11\) as seen with HCC lesions. Unlike contrast agents currently used in CT and magnetic resonance imaging (MRI), the UCAs stay in the intravascular space, and, with high patient tolerance, more than one ‘dose’ can be administered at any time.\(^5,11\) The greatest advantage of CEUS is that it allows for real-time observation.\(^2,8,9,11\) This is a limitation of CT and MRI; enhancement can be missed if arterial phase scans are not optimally timed,\(^2\) or if there is poorly controlled patient respiration.

**Conclusion**

Patients with cirrhosis and HCC are at an increased risk of developing PVT, which, if malignant, may exclude them from treatment. Studies have shown that CEUS is an excellent method for identification of malignant PVT, as demonstrated in this case, owing to its unique qualities of real-time observation and detection of microvasculature. These capabilities of CEUS may also have applications in gut, kidneys, bladder, small parts, spleen, lung and vascular cases.\(^12\)

**References**

1. Ponziani FR, Zocco MA, Campanale C, Rinninella E, Tortora A, Di Maurizio L, et al. Portal vein thrombosis: insight into physiopathology, diagnosis and treatment. *World J Gastroenterol* 2010; 16 (2): 143–55.
2. Tarantino I, Francica G, Sordelli I, Esposito F, Giorgio A, Sorrentino P. Diagnosis of benign and malignant portal vein thrombosis in cirrhotic patients with hepatocellular carcinoma: colour Doppler US, contrast-enhanced US, and fine-needle biopsy. *Abdom Imaging* 2006; 31: 537–44.
3. Parikh S, Shah R, Kapoor P. Portal vein thrombosis. *Am J Med* 2010; 123: 111–19.
4. Dānilā M, Sporea I, Popescu A, Sirli R, Sendreiţ. The value of Contrast Enhanced Ultrasound in the evaluation of the nature of portal vein thrombosis. *Medical Ultrasonography* 2011; 13 (2): 102–07.
5. Ueno N, Kawamura H, Takahashi H, Fujisawa N, Yoneda M, Kirikoshi H. Characterisation of portal vein thrombus with the use of contrast-enhanced sonography. *J Ultrasound Med* 2006; 25: 1147–52.
6 Rumack CM, Wilson SR, Charboneau JW. *Diagnostic Ultrasound, vol 2.* 3rd ed. Missouri: Elsevier Mosby; 2005.

7 Henningson C. *Clinical Guide to Ultrasonography.* Missouri: Mosby; 2004.

8 Rossi S, Ghittoni G, Ravetta V, Viera FT, Rosa L, Serassi M, *et al.* Contrast-enhanced ultrasonography and spiral computed tomography in the detection and characterisation of portal vein thrombosis complicating hepatocellular carcinoma. *Eur J Radiol* 2008; 18: 1749–56.

9 Sorrentino P, D'Angelo S, Tarantino L, Ferbo U, Bracigliano A, Vecchione R. Contrast-enhanced sonography versus biopsy for the differential diagnosis of thrombosis in hepatocellular carcinoma patients. *World J Gastroenterol* 2009; 15 (18): 2245–51.

10 Sorrentino P, Tarantino L, D'Angelo S, Terracciano L, Ferbo U, Bracigliano A, *et al.* Validation of an extension of the international non-invasive criteria for the diagnosis of hepatocellular carcinoma to the characterisation of macroscopic portal vein thrombosis. *J Gastroenterol Hepatol* 2011; 26: 669–77.

11 Claudon M, Cosgrove D, Albrecht T, Bolondi L, Bosio M, Calliada F, *et al.* Guidelines and Good Clinical Practice Recommendations for Contrast Enhanced Ultrasound (CEUS) – Update 2008. *Ultraschall Med* 2008; 29 (1): 28–44.

12 Piscaglia F, Nolsoe C, Dietrich CF, Codgrove DO, Gilja OH, Bachmann Nielsen M, *et al.* The EFSUMB Guidelines and Recommendations on the Clinical Practice of Contrast Enhanced Ultrasound (CEUS): Update 2011 on non-hepatic applications. *Ultraschall in Medicine.* 2011 Aug 26 Available from: http://www.efsumb.org/asp/detail00.asp?ref=280&url=/intro/home.asp?ref=1 [verified January 2012].