Case Report: Gallbladder Varices in a Patient with Portal Vein Thrombosis Secondary to Hepatocellular Carcinoma

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ABSTRACT

Gallbladder varices are a rare form of collateralization that develop in patients with portal hypertension. We present here a case of gallbladder varices accurately diagnosed by contrast enhanced CT imaging of the abdomen and confirmed by Color Doppler Sonography. A 76-year-old patient with hepatocellular carcinoma developed portal vein thrombosis due to tumor extension during the course of treatment and was incidentally discovered to have gallbladder varices. While most commonly asymptomatic, gallbladder varices are associated with increased risk of massive bleeding, either spontaneously or during cholecystectomy. As a result, the existence of such varices should be well documented if the patient is to undergo any abdominal surgical procedures. In addition, because of a particular association with portal vein thrombosis, patients with portal hypertension that are found to possess gallbladder varices should be evaluated for portal vein thrombosis.

CASE REPORT

CASE REPORT

A 76-year-old male with a past medical history relevant for Hepatitis C Cirrhosis, Child-Pugh Class A, and Diabetes Mellitus underwent an MRI which revealed three lesions within the liver; a mass within the left hepatic lobe demonstrated imaging characteristics compatible with hepatocellular carcinoma and a large, but indeterminate, hepatic mass at the junction of Couinaud segments 5 and 8 later confirmed by biopsy to be focal nodular hyperplasia (Fig. 1). The patient underwent a left lateral liver resection. A follow up MRI was performed 3 months later revealing three new hypervascular lesions within segments 8, 6, and 4b. In addition, punctate foci of enhancement were noted within the right lobe of the liver surrounding the dominant mass, which was suspicious for hepatocellular cancer. In addition, new tumor thrombus was noted within the anterior division of the

right portal vein (Fig. 2). Patient subsequently underwent chemoembolization with doxorubicin 3 months later. A follow up MRI performed approximately 14 months later revealed recurrence of hepatocellular carcinoma as well as further expansion of the tumor thrombus within the portal vein, now extending from the extrahepatic main portal vein into the intrahepatic branches of the right and left portal veins (Fig. 3). On the most recent CT performed approximately 1 year after the previous MRI, after beginning a new oral chemotherapy agent under trial for treatment of widespread HCC, the previous ablation zone in the right hepatic lobe demonstrated no evidence of residual recurrent disease. The innumerable previously described arterially enhancing lesions noted throughout the remaining liver were also found to be much less conspicuous. Again noted was an enhancing occlusive tumor within the right and left portal veins (Fig. 4). Also of note was the new finding of gallbladder wall thickening with prominent

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vessels within the gallbladder wall consistent with gallbladder varices (Fig. 5 and 6). This finding was confirmed by Color Doppler Sonography performed shortly after the most recent CT (Fig. 7 and 8). As of submission of this case report, the patient's recurrent hepatocellular carcinoma shows responsiveness to the experimental chemotherapy treatment. Despite a one-day admission for workup of asymptomatic anemia (hemoglobin recorded at 5.7 g/dL), patient has remained in fair health. The portal vein thrombus and gallbladder varices remain unchanged.

DISCUSSION

Etiology & Demographics:

Gallbladder varices (GBV) are a rare form of collateralization that develops in patients with portal hypertension. GBV are thought to represent a portosystemic shunt between the cystic vein branch of the portal vein and the systemic veins of the anterior abdominal wall or possibly a porto-portal bypass around a focally thrombosed segment of the portal vein[1, 2]. Prevalence rates have been reported between 12-30% of patients with portal hypertension, and occur with similar incidence in children and adults [1, 3, 4]. While literature has described gallbladder varices in relation with portal hypertension, there seems to be a particularly strong association with portal vein thrombosis as a source of portal hypertension among adults and children [1, 3, 5, 6]. Multiple studies have described the common causes of portal vein thrombosis include hypercoagulable states, cirrhosis, infectious and inflammatory disorders, and interventional complications [3, 5]. In our case, portal vein thrombosis developed secondary to extension of hepatocellular carcinoma to the portal vein.

Imaging Findings:

Color Doppler Sonography is the accepted gold standard across multiple studies for diagnosis of GBV, which will typically show "serpentine" areas of venous flow within or around a thickened gallbladder wall [3, 7, 8]. However, with technological advancements in CT and MR imaging, it is possible that these modalities are equally capable of identifying GBV, but no recent case study comparing modalities has been published to date. In our patient, the varices were initially diagnosed on CT imaging of the abdomen, but were also clearly visualized on follow up MRI and Color Doppler Sonography. CT and MRI commonly show irregular, nodular enhancement of the gallbladder wall and/or multiple enhancing small vessels in the pericholecystic fat [1]. Regardless of the modality used, GBV can often go undetected because of the small caliber of these collateral vessels as well as the often numerous additional collaterals that develop in the porta hepatis and hepatoduodenal ligament [1].

Differential Diagnosis:

GBV are a rare diagnosis for gallbladder wall thickening. Broad differential considerations include primary gallbladder pathologies such as inflammatory processes, like cholecystitis, porcelain gallbladder, or gallbladder carcinoma, as well as benign processes, like adenomyomatosis of the gallbladder [9, 10]. Acute cholecystitis, as opposed to chronic cholecystitis, presents with thickening of the gallbladder wall, but will typically also present with pericholecystic inflammation. Porcelain gallbladder has a pathognomonic radiographic imaging appearance and will demonstrate a thin layer of mineralization outlining the wall as opposed to vascular enhancement. Gallbladder carcinoma may present as diffuse mural thickening, however associated features such as local invasion of adjacent soft tissue or metastatic lesions may help distinguish this from other pathologies [10]. The pattern of wall thickening in adenomyomatosis can be very similar to that of more malignant processes; however a finding of comet-tail artifact on ultrasound, or echogenic intramural foci forming a V-shaped comet tail reverberation, is highly specific for adenomyomatosis [11]. Systemic processes can lead to thickening of the gallbladder wall in individuals who do not have primary gallbladder pathology, including liver cirrhosis, hepatitis, congestive heart failure, or pancreatitis [9, 10]. While a wide differential is considered in the setting of gallbladder wall thickening, demonstration of "serpentine" areas of venous flow within or around the gallbladder wall on Color Doppler Sonography confirms diagnosis of GBV [3, 7, 8].

Treatment and Prognosis:

Generally, GBV are an incidental radiographic finding with the majority of patients being asymptomatic. While they have been found to affect gallbladder contractility, they have not been associated with gallstone formation and do not seem to affect gallbladder functioning [3]. However, GBV possess an increased risk of massive bleeding. They have been found to be a rare cause of spontaneous hemobilia, intraabdominal bleeding or gallbladder rupture[7]. GBV bleeding is extraordinarily rare, but can be catastrophic. And there have been rare case reports of mortality related to GBV bleeding [12, 13]. Because GBV can be a major source of blood loss, communication of these findings to surgeons is necessary, especially if surgery is planned on patients with portal hypertension [1].

In conclusion, GBV are rare development in patients with portal hypertension, particularly as a result of portal vein thrombosis. Therefore, patients with radiographic evidence of GBV should be evaluated for possible portal vein thrombosis. Similarly, GBV should be included in the diagnosis of patients with gallbladder wall thickening who have a known history of portal hypertension. Because of the propensity for bleeding of gallbladder varices, it is important for surgeons to be made aware of their existence before operating.

TEACHING POINT

Gallbladder varices are found in up to 30% of patients with portal vein thrombosis and, therefore, if discovered in a patient with portal hypertension, there should be increased concern for possible portal vein thrombosis. Because of the increased risk of bleeding, the finding of gallbladder varices should be well documented and communicated to any surgeons who are to operate on the patient.

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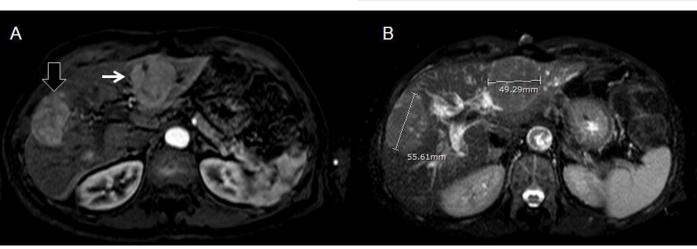


Figure 1: 76-year-old male with Gallbladder Varices.

TECHNIQUE: 1.5 T MRI of the abdomen with and without contrast (15 cc of intravenous Gadovist 469 mg/ml was administered).

(A) Axial T1 weighted THRIVE pre-contrast sequence. TR 4.21, TE 2.07, slice thickness 4 mm.

(B) Axial T1 weighted THRIVE post-contrast sequence. TR 4.21, TE 2.07, slice thickness 4 mm.

(C) Axial T1 weighted THRIVE delayed sequence. TR 4.21, TE 2.07, slice thickness 4 mm.

(D) Axial T2 weighted SPAIR sequence. TR 431.67, TE, slice thickness 7 mm.

FINDINGS: There is a 4.9 x 5.1 x 4.8 cm well circumscribed mass (small white arrow) within the left hepatic lobe, which demonstrates mild diffuse arterial enhancement on the T1 Fat-saturated images (A, pre-contrast, and B, post-contrast) without central hypoenhancement and heterogeneous T2 hyperintense signal (D). Washout was seen on the delayed phase images (C). These findings are compatible with hepatocellular carcinoma. At the junction of segments V and VIII there is a 4.0 x 5.6 x 4.4 cm mass (large black arrow), which demonstrates mild arterial enhancement on T1 Fat-saturated images (A, pre-contrast, and B, post-contrast) and mild hyperintense T2 signal (D). The lesion did not washout on the delayed images (C) and was later biopsy proven to represent focal nodular hyperplasia.

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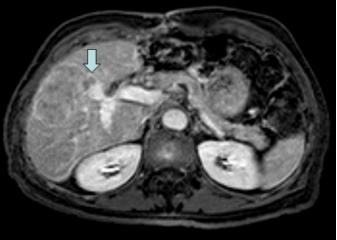


Figure 2: 76-year-old male with Gallbladder Varices. TECHNIQUE: 1.5 T MRI of the abdomen with and without administration of 15 cc of intravenous Gadovist 469 mg/ml. (A) Axial T1 weighted THRIVE pre-contrast sequence. TR 4.03, TE 1.95, slice thickness 4 mm.

(B) Axial T1 weighted THRIVE post-contrast sequence. TR 4.03, TE 1.95, slice thickness 4 mm.

(C) Axial T1 weighted THRIVE delayed sequence. TR 4.03, TE 1.95, slice thickness 4 mm.

(D) Axial T2 weighted sequence. TR 489.86, TE 80, slice thickness 7 mm.

FINDINGS: New thrombus (large black arrow) visualized within the anterior division of the right portal vein. This thrombus is an extension of a 6.9 x 6.5 x 4.4 cm mass (small white arrow) seen at the junction of segments V and VIII. The tumor thrombus, similar to the mass lesion, has isointense T1 signal (A) and mildly increased T2 signal (D). There is heterogeneous arterial enhancement (B) with partial washout on the delayed phases of imaging (C).

Figure 3: 76-year-old male with Gallbladder Varices. TECHNIQUE: 1.5 T MRI of the abdomen with and without administration of 14 cc of intravenous Magnevist 469 mg/ml. (A) Axial T1 weighted THRIVE pre-contrast sequence. TR 4.37, TE 2.16, slice thickness 5 mm.

(B) Axial T1 weighted THRIVE post-contrast arterial-phase sequence. TR 4.37, TE 2.16, slice thickness 5 mm.

(C) Axial T1 weighted THRIVE post-contrast venous-phase sequence. TR 4.37, TE 2.16, slice thickness 5 mm.

(D) Axial T2 weighted sequence. TR 471.25, TW 80, slice thickness 6 mm.

FINDINGS: The portal vein is expanded and filled with tumor thrombus (white arrow) that extends from the extrahepatic main portal vein into the intrahepatic branches of the right and left hepatic veins consistent with tumor thrombus. Tumor thrombus exhibits isointense T1 signal (A) and mildly increased T2 signal (D). There is heterogeneous arterial enhancement (B) with partial washout on the delayed phases of imaging (C).

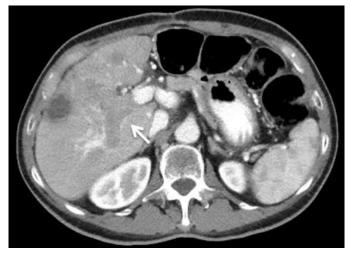


Figure 4: 76-year-old male with Gallbladder Varices.

TECHNIQUE: Enhanced, helical axial (A) and magnified axial (B) images via Philips iCT 256-slice were obtained of the abdomen and pelvis after the uneventful administration of oral contrast and 100ml Omnipaque 350 at 4.5 cc/sec, 120 kV and 30 mAs, slice thickness 2.5 mm.

FINDINGS: Axial CT with IV and oral contrast showing persistent tumor (white arrow) which extends from the extrahepatic main portal vein into the intrahepatic branches of the right and left hepatic veins.



Figure 5: 76-year-old male with Gallbladder Varices.

TECHNIQUE: Enhanced, helical axial (A) and magnified axial (B) images via Philips iCT 256-slice were obtained of the abdomen and pelvis after the uneventful administration of oral contrast and 100 ml Omnipaque 350 at 4.5 cc/sec, 120 kV and 30 mAs, slice thickness 2.5mm.

FINDINGS: Axial CT with oral and IV contrast showing gallbladder wall thickening and edema as well as varices (white arrow) within the gallbladder wall.

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Figure 6: 76-year-old male with Gallbladder Varices.

TECHNIQUE: Enhanced, helical sagittal (A), sagittal magnified (B), coronal (C), and coronal magnified (D) images via Philips iCT 256-slice were obtained of the abdomen and pelvis after the uneventful administration of oral contrast and 100 ml Omnipaque 350 at 4.5 cc/sec, 120 kV and 30 mAs, slice thickness 2.5 mm.

FINDINGS: Sagittal (A and B) and coronal (C and D) plane CT with oral and IV contrast again showing gallbladder wall thickening and edema as well as varices (white arrow) within the gallbladder wall.



Figure 7 (left): 76-year-old male with Gallbladder Varices. TECHNIQUE: Ultrasonography, transabdominal probe, 1-5 MHz. Grayscale image.

FINDINGS: Grayscale ultrasound image demonstrates gallbladder wall thickening, measuring up to 5 mm.

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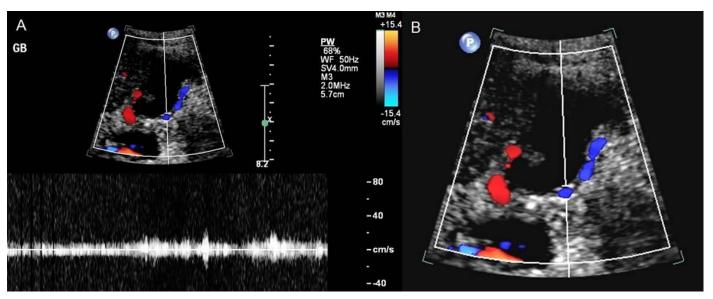


Figure 8: 76-year-old male with Gallbladder Varices.

TECHNIQUE: Ultrasonography, transabdominal probe, 1-5 MHz. Spectral Wave (A) and Color Doppler (B) Sonography images. FINDINGS: Venous flow is visualized within the thickened gallbladder wall on Spectral Wave Sonography (A) with a "serpentine" pattern illustrated on Color Doppler Sonography (B).

Etiology	In patients with portal hypertension, varices proliferate in the porta hepatis involving venous		
	channels in and around the biliary system. Gallbladder varices are thought to represent a		
	portosystemic shunt between the cystic vein branch of the portal vein and the systemic veins of the		
	anterior abdominal wall or possibly a porto-portal bypass around a focally thrombosed segment of		
	the portal vein.		
Incidence	12-30% of patients with portal hypertension according to multiple studies		
Gender ratio	No known significant male or female dominance		
Age predilection	Similar incidence seen in adults and children		
Risk factors	They are a rare development in patients with portal hypertension, however, there is a particularly high association among patients with portal hypertension due to portal vein thrombosis		
Treatment	Conservative		
Prognosis	Most commonly asymptomatic, but are a rare cause of spontaneous hemobilia, intraabdominal bleeding or gallbladder rupture		
Findings on Imaging	• Color Doppler Ultrasonography: "serpentine" areas of venous flow within or around a thickened		
	gallbladder wall		
	• Computed Tomography: Irregular, nodular enhancement of the gallbladder wall and/or multiple		
	enhancing small vessels in the pericholecystic fat		
	• Magnetic Resonance Imaging: MRI will have similar findings as CT, but it doesn't seem to add		
	further information compared to ultrasound and CT		

 Table 1: Summary table for Gallbladder Varices.

Differential Diagnosis	Color Doppler Ultrasonography	Computed Tomography	Magnetic Resonance Imaging
Gallbladder Varices	"Serpentine" areas of venous flow within or around a thickened gallbladder wall.	CT and MRI commonly show irregular, nodular enhancement of the gallbladder wall and/or multiple enhancing small vessels in the pericholecystic fat	CT and MRI commonly show irregular, nodular enhancement of the gallbladder wall and/or multiple enhancing small vessels in the pericholecystic fat
Acute/Chronic Cholecystitis	Gallbladder wall thickening and/or evidence of cholelithiasis. Pericholecystic inflammation is usually absent in chronic forms.	CT and MRI commonly show cholelithiasis and gallbladder wall thickening. The gallbladder may appear contracted or distended, and pericholecystic inflammation is usually absent in chronic forms.	CT and MRI commonly show cholelithiasis and gallbladder wall thickening. The gallbladder may appear contracted or distended, and pericholecystic inflammation is usually absent in chronic forms.
Gallbladder Carcinoma	Marked generalized gallbladder wall thickening, single or multiple intraluminal mass, extraluminal mass that extends to the liver, and/or polyps larger than 1 cm in diameter.	Most exhibit a heterogeneous mass that replaces the gallbladder. Focal or diffuse wall thickening is seen in some patients as well as a discrete intraluminal mass that enhances heterogeneously is visualized after the administration of intravenous contrast.	Findings are similar to those on CT. Additionally, tumor is usually bright on T2-weighted images and is poorly marginated. On T1- weighted images, the GB carcinoma ranges from isointense to hypointense.
Adenomyomatosis of the Gallbladder	Thickening of the gallbladder wall and/or "comet-tail artifact" described as echogenic intramural foci with V-shaped comet tail reverberation.	There is abnormal gallbladder wall thickening and enhancement and possibly a "rosary sign" formed by enhancing epithelium within intramural diverticula surrounded by the relatively unenhanced hypertrophied gallbladder muscularis.	The "pearl necklace" sign is a curvilinear arrangement of multiple rounded hyperintense intraluminal cavities visualized at T2-weighted MR imaging.
Porcelain Gallbladder	The gallbladder will demonstrate dense shadowing, which can be mistaken for gallstones or gas within the wall or lumen of the gallbladder.	A thin layer of mineralization outlining the gallbladder wall is pathognomonic.	Calcification in the wall of the gallbladder may appear as low T1 and low T2 signal.
Secondary Gallbladder Wall Thickening (e.g. Hepatitis)	Thickened striated gallbladder walls as well as pericholecystic edema.	CT and MRI will show gallbladder wall thickening, though subserosal edema cannot be well differentiated from surrounding ascites.	CT and MRI will show gallbladder wall thickening, though subserosal edema cannot be well differentiated from surrounding ascites.

 Table 2: Differential diagnosis table for Gallbladder Varices.

ABBREVIATIONS

CT = Computed Tomography GBV = Gallbladder Varices MRI = Magnetic Resonance Imaging SPAIR = Spectral Attenuated Inversion Recovery THRIVE = T1 High Resolution Isotropic Volume Excitation

KEYWORDS

Gallbladder varices; Portal hypertension; portal vein thrombosis; hepatocellular carcinoma; liver

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