Pathologic Intracardiac Bubbles in Patients With Cirrhosis: The Case for an Intestinal Origin

Zain Azzo, MD, FACC, Mays Albeer, MBChB, and Gerald I. Cohen, MD, FASE, FACC,
Detroit, Michigan; and Hamburg, Germany

INTRODUCTION

Microbubbles may be detected in the heart in the absence of an active infusion. Bubbles may form in the vicinity of prosthetic valves because local pressure drop causes gas to separate from liquid, which is called degassing.[1] Spontaneous microbubbles have also been described in the setting of congestive heart failure, mitral valvular disease, tricuspid regurgitation, pulmonary hypertension, and pulmonary embolism.[2-4]

These bubbles may have a gastrointestinal origin and be pathologic rather than spontaneous. Abraham *et al*[5] described bilateral intracardiac bubbles on transthoracic echocardiography in a neonate with complete atrioventricular septal defect, no active intravenous infusion, and radiographic pneumatosis intestinalis. Subcostal imaging showed portal vein and hepatic vein bubbles streaming into the inferior vena cava (IVC). Labbé and Hafiani[6] described a 78-year-old man with a central line clear of air, bilateral echocardiographic intracardiac bubbles, and computed tomographic findings of portal vein gas and intestinal pneumatosis.

Liver disease may also be associated with pathologic intracardiac bubbles. Akasaka *et al*[2] described microbubbles in eight patients, three with prosthetic valves and six with liver disease. In one patient, portal and mesenteric vein bubbles were noted and illustrated on M-mode echocardiography. Portal vein bubbles may reach both sides of the heart because of distinct pathophysiology associated with severe liver disease. To illustrate this, we present findings in two patients with cirrhosis.

CASE PRESENTATIONS

Case 1

A 48-year-old man with alcoholic hepatic cirrhosis, chronic obstructive pulmonary disease on home oxygen, and severe biventricular failure was brought in to the emergency department after cardiac arrest with pulseless electrical activity at his extended-care facility. He was intubated at the scene and arrived hypotensive with generalized edema. Oxygen saturation on mechanical ventilation was 100%. A computed tomographic scan of the chest and upper abdomen showed no pulmonary embolism, intracardiac gas, or intrahepatic gas. Portal venous congestion, marked IVC dilation, and cirrhosis were noted. Transthoracic echocardiography showed severe tricuspid regurgitation and a large number of microbubbles in the right atrium and ventricle, though the intravenous line was static, and a moderate number of bubbles in the left atrium and ventricle that appeared to emerge from the right lower pulmonary vein (Figure 1, Video 1). Bubbles were also present in the IVC and hepatic veins (Figure 2). There was systolic reversal of bubble motion in the haptic veins that was consistent with findings of severe tricuspid regurgitation on color and spectral Doppler (Video 2). The bubbles could also be visualized within the liver parenchyma and a portal vein (Videos 3 and 4).

Bubbles in the right and left cardiac chambers were also evident on parasternal two-dimensional imaging (Figure 3, Video 5) and had a distinct appearance on M-mode echocardiography. Systolic function was severely reduced in both ventricles. An abdominal ultrasound examination showed severe ascites and ileus and the nonspecific bubbles within the bowel. Abdominal radiography showed marked distention of bowel with intraluminal but not intramural gas.

Case 2

A 59-year-old woman with hepatic cirrhosis, alcohol and cocaine abuse, and portal hypertension presented to the hospital with altered mental status. She had stopped taking her lactulose and developed left-sided weakness and severe lethargy. Oxygen saturation on room air was 93%. Findings on cardiovascular examination were normal. She had abdominal distention. Blood work revealed high ammonia of 154 mg/dL and low albumin of 2.6 mg/dL and a platelet count of 59,000/mL. Transthoracic echocardiography for stroke workup showed a moderate number of microbubbles in the right ventricle and few bubbles in the left ventricle (Figure 4, Videos 6 and 7), even though a static intravenous Hep-Lock was in place. Other findings included normal left ventricular systolic function, increased left ventricular wall thickness, grade 2 diastolic dysfunction, biatrial dilation, mild right ventricular dilation and dysfunction, and moderate pulmonary hypertension. Subcostal images were suboptimal. Abdominal computed tomography showed liver cirrhosis with two solid enhancing hepatic masses suggestive of carcinoma and signs of portal hypertension with splenomegaly, ascites, and numerous gastroesophageal and perisplenic varices. No air was detected on computed tomography in the bowel wall, liver, or heart (Figure 5).

DISCUSSION

Our case reports describe the spontaneous appearance of bilateral intracardiac bubbles in two patients with cirrhosis. In the first patient, bubbles were also detected in or originating from a pulmonary vein, the IVC, and the hepatic and portal veins. The association of pathologic intracardiac bubbles in patients with cirrhosis has been previously reported.[2]

Previous studies and portal vein gas in our first case suggest that intracardiac bubbles came from the bowel. Both of our patients were at risk for this because of ileus, bowel dilation, and possible ischemia after cardiac arrest in our first patient and gastrointestinal

From the Division of Cardiology, St. John Hospital and Medical Center, Detroit, Michigan (Z.A., G.I.C.); and Kassenärztliche Vereinigung, Hamburg, Germany (M.A.).

Keywords: Microbubbles, Cirrhosis, Portosystemic shunt, Hepatopulmonary syndrome

Conflicts of interest: Dr. Cohen speaks on behalf of Lantheus Medical Imaging (Billerica, MA). The other authors report no actual or potential conflicts of interest relative to this document.

2468-6441

https://doi.org/10.1016/j.case.2018.09.005

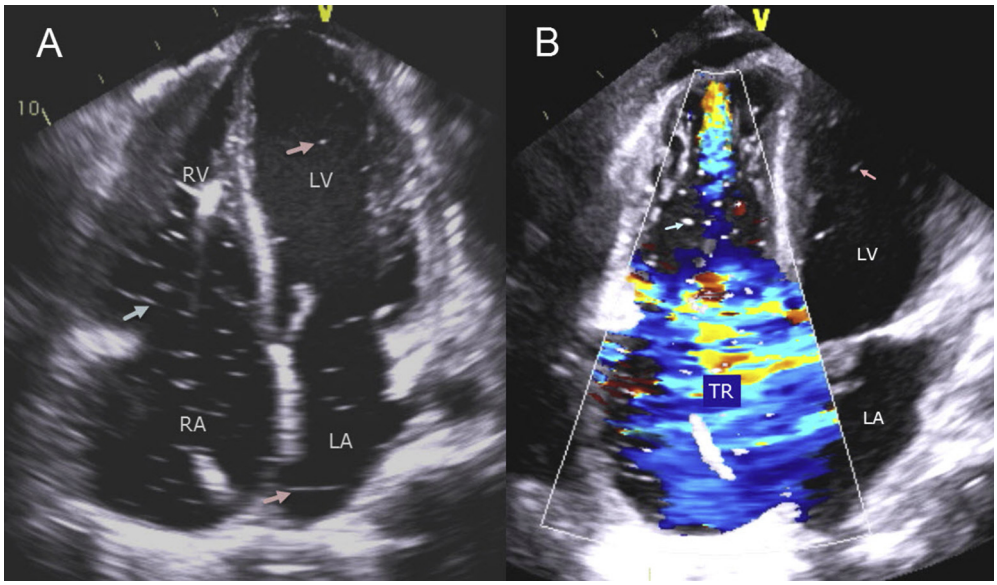

Figure 1 Transthoracic apical four-chamber view depicting severe right atrial and right ventricular dilation **(A)** and severe tricuspid regurgitation (TR) with added color Doppler **(B)**. Bubbles (*arrows*) are evident in all four chambers, but more on the right side. A pacing wire and leftward deviation of the atrial septum are also shown. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

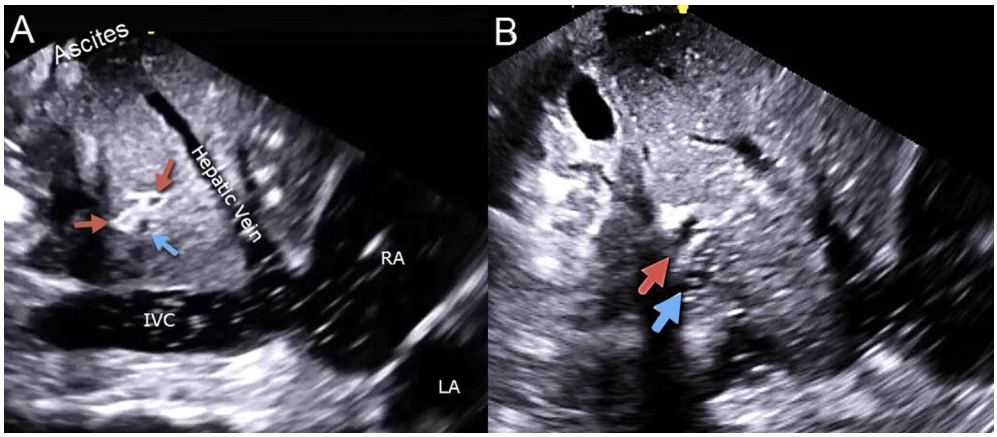

Figure 2 Subcostal view depicting bubbles in the right atrium (RA), IVC, and branches of the hepatic and portal veins, with the latter shown in short-axis **(A)** and long-axis **(B)** views (*blue arrow*). In the short-axis view, three structures of a portal triad are shown: the portal veins (*blue arrow*) and a hepatic artery and bile duct branch (*red arrows*), which were not distinguishable without color Doppler. In its long axis, bubbles are seen in the portal vein (*blue arrow*), unlike the other bubble-free component of the portal triad (*red arrow*). The portal vein trajectory is different than that of the hepatic vein, which is toward the IVC. In addition, the wall of the portal vein is echogenic, unlike the hepatic vein. Ascites is also shown. *LA*, Left atrium.

disease with suspected malignancy in our second patient.[7] Portal vein gas has been associated with bowel wall gas or pneumatosis intestinalis.[5,6,8,9] Passage of gas from the bowel into the portal circulation may occur because of disruption of intestinal wall integrity.[9]

Examination of the portal veins is not a routine part of echocardiographic examination, but a number of findings help in their recognition. First, portal vein branches are associated with other structures that are part of a triad that also includes a hepatic artery and bile duct branch (Figure 2). Portal vein walls have more circumferential echogenicity, while the walls of hepatic veins are generally indistinct or minimal.[10] Doppler findings may help in the distinction, though Doppler studies were not performed in our patients. The two-dimensional phasic motion of the portal vein bubbles in our first patient appeared to be toward the center of the liver and contrasted with the to-and-fro motion of bubbles in the hepatic veins from severe tricuspid regurgitation. The hepatic veins were also distinguished by their emergence from the hepatic parenchyma and drainage into the IVC.

For portal vein bubbles to have been able to reach cardiac chambers in our patients, they would have had to bypass the filtration of the hepatic parenchyma. Portal-to-systemic venous shunts may be due to back pressure from portal hypertension that opens up collateral veins[11] to the IVC, perihepatic veins, and much less commonly to the hepatic veins. In our patient, severe tricuspid regurgitation may have

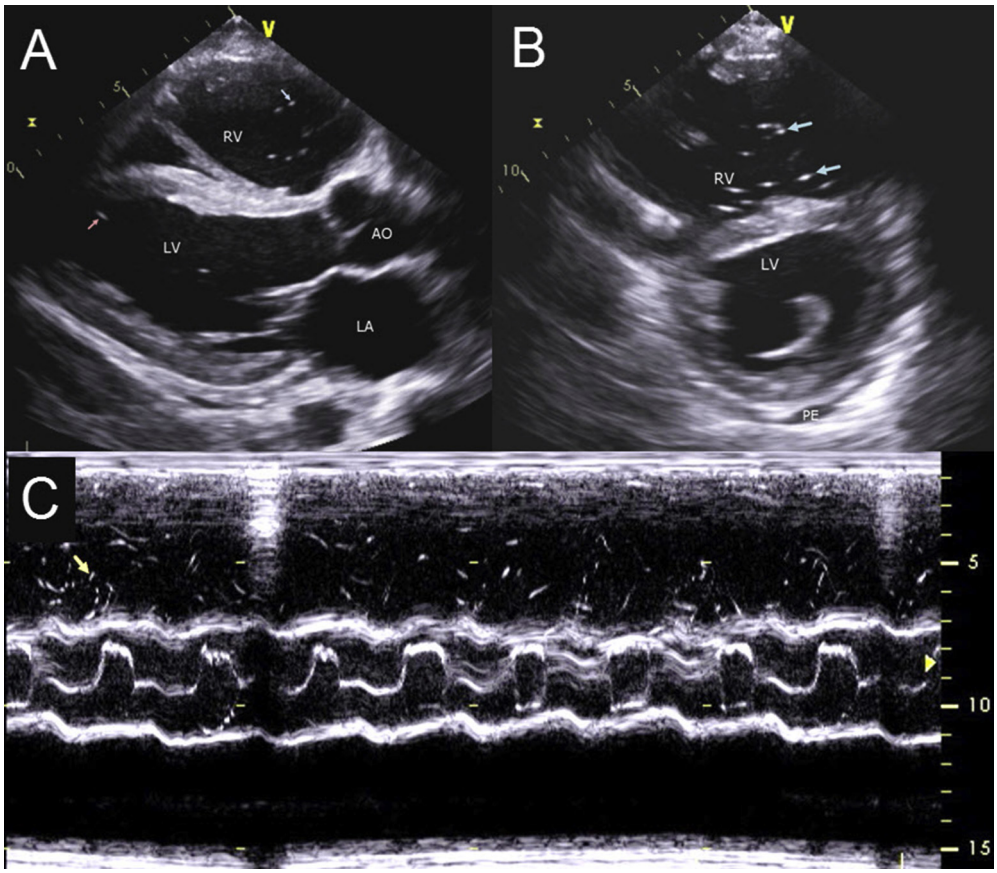

Figure 3 Transthoracic parasternal long-axis **(A)** and short-axis **(B)** views depicting bubbles (*arrows*) in the right ventricle (RV) and left ventricle (LV). Linear motion of the bubble reflectors appears chaotic on M-mode image **(C)**. *AO*, Aorta; *LA*, left atrium.

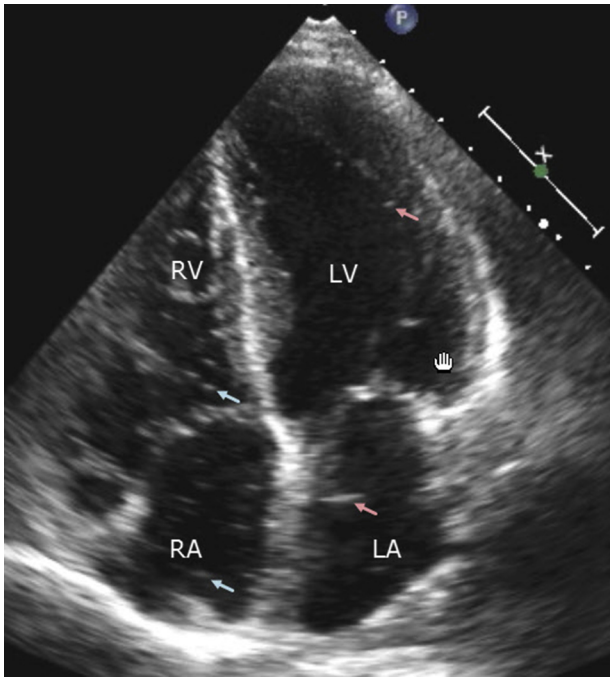

Figure 4 Transthoracic four-chamber view depicting bubbles (*arrows*) in all cardiac chambers but more so in the right heart. Mild right ventricular dilation and increased left ventricular wall thickness are also shown. *LA*, Left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle.

also pushed bubbles from the IVC into the hepatic veins and caused the bubbles to persist in the right heart.

After entering the IVC, bubbles would naturally flow into the right atrium and right ventricle. Their passage to the left heart may be explained by pulmonary arteriovenous communications associated with liver disease. This is known as the hepatopulmonary syndrome, is due to dilation of the pulmonary microvasculature and angiogenesis, and is mediated by a number of factors released because of hepatic injury and increased nitric oxide production. The syndrome is associated with digital clubbing, cyanosis, and hypoxemia.[12,13]

Pulmonary arteriovenous shunting may be diagnosed by intravenous injection of agitated saline and the delayed appearance of bubbles after five cardiac cycles in the left heart compared with the faster passage that is observed when a foramen ovale is present.[12-14] Timing the shunt depends on first seeing the bubbles opacify the right atrium and counting the cycles until bubbles arrive for a resting shunt or adding respiratory or abdominal maneuvers to increase right atrial pressure to shift the septum toward the left atrium. A number of factors can confound making a correct distinction on the basis of timing alone.[15] Therefore, it is also helpful to actually see the bubbles enter the left atrium through the septum or, as in our first patient, from the pulmonary veins. Distinction may also be aided by (1) color Doppler imaging of the septum with a reduced Nyquist limit, especially if the left atrium is dilated and the septum is deviated toward the right atrium; (2) transesophageal echocardiography for better visualization and localization of shunting; and (3) consideration of other findings, such as an atrial septal aneurysm or liver disease.[15]

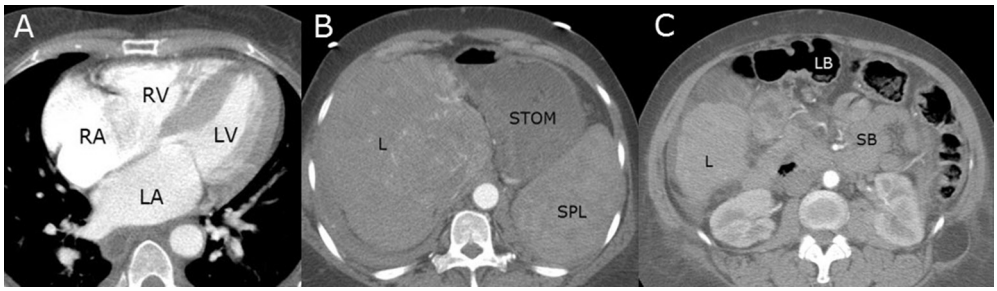

Figure 5 Abdominal and chest computed tomographic scan with contrast. **(A)** Four-chamber view with no visible intracardiac gas or bubbles. **(B)** Hepatic cirrhosis and enlarged spleen. No gas was seen in the liver or the wall of the stomach. **(C)** No bowel wall thickening or intramural gas was detected. Ascites was present. *L*, Liver; *LB*, large bowel; *SB*, small bowel; *SPL*, spleen; *STOM*, stomach.

Limitations

This report and discussion of prior studies indicate how bubbles can appear on both sides of the heart in patients with cirrhosis. More direct evidence would follow ingested bubbles or other imaging tracers from the bowel to the portal vein in the setting of cirrhosis. Future studies might evaluate the safety and efficacy of different agents, such as a carbonated beverage, synthetic bubbles of different sizes, and nuclear agents to determine the continuum of intestinal wall integrity, portal to systemic venous shunts, and pulmonary arteriovenous communications.

The prevalence of hepatic and cardiac bubbles among patients with cirrhosis and other gastrointestinal and liver diseases is not known. Not all patients may have the same number of bubbles, which was different between our two patients and in the study by Akasaka *et al.*[2] When few bubbles are present, they may be overlooked or incorrectly attributed to intravenous infusion when none is present.

A limitation of this report is our inability to clinically establish hepatopulmonary syndrome in either of our patients. Clubbing was not noted on review of records. The first patient had chronic obstructive pulmonary disease. The second patient had polysubstance abuse and low normal oxygen saturation.

CONCLUSION

We have presented two cases of patients with cirrhosis and spontaneous bubbles on both sides of the heart. Detection of bubbles in the portal veins in the first patient and observations in the literature suggest a mechanism whereby bowel gas enters the portal veins, shunts past the liver into the IVC or hepatic veins, enters the right heart, and then shunts past the lungs to enter the left atrium and left ventricle, akin to "cardiac flatulence." When interpreting echocardiograms of patients with cirrhosis, readers should be aware that pathologic intracardiac bubbles may be present that are not from an intravenous line.

ACKNOWLEDGMENTS

We acknowledge and thank Dr. Richard G. Barr (Professor of Radiology, Northeastern Ohio Medical University Southwoods Imaging, Youngstown, OH) and Dr. David T. Fetzer (Assistant Professor, The University of Texas Southwestern Medical Center, medical director of ultrasound, Dallas, Texas) for reviewing the manuscript and images of the liver.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2018.09.005.

REFERENCES

1. Kerut EK. Microbubbles in the left ventricle associated with mechanical aortic valve regurgitation signifies valvular (not peri-valvular) regurgitation. Echocardiogr 2014;31:540-2.
2. Akasaka T, Yoshikawa J, Yoshida K, Kato H, Yanagihara K, Okumachi F, et al. Echocardiographic characteristics and clinical significance of the spontaneous contrast echoes. J Cardiol 1987;17:159-68.
3. Segal R, Baltazar RF, Mower MM, Steward C. Spontaneous contrast visualization on the right side of the heart during echocardiography. Am J Med Sci 1986;292:363-6.
4. Iliceto S, Papa A, Ciociola G, Sorino M, Girardi F, Biasco G. Spontaneous microbubbles in right cardiac chambers. G Ital Cardiol 1984;14:577-82.
5. Abraham BP, Sachdeva R, Vyas PG, Collins RT. An unusual presentation of necrotizing enterocolitis on an echocardiogram. Pediatr Cardiol 2012;33:1427-9.
6. Labbé V, Hafiani EM. Echocardiographic air bubbles. Early sign of intestinal pneumatosis. Am J Respir Crit Care Med 2015;192:e44.
7. McElvanna K, Campbell A, Diamond T. Hepatic portal venous gas—three non-fatal cases and review of the literature. Ulster Med J 2012;81:74-8.
8. Mallappa S, Warren OJ, Kantor R, Mohsen Y, Harris S. Pneumatosis intestinalis and hepatic portal venous gas on computed tomography—a non-lethal outcome. JRSM Short Rep 2011;2:88.
9. Sebastia C, Quiroga S, Espin E, Boyé R, Alvarez-Castells A, Armengol M. Portomesenteric vein gas: pathologic mechanisms, CT findings, and prognosis. Radiographics 2000;20:1213-24.
10. Wachsberg RH, Angyal EA, Klein KM, Kuo HR, Lambert WC. Echogenicity of hepatic versus portal vein walls revisited with histologic correlation. J Ultrasound Med 1997;16:807-10.
11. Sharma M, Rameshbabu CS, Rai J. Collateral pathways in portal hypertension. J Clin Exp Hepatol 2012;2:338-52.
12. Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome — a liver-induced lung vascular disorder. N Engl J Med 2008;358:2378-87.
13. Surani SR, Mendez Y, Anjum H, Varon J. Pulmonary complications of hepatic diseases. World J Gastroenterol 2016;22:6008-15.
14. Gudavalli A, Kalaria VG, Chen X, Schwarz KQ. Intrapulmonary arteriovenous shunt: diagnosis by saline contrast bubbles in the pulmonary veins. J Am Soc Echocardiogr 2002;15:1012-24.
15. Attaran RR, Ata I, Kudithipudi V, Foster L, Sorrell VL. Protocol for optimal detection and exclusion of a patent foramen ovale using transthoracic echocardiography with agitated saline microbubbles. Echocardiogr 2006;23:616-22.