UTILITY OF ENDOSCOPIC ULTRASOUND IN THE EVALUATION OF PRE AND POST CYANOACRYLATE GASTRIC VARICEAL INJECTION

KJS Cham; LBC Corral; RGG Bondoc; EG Ong
Metropolitan Medical Center

INTRODUCTION

Acute gastrointestinal bleeding is a life-threatening emergency that remains a common cause of morbidity and mortality. Among which, bleeding from esophageal and gastric varices is the most common and severe complication of liver cirrhosis and portal hypertension. The prevalence of varices is about 50% among all cirrhotics.[1]They develop varices at a rate of 10% per year. Variceal hemorrhage will complicate the clinical course of chronic liver disease in about 30% of patients[2]and accounts for 80 to 90 percent of bleeding in those patients.[3]

The mortality of each episode of variceal bleeding is about 20 to 30 percent and as many as 70 percent of survivors have recurrent bleeding after their first variceal hemorrhage.[4]Gastric varices (GV) are less common than esophageal varices, with a prevalence of about 20 percent in patients with portal hypertension.[5,6] Although gastric varices bleed less frequently and with lower pressure than esophageal varices, bleeding from GV is more severe, have a higher risk of rebleeding and a decreased rate of survival.

Early detection of portal hypertension and the presence of gastroesophageal varices is the mainstay in the management of portal hypertension. Once gastroesophageal varices are detected and assessed based on its risks of bleeding, intervention is applied. Either pharmacotherapy and/or endoscopic band ligation is considered based on whether primary prophylaxis (no previous variceal bleeding) or secondary prophylaxis (previous variceal bleeding) is encountered.

The endoscopic treatment of esophageal varices has been addressed successfully with the use of rubber band ligation and injection sclerotherapy. For gastric varices, the optimum endoscopic treatment remains to be defined. Band ligation and sclerotherapy with various agents has been tried with various results, but a high risk of rebleeding was found in most studies.[7,8] The treatment of

gastric varices with cyanoacrylate gives very good results, with high hemostasis rate and reduced early and late rebleeding rate compared to other endoscopic treatment modalities.[9,10]

In almost 90% of the cases of gastrointestinal bleed, an identifiable source can be seen by upper and lower digestive tract endoscopy, however there are other situations, called obscure gastrointestinal bleeding, in which the origin was missed or no active bleeding was found on the initial examination. Other endoscopic techniques, such as small bowel endoscopy, endoscopic ultrasound (EUS) or angiography can subsequently be used.

Endoscopic ultrasound with its ability to provide both endoscopic and ultrasonographic visualization has expanded the diagnostic and therapeutic armamentarium in patients with portal hypertension. Earlier studies revealed EUS was inferior to endoscopy in detecting and grading esophageal varices.[11,12] However, with improved instrumentation and increased availability and training in thefield of endosonography, EUS has enhanced the diagnostic and therapeutic approach to patients with portal hypertension.

EUS has a higher sensitivity for detection of varices than gastroduodenoscopy. With a careful examination of the gastroesophageal junction by esophagogastroduodenoscopy, it can detect almost all cases of large esophageal varices, but small varices may not be readily seen and gastric varices may not be easily detected. A large part of portal venous system and the paragastric and para-esophageal collateral circulation is within the reach of endoscopic ultrasound. EUS can accurately distinguish GV from thickened gastric folds. The EUS has also been used to monitor the completeness of GV obturation after glue injection. There are limited data that this strategy may be clinically beneficial to prevent GV re-bleed.

CASE REPORT

We present the case of a 64 year old diabetic female patient who came in with a chief complaint of melena. No complaints of jaundice, abdominal pain or hematemesis. She has been diabetic for more than 15 years on dual oral hypoglycemic agents and was diagnosed with fatty liver

disease a year ago. On the first admission, she was hemodynamically stable, anemia was corrected and gastroscopy revealed a Grade 1 esophageal varix, portal hypertensive gastropathy and a prominent thickened fold at the gastric cardia. No point of bleeding was isolated at this time so colonoscopy was done which revealed internal hemorrhoids only. We advised further work ups for occult GI bleed, however patient preferred it on an outpatient basis. She was treated for cirrhosis secondary to NAFLD and primary prophylaxis with beta blockers were given for the patient.

Three months from initial presentation, there was recurrence of melena. The patient was readmitted for correction of anemia and repeat gastroscopy showed that the previously noted gastric fold at the cardia now appeared as a medium sized varix which was soft upon tactation with a catheter. We then proceeded with injection of 1cc total of undiluted histoacryl. The patient tolerated the procedure well and was discharged improved.

Two weeks post enbucrylation, patient came back for reassessment of GV. Gastroscopy showed faint reddish hematin spots atop the gastric varix without evidence of recent bleed. The variceal surface was hard on tactation. Endoscopic ultrasound done showed a hyperechoic structure near the aorta surrounded by small vessels with small amount of paraesophageal vascular structures.

Ten months from initial presentation, there was recurrence of melena. A pre gastroscopy EUS revealed hypoechoic and serpiginous structures with Doppler signal at the area of the GE junction. Injection of 0.5cc of undiluted histoacryl was done. Post enbucrylation EUS showed marked diminution of the vascular echoes. At present, no recurrence of bleeding eight months post obliteration.

DISCUSSION

In common clinical practice, varices are classified simply by their location into esophageal and gastric varices. Esophageal varices are graded according to size. In most cases the gastric and esophageal varices are diagnosed by endoscopy.The experienced endoscopist can identify GV

easily in the vast majority of cases. If there is doubt and the nature of an enlarged suspicious fundal "fold" cannot be determined, endoscopic ultrasound is the test of choice for confirmation.[13] Alternatively, transabdominal ultrasound with Doppler, computed tomography scan with contrast, magnetic resonance angiography, portovenography and interventional angiography can be used to identify GV, with the latter test being the most sensitive to recognize the presence and the anatomy of gastric and esophageal varices.

Large size of the varices, presence of ascites, advanced chronic liver disease (Child-Pugh class C cirrhosis), high portal pressure (hepatic venous pressure gradient > 12 mm hg) and red marks indicate high risk of variceal bleeding.[5,14] In acute upper gastrointestinal bleeding, the identification of esophageal varices is not difficult, but the appearance of esophageal varices on endoscopy is important, if there is no bleeding present at the time of the procedure. Signs indicating recent variceal bleeding or high risk of bleeding are the red wale marks. The presence of a venous plug or nipple on a varix indicates the probable site of rupture.

Isolated gastric varices (IGV1) are by themselves a risk factor of variceal bleeding. The risk of bleeding from GV was shown to correlate with variceal size (>10 mm), Child class and the presence of a red spot on the varices. The management of gastric varices has not been as well studied as that of esophageal varices. Controversy exists on the evaluation and possible pharmacologic and endoscopic treatment in those who have never bled. In addition there have currently not been any randomized controlled studies on the role of endoscopy and pharmacotherapy in the management of patients that have bled.

In geographic areas where glue is available there is no role for sclerotherapy and/or band ligation. Band ligation can be used only for small gastric varices. There is growing evidence that treatment with cyanoacrylate (tissue glue N-butyl-2-cyanoacrylate, bucrilate) is the most effective method for the treatment of GV. In a randomized, controlled study of various agents for endoscopic injection sclerotherapy of bleeding canine GV, cyanoacrylate was found to be the best agent overall in terms of immediate efficacy, low volume requirement, time required for initial hemostasis and reduction of gastric variceal size.[15] A randomized controlled trial showed that cyanoacrylate was more effective and achieved GV obliteration faster than injection sclerotherapy with alcohol.[6]

Endoscopic ultrasound (EUS) has revolutionized the diagnostic and therapeutic approach to patients with gastrointestinal disorders. Gastric varices are depicted by EUS as serpiginous, anechoic channels in the gastric submucosal and mucosal layers, below the esophagogastric junction. Several studies have shown that EUS is superior to conventional endoscopy for the diagnosis of GV.[16-18] Endoscopic ultrasound is also more sensitive than gastroscopy to distinguish GV from enlarged gastric folds.[11,18] Boustière et al reported a more than 6-fold increase in the rate of GV detection by using EUS compared with gastroscopy.[17]Using EUS as the gold standard, the sensitivity, specificity, positive-predictive value (PPV), and negative-predictive value (NPV) of endoscopy for the diagnosis of GV were 44%, 94%, 78%, and 79%, respectively.[19] Moreover, EUS can more accurately detect the variceal size, and by measuring the radius of the external and internal walls of the varices, one can also determine the variceal wall thickness.[20]

An EUS with color and pulsed Doppler facilities allows a detailed structural and hemodynamic evaluation of the upper abdominal collateral circulation in portal hypertension, with a potential for directed therapeutics. The potential application of EUS for improving outcomes in GV treatment includes as follows: EUS can improve the detection and diagnosis of gastroesophageal varices and collateral veins, provide endoscopic therapy of gastroesophageal varices by allowing more accurate EUS guided delivery of glue into the GV, provide knowledge on the efficacy of pharmacotherapy of portal hypertension by confirming complete GV obturation after glue injection and provide assessment and prediction of variceal recurrence after endoscopic therapy and assessment of portal hemodynamics.

Most series from India, Japan, Europe, and the United States report good initial hemostasis rates of over 90%. However, the re-bleeding rates from GV may be 15–30% after glue injections.[6] The risk of re-bleeding is mainly related to incomplete obturation of the gastric vascular channels. As a result of the deep-seated location of GV in the submucosal layer of the stomach, residual GV are difficult to detect and eradicate. Mucosal ulceration and scarring after sclerotherapy also make subsequent endoscopic assessment of variceal patency more difficult, and a treatment end point is difficult to define.

Immediately after therapy, the shape and size of the varices may not show any changes under endoscopic observation, but with EUS evaluation the varices are seen to become echogenic, and blood flow can no longer be detected by Doppler. The EUS can thus provide an objective end point for gastric variceal eradication. The paragastric large collateral channels usually persist after glue obturation of the intramural channels. There is evidence that persistence of large para-esophageal collaterals after esophageal variceal eradication is associated with increased rates of variceal recurrence and bleeding. However, there are no data which suggest that the size or number of persisting paragastric vascular channels is associated with increased recurrence or bleeding from GV.

CONCLUSION

Endoscopic ultrasound has the ability to identify the presence of gastric varices when endoscopic evaluation is uncertain. Moreover, it can be used to evaluate the efficacy of variceal glue injection as well as the possibility for monitoring the degree of vascularity.

REFERENCES

1. Luketic VA, Sanyal AJ. Esophageal varices. I. Clinical presentation, medical therapy and

endoscopic therapy. GastroenterolClin North Am 2000;29:337-385.

2. Williams SGJ, Westaby D. Management of variceal bleeding. British Medical Journal 1994; 308:1213-1217.

3. Sharara AI, rockey DC. Gastroesophagealvariceal hemorrhage. New England Journal of Medicine 2001; 345:669- 681.

4. Soderlund C. long-term survivors after varicealhaemor- rhage.Follow-up of a controlled study of endoscopic sclerotherapy versus conservative management. Scandinavian Journal of Gastroenterology 1987; 22:665-671.

5. Kim T, Shijo h, Kokawo h, al e. risk factors for hemorrhage from gastric fundal varices. hepatology 1997; 25:307-312. 6. Sarin SK, Jain AK, Jain M, Gupta r. A randomized con- trolled trial of cyanoacrylate versus alcohol injection in patients with isolated fundicvarices. American Journal of Gastroenterology 2002; 97:1010-1015.

6. Sarin SK, Jain AK, Jain M, Gupta r. A randomized con- trolled trial of cyanoacrylate versus alcohol injection in patients with isolated fundicvarices. American Journal of Gastroenterology 2002; 97:1010-1015.

7. Chen WC, hou MC, TsaySh, et al. Gastric perforation af- ter endoscopic ligation for gastric varices. Gastrointestinal Endoscopy 2001; 54:2001.

8. Shiha G, El-Sayed SS. Gastric variceal ligation: a new tech- nique. Gastrointestinal Endoscopy 1999; 49:437-441.

9. Feretis C, Tabakopoulos D, Benakis P, et al. Endoscopic he- mostasis of esophageal and gastric variceal bleeding with histoacryl. Endoscopy 1990; 22:282-284.

10. Soehendra N, Grimm h, Nam VC, Berger B. N-butyl-2-cy- anoacrylate: a supplement to endoscopic sclerotherapy. En- doscopy 1987; 19:221-224.

11. Caletti G, Brocchi E, Baraldini M, Ferrari A, Gibilaro M, Barbara L. Assessment of portal hypertension by endo- scopic ultrasonography. *GastrointestEndosc*1990;36: S21-S27 [PMID: 2184082]

12. Choudhuri G, Dhiman RK, Agarwal DK. Endosonographic evaluation of the venous anatomy around the gastro-esoph- ageal junction in patients with portal hypertension. *Hepato-gastroenterology* 1996; 43: 1250-1255 [PMID: 8908559]

13. Lee YT, Chan FKl, Ng EKW, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. Gastrointesti- nal Endoscopy 2000; 52:168-174.

14. HegabAM, luketic VA. Bleeding esophageal varices. Post- graduate Medicine 2001; 109:75-89.

15. Jutabha r, Jensen DM, See J, et al. randomized, controlled study of various agents for endoscopic injection sclerother- apy of bleeding canine gastric varices. Gastrointestinal Endoscopy 1995; 41:206-211.

16. Lee YT, Chan FK, Ching JY, et al. Diagnosis of gastroesophagealvarices and portal collateral venous abnormalities by endosonog- raphy in cirrhotic patients. *Endoscopy* 2002;34:391–8.

17. Boustière C, Dumas O, Jouffre C, et al. Endoscopic ultrasonogra- phy classification of gastric varices in patients with cirrhosis. Comparison with endoscopic findings.*J Hepatol*1993;19: 268–72.

18. Burtin P, Calès P, Oberti F, et al. Endoscopic ultrasonographic signs of portal hypertension in cirrhosis. *GastrointestEndosc*1996;44:257–61.

19. Sgouros SN, Bergele C, Avgerinos A. Endoscopic ultrasonography in the diagnosis and management of portal hypertension. Where are we next? *Dig Liver Dis* 2006;38:289–95.

20. Schiano TD, Fisher RS, Parkman HP, et al. Use of high-resolution endoscopic ultrasonography to assess esophageal wall damage after pneumatic dilation and botulinum toxin injection to treat achalasia. *GastrointestEndosc*1996;44:151–7.