Clinical Case Report

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Upper gastrointestinal ectopic variceal bleeding treated with various endoscopic modalities

Case reports and literature review

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Abstract

Rationale: Ectopic variceal bleeding is a rare (2–5%) but fatal gastrointestinal bleed in patients with portal hypertension. Patients with ectopic variceal bleeding manifest melena, hematochezia, or hematemesis, which require urgent managements. Definitive therapeutic modalities of ectopic varices are not yet standardized because of low incidence. Various therapeutic modalities have been applied on the basis of the experiences of experts or availability of facilities, with varying results.

Patient concerns: We have encountered eight cases of gastrointestinal ectopic variceal bleeding in five patients in the last five years.

Diagnoses: All patients were diagnosed with liver cirrhosis presenting melena or hematemesis.

Interventions: All patients were treated with various endoscopic modalities (endoscopic variceal obturation [EVO] with cyanoacrylate in five cases, endoscopic variceal band ligation (EVL) in two cases, hemoclipping in one case).

Outcomes: Satisfactory hemostasis was achieved without radiologic interventions in all cases. EVO and EVL each caused one case of portal biliopathy, and EVL induced ulcer bleeding in one case.

Lessons: EVO generally accomplished better results of variceal obturations than EVL or hemoclipping, without serious adverse events. EVO may be an effective modality for control of ectopic variceal bleeding without radiologic intervention or surgery.

Abbreviations: BP = blood pressure, BRTO = balloon-occluded retrograde transvenous occlusion, EGD = esophagogastroduodenoscopy, EVL = endoscopic variceal band ligation, EVO = endoscopic variceal obturation, HBV = hepatitis B virus, HCC = hepatocellular carcinoma, SRH = stigmata of recent hemorrhage, TIPS = transjugular intra-hepatic portosystemic shunt.

Keywords: adverse event, cyanoacrylate, ectopic, modalities, varices

1. Introduction

Varices located anywhere other than gastroesophageal region are called ectopic varices; such bleeding is rare, accounting for 2% to 5% of variceal bleeds.[1,2] Ectopic variceal bleeding can be fatal with a high mortality rate of up to 40% in duodenal variceal bleeding.[3,4] Many therapeutic modalities have been developed, including endoscopic treatments [endoscopic variceal obturation (EVO), endoscopic variceal band ligation (EVL)], radiologic interventions such as balloon-occluded retrograde transvenous occlusion (BRTO), transjugular intrahepatic portosystemic shunt (TIPS), and surgeries. There is no definitive standard therapy because of the rarity of cases, which makes diagnosis and treatment difficult. We present 5 patients, all with liver cirrhosis and variceal bleeding (3 with duodenal and 2 with jejunal) treated only with various endoscopic modalities and achieving successful hemostasis.

2. Methods

We have encountered 8 cases of gastrointestinal ectopic variceal bleeding in 5 patients in the last 5 years, successfully treated with various endoscopic modalities (EVO with cyanoacrylate in 5 cases, EVL in 2 cases, hemoclipping in 1 case). Written informed consent was obtained from all of the patients or the next of kin, and this study was performed in compliance with the Declaration of Helsinki.

3. Case reports

We investigated clinical cases of upper gastrointestinal ectopic variceal bleeding retrospectively between the years 2011 and 2015. All patients were provided written informed consent to undergo endoscopy. Endoscopic and clinical characteristics of the patients were analyzed (Table 1).

3.1. Patient 1

A 75-year-old man with alcoholic liver cirrhosis visited our center experiencing melena and hematochezia. On admission, his

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SWP and EC contribute equally to this work.

Written informed consent was obtained from all of the patients or the next of kin, and this study was performed in compliance with the Declaration of Helsinki.

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Table 1

Characteristics and clinical outcome of the enrolled patients.

Case no. (Pt no.)	Age/Sex	Cause	Location	Tx method	Hemostasis	Varix obturation	Rebleeding	Bleeding-related death	Complication
#1 (Pt. 1)	75/M	LC (A) s/p total gastrectomy	Jejunum	Cyanoacrylate 1 cc	Yes	Yes	No	No	None
#2 (Pt. 2)	67/M	LC (B)	Duodenum	Cyanoacrylate 1 cc	Yes	N/A	Yes	No	None
#3 (Pt. 2)	69/M	LC (B)	Duodenum	Cyanoacrylate 0.5 cc	Yes	N/A	No	Yes	None
#4 (Pt. 3)	55/M	LC (A)	Duodenum	Cyanoacrylate 1 cc	Yes	Yes	No	No	Portal biliopathy (Portal vein thrombosis)
#5 (Pt. 4)	69/F	LC (B), HCC	Duodenum	Hemoclipping	Yes	No	Yes	No	None
#6 (Pt. 4)	70/F	LC (B), HCC	Duodenum	EVL	Yes	Yes	No	No	EVL-induced ulcer bleeding with exposed vessel
#7 (Pt. 5)	60/M	LC (B), HCC, s/p Total gastrectomy	Jejunum	EVL	Yes	No	Yes	No	None
#8 (Pt. 5)	61/M	LC (B), HCC, s/p Total gastrectomy	Jejunum	Cyanoacrylate 0.5 cc	Yes	Yes	No	No	None

means Event of ectopic variceal bleeding. EVL = endoscopic variceal band ligation, LC(A) = alcoholic liver cirrhosis, LC(B) = HBV-associated liver cirrhosis, N/A = nonavailable, Pt. = patient.

hemoglobin level was 4.0 g/dL and blood pressure (BP) was 90/60 mm Hg. The patient had undergone total gastrectomy 16 years earlier because of early gastric cancer. He underwent emergent esophagogastroduodenoscopy (EGD; GIF Q 260; Olympus, Tokyo, Japan), which revealed esophageal varices without bleeding stigmata, and a polypoid jejunal varix with a whitish nipple sign just below the esophago-jejunal anastomosis site. A 2 mL 1 : 1 mixture of cyanoacrylate and ethiodized oil (Lipiodol) was injected into the jejunal varix without adverse event. Follow-up EGD after 3 weeks showed near resolution of the jejunal varix and a large amount of extruded glue casts (Fig. 1). He was discharged from the hospital, and no further bleeding was noted through 4 months of follow-up.

3.2. Patient 2

A 72-year-old man with hepatitis B virus (HBV)-associated liver cirrhosis visited our center with hematemesis. His hemoglobin level was 9.4 g/dL and BP was 100/60 mm Hg on admission. Emergent EGD showed scattered blood clots and duodenal varices, with a small erosion in the second portion of the duodenum considered stigmata of recent hemorrhage (SRH). After injection of 2 mL of the cyanoacrylate and Lipiodol mixture without adverse events, he was followed up for 18 months in the outpatient department without further bleeding.

He was readmitted to our hospital with hematemesis 1 year later. His hemoglobin level was 7.0 g/dL and BP was 90/60 mm Hg. Emergent EGD showed a duodenal varix with hematocystic spots, considered the bleeding focus, more proximally than the previous site in the duodenal bulb. EVO with 1 mL of the cyanoacrylate and Lipiodol mixture was performed to control the variceal bleeding. Despite hemodynamic stability and no further bleeding episodes, hepatic failure progressed and he expired on the fifth day of admission.

3.3. Patient 3

A 55-year-old man with alcoholic liver cirrhosis was admitted with melena. Emergent EGD showed duodenal varix with erosion, which was considered SRH. EVO was done with 2 mL of the cyanoacrylate and Lipiodol mixture in the second to third portion of the duodenum (Fig. 2). He was closely observed and discharged without further signs of bleeding.

The patient returned to our hospital 6 months later with intermittent fever, abdominal pain, and jaundice. Laboratory results showed a cholestatic pattern of liver function test abnormalities. Abdominal computed tomography scan demonstrated disappearance of the previous duodenal varix with Lipiodol remaining in the periduodenal vessel and superior mesenteric vein, but revealed a newly developed thrombosis in the main and left portal veins and superior mesenteric vein. We could also see the enhanced and compressed common bile duct beside the thrombus in the main portal vein, suggesting portal biliopathy. After endoscopic decompression and biliary drainage of the common bile duct, clinical symptoms and laboratory findings improved and the patient was discharged. Follow-up EGD 4 months after discharge showed obturation of the duodenal varix. He has had no further bleeding, relapse of pylephlebitis, or portal biliopathy through 8 months of follow-up.

3.4. Patient 4

A 69-year-old woman with HBV-associated liver cirrhosis and hepatocellular carcinoma (HCC) was admitted with melena. Her hemoglobin was 5.2 g/dL with BP of 90/60 mm Hg. Emergent EGD showed irregular venous engorgement with suspicious hematocystic spot lesions in the second portion of the duodenum, without esophageal or gastric varices. Four hemoclips were deployed at the duodenal lesion, and she became hemodynamically stable and discharged from hospital. However, follow-up EGD performed 3 months later demonstrated a remaining duodenal varix.

Seven months later, she was readmitted with melena. Her hemoglobin was 7.3 g/dL and BP was 80/50 mm Hg. On EGD, bluish nodular venous engorgements with oozing blood were seen in the second portion of the duodenum. These were treated with EVL using 3 bands, but she experienced melena and decreased hemoglobin after 5 days. Fresh blood was found on EGD, with exposed vessels and ulcers at previous EVL sites. Hemostasis was accomplished after application of 3 hemoclips

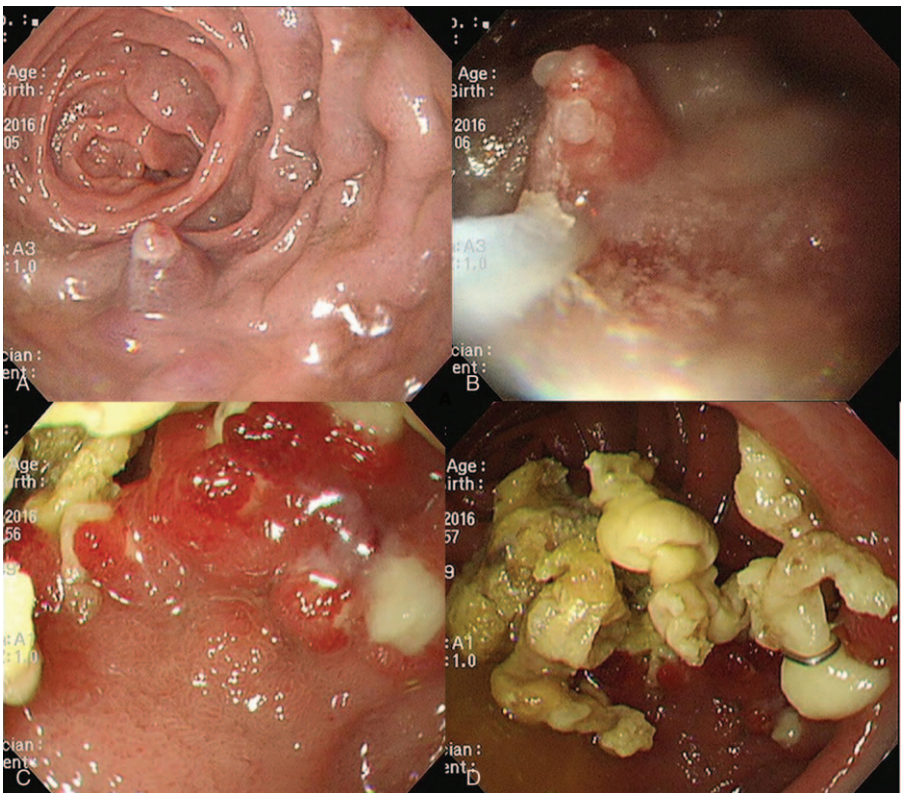

Figure 1. (Patient 1) Initial esophagogastroduodenoscopy (EGD) showed a polypoid jejunal varix with a whitish nipple sign just below the esophago-jejunal anastomosis site (A). A total of 2 mL of cyanoacrylate and lipiodol 1 : 1 mixture was injected into the jejunal varix (B). After 3 weeks, previously seen jejunal varices nearly disappeared (C) and a large amount of glue extrusion is observed (D).

(Fig. 3). She did not rebleed during 2 years of follow-up, and obturation of the duodenal varix was confirmed on EGD 5 months after discharge. However, her condition became worse and she finally died because of HCC aggravation.

3.5. Patient 5

A 62-year-old man with HBV-associated liver cirrhosis and HCC was admitted to our hospital with melena. His initial hemoglobin level was 7.9 g/dL and BP was 100/70 mm Hg. The patient had a history of total gastrectomy with Roux-en-Y anastomosis 10 years ago because of early gastric cancer. Emergent EGD was performed, and 2 hematocystic lesions considered SRH were noted just below the esophago-jejunal anastomosis site. He was treated with EVL using bands at each lesion and discharged after 5 days.

Fourteen months later, he was readmitted with melena. His hemoglobin decreased to 7.7 g/dL and BP was 80/50 mm Hg. Emergent EGD revealed oozing vessels just below the esophago-jejunal anastomosis site. EVO using 1 mL of the cyanoacrylate and Lipiodol mixture was administered without adverse events. There was no further bleeding for 5 days, and he was discharged. Follow-up EGD after 2 months demonstrated obturation of the jejunal varices. Until then, he had received 4 times of transarterial

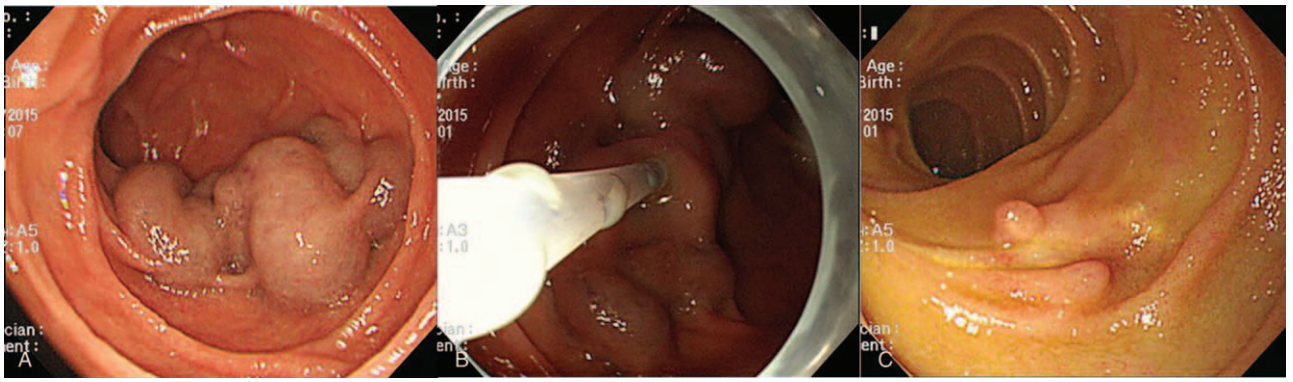

Figure 2. (Patient 3) EGD of the duodenum showed varices with erosion in the second to third portion of the duodenum is seen (A). A total of 2 mL of cyanoacrylate and lipiodol 1 : 1 mixture was injected into the duodenal varices (B). Previously seen duodenal varices nearly disappeared (C).

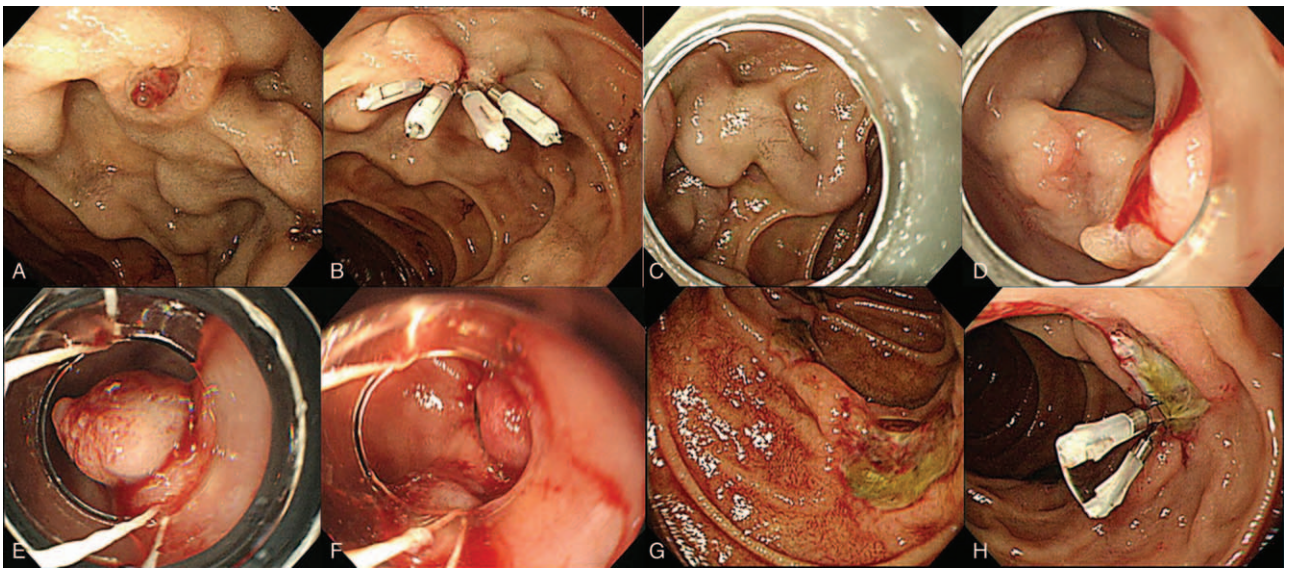

Figure 3. (Patient 4) EGD performed at first admission showed irregular venous engorgement with suspicious hematocystic spot in the 2nd portion of duodenum (A) and 4 hemoclips were applied (B). Three months later, remained duodenal varices were seen (C). Seven months later, EGD performed due to rebleeding demonstrated bluish nodular venous engorgements with bloody oozing in the 2nd portion of duodenum (D) and treated with EVL using 3 bands (E, F). EGD performed after 5 days of EVL showed ulcer bleeding with exposed vessel at previous EVL sites (G) and 3 hemoclips were applied (H).

chemoembolizations for HCC. However, during 5 months of follow-up, HCC aggravated and he expired as a consequence of hepatic failure.

4. Discussion

There are many studies evaluating efficacy and adverse events of treatment modalities for esophageal and gastric variceal bleeding.[5,6] Most of the available information about upper gastrointestinal ectopic variceal bleeding control is acquired from case reports or small case series. Randomized controlled trials have also not been reported. As a result, there is no proven, absolutely superior treatment modality for controlling ectopic variceal bleeding. We present 8 cases showing successful initial hemostasis using various endoscopic modalities, without radiologic intervention or surgery. Our experience may reinforce the evidence for selection of a best, most effective modality, and aid in making guidelines for the management of ectopic variceal bleeding.

Norton et al[1] reviewed 169 cases of ectopic variceal bleeding, and reported peristoma, duodenum, and jejunum and ileum as the common sites of ectopic variceal bleeding. Recognized causes of ectopic varices are intra- and extrahepatic portal hypertension, surgical procedures, anomalies of venous outflow vessels, abdominal vascular thromboses, rare familial conditions, and so on.[2] Three of five of our patients were bleeding from duodenal varices, and the other 2 from jejunal varices. In all patients, these varices were caused by liver cirrhosis: intrahepatic portal hypertension associated with alcoholic liver cirrhosis in two patients, and liver cirrhosis associated with HBV in 3 patients. Two patients with jejunal varices had a history of total gastrectomy because of early gastric cancer, resulting in anomalies of venous outflow.

In the past, preferred treatment of ectopic variceal bleeding included surgical options such as variceal suture ligation or resection, and portocaval shunt. Given the high mortality rate of up to 30% to 40% and reported rebleeding up to 40%,[3,7] surgery is now rarely performed. Surgical intervention may nevertheless be considered a salvage method in patients in whom nonsurgical modalities, such as endoscopic or radiologic interventions, have failed to achieve hemostasis. Recently, nonsurgical modalities such as EVL, EVO using cyanoacrylate were tried with effective, satisfactory outcomes, and lower adverse events than surgical methods. Akazawa et al[8] showed successful management of duodenal variceal bleeding by EVL and subsequent BRTO. Malik et al[9] and Mora-Soler et al[10] reported 1 and 5 patients with duodenal variceal bleeding treated successfully with cyanoacrylate injection, respectively. Schmeltzer et al[11] presented a case of duodenal variceal bleeding successfully treated with EVL. Kitagawa et al[12] showed a patient with jejunal variceal after choledochojejunostomy treated with EVO with cyanoacrylate. In our case series, all bleeding was completely controlled using only endoscopic modalities without surgeries or radiologic interventions such as BRTO[13,14] or TIPS.[15] We accomplished excellent hemostasis by cyanoacrylate injections in 5 cases, endoscopic variceal ligation in 2 cases, and hemoclipping in 1 case. The most frequently used modality in our cases was cyanoacrylate injection. Only 1 of 5 cyanoacrylate injection cases rebled. We saw obturation of varices in 3 of 5 cases; the rest were unavailable. In concordance with other reported cases,[9,11,16] cyanoacrylate injection seems to be effective and safe without serious adverse events.

EVL and hemoclipping were performed in 2 cases and 1 case, respectively. Variceal obturation was achieved in only 1 of 2 cases in the EVL group, and rebleeding also occurred in 1 case. Hemoclipping failed in both variceal obturation and prevention of rebleeding.

Adverse events of both EVL and EVO are treatment-induced ulcer, perforations, and strictures. Unlike EVL, EVO can also cause embolic events, bleeding due to cast extrusion from the injector needle site, and portal biliopathy.[17–19] In our series, 2 of 8 cases showed adverse events; patient 3 experienced portal biliopathy and pylephlebitis that developed 6 months after EVO, and patient 4 represented with an EVL-induced ulcer with

exposed vessel at the previous EVL site. Endoscopic treatment modalities for ectopic variceal bleeding were effective and easily accessible compared with surgical or radiologic interventions. Furthermore, adverse event of endoscopic treatment modalities for ectopic variceal bleeding was minor and easily controlled. Endoscopic therapeutic modalities, especially EVO, should therefore be considered to control ectopic variceal bleeding.

It is difficult to judge because of the rarity of cases, but endoscopic modalities for control of ectopic variceal bleeding have a high hemostasis rate. Rebleeding of ectopic varices after initial endoscopic modalities may occur, and can be treated successfully with additional endoscopic modalities. Our cases can contribute to strengthening the acceptance of endoscopic therapeutic modalities, especially EVO with cyanoacrylate, as useful in controlling ectopic variceal bleeding, which lacks a fully evaluated and established best treatment modality.

5. Conclusion

Ectopic variceal bleeding has a high risk of fatal massive bleeding because of delayed diagnosis and limited visualization during EGD compared with esophageal and gastric varices. Physicians should be cautious not to overlook ectopic variceal bleeding when assessing upper gastrointestinal bleeding or anemia of obscure origin in patients with portal hypertension. In the absence of consensus regarding treatment for ectopic variceal bleeding, endoscopic interventions, such as EVO, should be attempted before radiologic or surgical interventions.

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