

Successful treatment of repeated hematemesis secondary to post-sclerotherapy esophageal ulcer in a cirrhotic patient: A case report

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Summary

Esophageal variceal bleeding is a common lethal complication of cirrhosis. Endoscopic injection sclerotherapy (EIS) is one of the major endoscopic approaches for treating esophageal variceal bleeding. However, complications may occur after EIS, which mainly include retrosternal discomfort/pain, dysphagia, re-bleeding, esophageal ulcer, esophageal strictures, and esophageal perforation, etc. In this article, we reported a 36-year-old male who developed esophageal ulcer related bleeding after EIS. Currently, there is no consensus on the treatment strategy for esophageal ulcer-related bleeding after EIS. In the present case, the following treatment strategy may be effective for ulcer related bleeding. The first step is to inhibit gastric acid secretion and reduce portal pressure by intravenous infusion of esomeprazole and somatostatin, respectively. The second is local hemostasis by oral norepinephrine and lyophilizing thrombin powder. The third is to protect digestive tract mucosa by oral Kangfuxin Ye and aluminum phosphate.

Keywords: Esophageal varices, endoscopic injection sclerotherapy, endoscopic band ligation, esophageal ulcer, portal hypertension

1. Introduction

Esophageal and gastric varices are common complications of chronic liver diseases. On the other hand, esophageal varices are one of the most common causes of acute upper gastrointestinal bleeding (1,2). The 6-week mortality rate of each variceal bleeding episode is 15-20%, ranging from 0% among patients with Child class A to approximately 30% among patients with Child class C (3-5). Before the 1970s, the major treatment options of variceal bleeding included vasoconstrictors and surgical intervention. Since the

mid-1970s, endoscopic injection sclerotherapy (EIS) has been gradually employed for the treatment of esophageal variceal bleeding (6). EIS is superior to vasoconstrictors or balloon tamponade in controlling acute esophageal variceal bleeding (7,8). However, EIS is associated with a number of complications, such as esophageal ulcer, stenosis, and perforation (9). Among them, the incidence of ulcer related bleeding after EIS is 4.3-12.8% (10-19). At present, there is no consensus on the treatment strategy for esophageal ulcer-related bleeding after EIS. In this article, we reported a case of esophageal ulcer related bleeding after EIS and discussed the management of this complication.

2. Case presentation

On June 17, 2018, a 36-year-old male with a 19-month history of hepatitis C virus related liver cirrhosis was admitted to the Department of Emergency of our hospital due to intermittent hematemesis for 11 hours.

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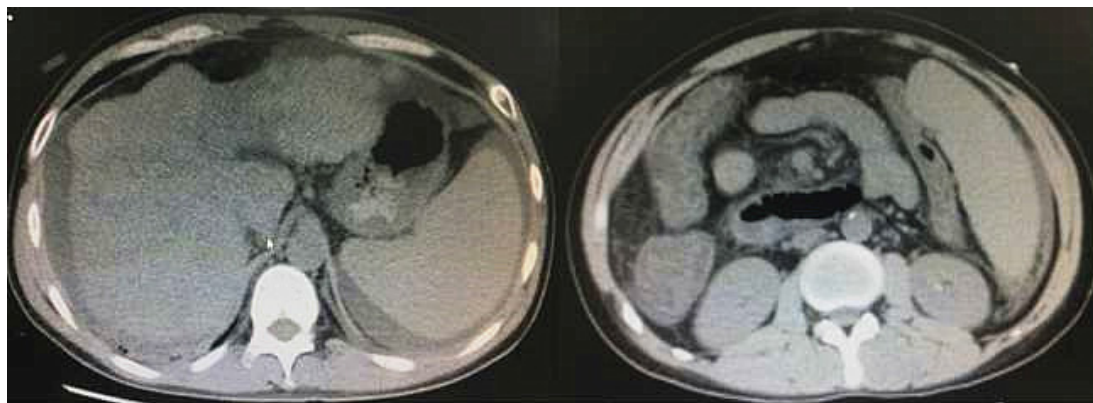


Figure 1. Abdominal CT scans showed cirrhosis, splenomegaly, ascites, and left renal calculus.

The volume of fresh blood vomited was about 300 mL. Immediately, infusion of terlipressin 2 mg, esomeprazole 80 mg, somatostatin 6 mg, hemocoagulase injection 2 u, and hydroxyethyl starch sodium chloride injection 500 mL was given at the Department of Emergency. He developed hematemesis again. The volume of fresh blood vomited was about 300ml. On June 18, 2018, he was transferred to our department. He had undergone endoscopic band ligation (EBL) with and without gastric variceal tissue adhesive injection for the treatment of acute variceal bleeding three times (on March 1, 2017, August 1, 2017, and March 27, 2018). He had a 10-year history of smoking and drinking.

After his admission, the patient did not have hematemesis or melena. Heart rate was 78 b.p.m. and blood pressure was 132/80 mmHg. Physical examinations demonstrated that his skin and sclera were yellow. On laboratory tests, red blood cell (RBC) was $4.05 \times 10^{12}/L$ (reference range: $4.0-5.5 \times 10^{12}/L$), hemoglobin (Hb) was 125 g/L (reference range: 110-150 g/L), hematocrit (HCT) was 38.2% (reference range: 35-45%), white blood cell (WBC) was $2.9 \times 10^9/L$ (reference range: $3.5-9.5 \times 10^9/L$), percentage of granulocyte (GR%) was 63.0% (reference range: 45-75%), total bilirubin (TBIL) was 62.2 $\mu\text{mol}/L$ (reference range: 5.1-22.2 $\mu\text{mol}/L$), direct bilirubin (DBIL) was 18.7 $\mu\text{mol}/L$ (reference range: 0-8.6 $\mu\text{mol}/L$), alanine amino-transaminase (ALT) was 30.43 U/L (reference range: 9-50 U/L), aspartate amino-transaminase (AST) was 61.38 U/L (reference range: 15-40 U/L), alkaline phosphatase (AKP) was 146.97 U/L (reference range: 45-125 U/L), γ -glutamyl transpeptidase (GGT) was 33.90 U/L (reference range: 10-60 U/L), prothrombin time (PT) was 21.5 seconds (reference range: 11.5-14.5 seconds), and international normalized ratio (INR) was 1.87. Abdominal computed tomography (CT) scans showed cirrhosis, splenomegaly, ascites, and left renal calculus (Figure 1). His Child-Pugh score was 12 points. Infusion of terlipressin 2 mg per 12 hours, esomeprazole 80 mg per 10 hours, polyene phosphatidylcholine 465 mg per day, isoglycyrrhizinate 150 mg per day, ademetionine 1,000 mg per day, and levofloxacin 0.5 g per day was given.

On June 19, 2018, the patient did not have hematemesis or melena. Laboratory tests demonstrated that WBC was $3.2 \times 10^9/L$, GR% was 63.0%, RBC was $3.85 \times 10^{12}/L$, Hb was 125 g/L, HCT was 36%, TBIL was 78.8 $\mu\text{mol}/L$, DBIL was 36.2 $\mu\text{mol}/L$, ALT was 29.03 U/L, AST was 53.49 U/L, AKP was 115.6 U/L, GGT was 31.46 U/L, albumin (ALB) was 31.3 g/L (reference range: 40-55 g/L), PT was 23.1 seconds, and INR was 2.04. Endoscopy showed three visible thrombi on the surface of the esophageal varices (Figure 2). Sclerotherapy with lauromacrogol 5 mL followed by tissue adhesive 0.5 mL was successfully performed by our endoscopist (Figure 2). After endoscopic treatment, terlipressin and esomeprazole were discontinued. Oral propranolol 10 mg per 12 hours was given.

On June 21, 2018, the patient developed hematemesis after sneezing. The volume of fresh blood vomited was about 100ml. Laboratory tests demonstrated that WBC was $4.8 \times 10^9/L$, GR% was 66.9%, RBC was $3.81 \times 10^{12}/L$, Hb was 117 g/L, HCT was 35.8%, TBIL was 53.9 $\mu\text{mol}/L$, DBIL was 34.5 $\mu\text{mol}/L$, ALT was 25.55 U/L, AST was 37.92 U/L, AKP was 124.34 U/L, GGT was 33.1 U/L, and ALB was 29.8 g/L. Infusion of somatostatin 3,000 u per 12 hours and esomeprazole 80 mg per 10 hours was given.

On June 22, 2018, endoscopy showed two ulcer lesions (Figure 3). At 15:00 o'clock, the patient developed hematemesis again. The volume of fresh blood vomited was about 100 mL. Laboratory tests demonstrated that WBC was $4.8 \times 10^9/L$, GR% was 76.1%, RBC was $3.65 \times 10^{12}/L$, Hb was 114 g/L, and HCT was 34.6%. Intravenous infusion of esomeprazole 80 mg per 10 hours was continued. The dosage of somatostatin was changed to 3,000 u per 6 hours. In addition, intravenous infusion of carbazochrome sodium sulfonate 80 mg per day and oral lyophilizing thrombin powder 5,000 u per day, norepinephrine 4 mg per day, and aluminum phosphate 20 g three times a day were given.

On June 24, 2018, the patient developed hematemesis again. The volume of fresh blood vomited was about 10 mL. Oral lyophilizing thrombin powder 5,000 u per day and norepinephrine 2 mg per day were given again.

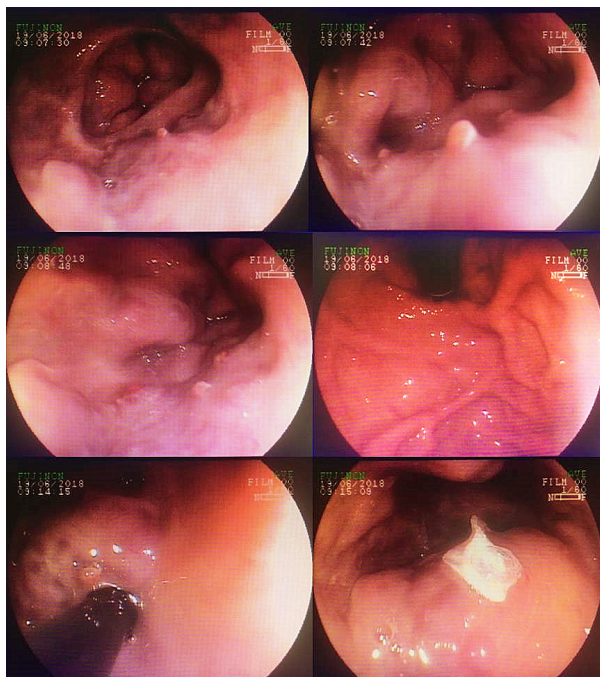


Figure 2. Endoscopy on June 19, 2018 showed three visible thrombi on the surface of esophageal varices, and then EIS was performed.

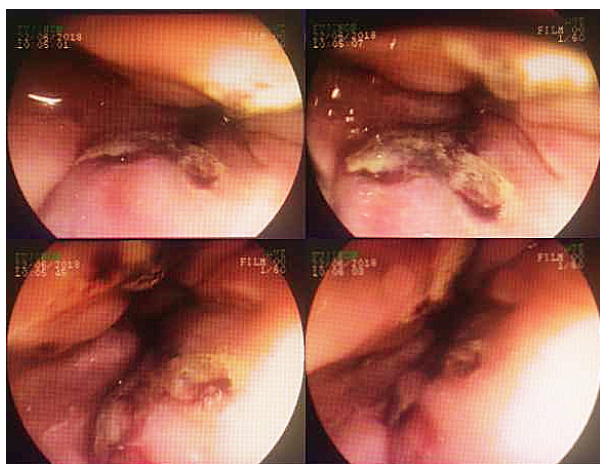


Figure 3. Endoscopy on June 22, 2018 showed two ulcer lesions.

On June 26, 2018, the patient did not have hematemesis or melena. Laboratory tests demonstrated that WBC was $4.1 \times 10^9/L$, GR% was 71%, RBC was $3.63 \times 10^{12}/L$, Hb was 116 g/L, HCT was 35.4%, TBIL was $45.5 \mu\text{mol}/L$, DBIL was $28.0 \mu\text{mol}/L$, ALT was 13.95 U/L, AST was 22.92 U/L, AKP was 108 U/L, GGT was 28.57 U/L, ALB was 27.0 g/L, PT was 23.4 seconds, and INR was 2.07. Isoglycyrrhizinate was discontinued. The dosage of somatostatin was changed to 3,000 u per 12 hours. Albumin 10 g per day was given. Oral Kangfuxin Ye, which is a traditional Chinese medicine drug for treatment of the damage of digestive tract mucosa, 10 mL per day was given.

On June 27, 2018, the patient developed hematemesis again. The volume of fresh blood vomited was about 30 mL. Intravenous infusion of somatostatin was changed to

3,000 u per 6 hours. Oral lyophilizing thrombin powder 5,000 u per day and norepinephrine 4mg per day were given again.

After that, he did not have hematemesis or melena. On June 30, 2018, laboratory tests demonstrated that WBC was $4.1 \times 10^9/L$, GR% was 71%, RBC was $3.63 \times 10^{12}/L$, Hb was 116 g/L, HCT was 35.4%, TBIL was $45.5 \mu\text{mol}/L$, DBIL was $28.0 \mu\text{mol}/L$, ALT was 13.95 U/L, AST was 22.92 U/L, AKP was 108 U/L, GGT was 28.57 U/L, ALB was 27.0 g/L, PT was 23.4 seconds, and INR was 2.07. The dosage of aluminum phosphate was changed to 20 g per day.

On July 1, 2018, the patient did not have hematemesis or melena. Somatostatin, levofloxacin, and carbazochrome sodium sulfonate were discontinued.

On July 4, 2018, the patient did not have hematemesis and then was discharged. Laboratory tests demonstrated that WBC was $3.2 \times 10^9/L$, GR% was 77%, RBC was $3.37 \times 10^{12}/L$, Hb was 111 g/L, HCT was 32.5%, TBIL was $31.7 \mu\text{mol}/L$, DBIL was $21.4 \mu\text{mol}/L$, ALT was 8.20 U/L, AST was 22.94 U/L, AKP was 103 U/L, GGT was 28.89 U/L, and ALB was 31.7 g/L. We recommended the patient to take medication at home, including oral Kangfuxin Ye 10 mL per day, aluminum phosphate 20 g per day, propranolol 10 mg twice a day, and polyene phosphatidylcholine 456 mg three times a day.

On August 6, 2018, the patient underwent follow-up endoscopic surveillance. Laboratory tests demonstrated that WBC was $2.2 \times 10^9/L$, GR% was 54%, RBC was $4.05 \times 10^{12}/L$, Hb was 129 g/L, HCT was 38.8%, TBIL was $39.9 \mu\text{mol}/L$, DBIL was $23.3 \mu\text{mol}/L$, ALT was 34.72 U/L, AST was 50.36 U/L, AKP was 159.70 U/L, GGT was 28.48 U/L, ALB was 36.1 g/L, PT was 19.5 seconds, and INR was 1.64.

On August 7, 2018, a follow-up endoscopy showed several esophageal varices with red color sign, and then EBL was performed. Mild varices were found in the gastric fundus (Figure 4).

On August 11, 2018, the patient did not have hematemesis or melena. Laboratory tests demonstrated that WBC was $2.5 \times 10^9/L$, GR% was 56.2%, RBC was $3.67 \times 10^{12}/L$, Hb was 117 g/L, HCT was 35%, TBIL was $38.4 \mu\text{mol}/L$, DBIL was $21 \mu\text{mol}/L$, ALT was 22.39 U/L, AST was 32 U/L, AKP was 170.49 U/L, GGT was 29.64 U/L, ALB was 32.1 g/L, PT was 20.6 seconds, and INR was 1.56. The patient was discharged. At the time of writing this manuscript, he is well without any other complaints.

3. Discussion

Currently, the first-line treatment option of acute variceal bleeding should be endoscopic treatment combined with vasoconstrictors (20). However, according to the current practice guideline, covered transjugular intrahepatic portosystemic shunt (TIPS) should be considered as the treatment of choice in the cases when endoscopic

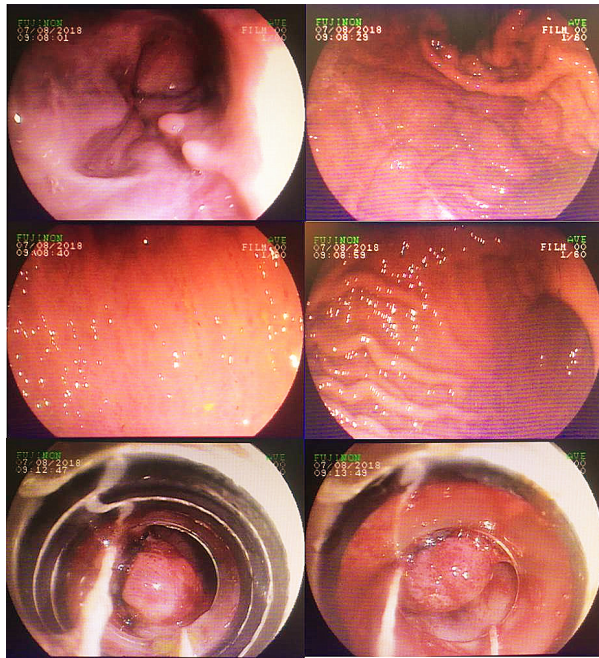


Figure 4. Endoscopy on August 7, 2018 showed mild varices on esophagus and gastric fundus with red color sign, and then EBL was performed.

treatment fails (21). Our case underwent endoscopic treatment for variceal bleeding many times. We recommended the use of TIPS, but he and his relatives refused.

EBL should be preferred, when endoscopic treatment is considered for the management of acute variceal bleeding in cirrhotic patients (20,21). Among the patients with acute esophageal variceal bleeding, the rate of re-bleeding in patients treated with EBL was lower than in those treated with EIS. The reason may be that EIS led to a sustained rise in hepatic venous pressure gradient, followed by an increased re-bleeding rate (22). A meta-analysis demonstrated that EBL was superior to EIS in terms of re-bleeding, complications, and variceal eradication (23). However, in our case, three visible thrombi were densely arranged on the surface of varices. Our endoscopist suggested that the ligation ring would pass over the thrombi and then lead to active bleeding during the procedure, if EBL was continued. Indeed, the American Society for Gastrointestinal Endoscopy (ASGE) guideline recommends that EIS may be performed in the case that EBL is technically difficult (24). After a comprehensive consideration, EIS was finally performed.

Adverse events of EIS include fever, retrosternal discomfort/pain, dysphagia, injection-induced bleeding, esophageal ulcers, esophageal strictures, esophageal perforation, pleural effusion, acute respiratory distress syndrome, and infection (9,25). Our case developed esophageal ulcer related bleeding after EIS (Figure 3). We reviewed the literature regarding the occurrence of re-bleeding secondary to esophageal ulcer after EBL or EIS (Table 1). As for most of esophageal ulcers

Table 1. Re-bleeding secondary to esophageal ulcer after EIS or EBL.

First author	Year	Country	Number of total cases	EIS			EBL		
				Incidence of ulcer after EIS	Incidence of re-bleeding after EIS	Re-bleeding caused by ulcer after EIS	Incidence of ulcer after EBL	Incidence of re-bleeding after EBL	Re-bleeding caused by ulcer after EBL
Laine	1993	USA	77	NA	43.6% (17/39)	12.8% (5/39)	NA	26.3% (10/38)	2.6% (1/38)
Lo	1995	China Taiwan	120	NA	50.8% (30/59)	8.5% (5/59)	NA	32.8% (20/61)	1.6% (1/61)
Baroncini	1997	Italy	111	NA	18.5% (10/54)	5.6% (3/54)	NA	15.8% (9/57)	8.8% (5/57)
Lo	1997	China Taiwan	71	8.8% (3/34)	33% (10/30)	NA	2.7% (1/37)	6/36 (17%)	NA
de la Peña	1999	Spain	88	4.3% (2/46)	50% (23/46)	4.3% (2/46)	7.1% (3/42)	28.6% (12/42)	7.1% (3/42)
Al Traif	1999	Saudi Arabia	60	NA	17% (5/29)	6.9% (2/29)	NA	23% (7/31)	9.7% (3/31)
Masci	1999	Italy	100	18% (9/50)	NA	NA	8% (4/50)	NA	NA
Robert	2001	USA	111	25.4% (15/59)	NA	NA	5.7% (3/52)	NA	NA
Zargar	2002	India	49	16.7% (4/24)	25% (6/24)	8.3% (2/24)	4% (1/25)	4% (1/25)	0% (0/25)
Awad	2012	Egypt	120	20% (12/60)	13.3% (8/60)	NA	16.7% (10/60)	10% (6/60)	NA
Overall				4.3-25.4%	13.3-50.8%	4.3-12.8%	2.7-16.7%	4-32.8%	0-9.7%

Abbreviations: EIS, endoscopic injection sclerotherapy; EBL, endoscopic band ligation; NA: not available.

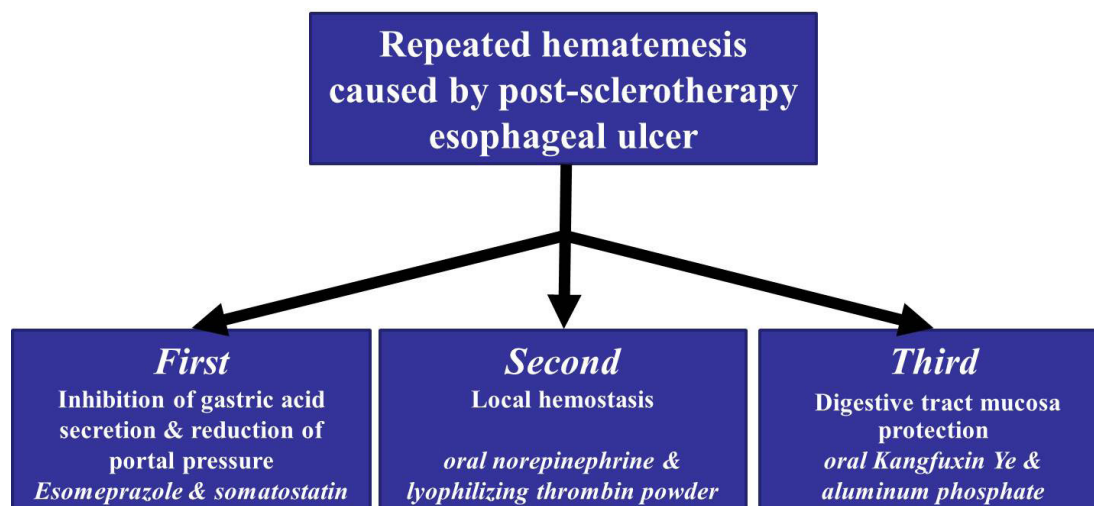


Figure 5. Treatment procedure in this patient.

without bleeding after EIS, no special treatment was required (15). The prophylactic use of acid suppression drugs after endoscopic treatment for gastroesophageal varices remains uncertain (26). By comparison, as for active bleeding secondary to esophageal ulcers, endoscopic injection of epinephrine might be useful for hemostasis (15). Our case had active ulcers bleeding after EIS. Our treatment strategy was as follows: the first was to inhibit gastric acid secretion and reduce portal pressure by intravenous infusion of esomeprazole and somatostatin, respectively; the second was local hemostasis by oral norepinephrine and lyophilizing thrombin powder; the third was to protect digestive tract mucosa by oral Kangfuxin Ye and aluminum phosphate (Figure 5). Despite his ulcer related bleeding stopped, the duration of treatment was long.

In conclusion, esophageal ulcer is a major cause of early re-bleeding after EIS. However, at present, there is no consensus regarding treatment strategy of esophageal ulcer related bleeding after EIS. Our successful treatment strategy may be validated in a large-scale study.

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