Chapter 34
Endoscopic Treatment of Gastric Varices: Histoacryl Method

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Abstract The endoscopic injection of cyanoacrylate glue (Histoacryl) has been successfully used to obliterate gastric varices in various parts of the world. To perform this treatment safely and effectively, the Histoacryl should be diluted with 5% Lipiodol (1:1) to lengthen the cyanoacrylate polymer and allow fluoroscopic monitoring. A mixture of Histoacryl and 5% Lipiodol should be injected to fill the gastric varices and the juxta-variceal portions of their inflow/outflow veins. Most gastric varices consist of a single varicose vessel and can be successfully obstructed with two injections. In the case of large gastric varices consisting of multiple varices, Histoacryl should be injected not only into the main varices but also into any small varices and connecting ramifications. The fluoroscopic monitoring of the injection procedure is very important for reducing the risk of complications and ensuring that gastric varices are completely obliterated. Assessments of variceal anatomy might provide useful clinical information that will lead to improvements in the treatment strategies for such patients. The endoscopic injection of cyanoacrylate glue (Histoacryl) under fluoroscopic guidance can rapidly halt life-threatening gastric variceal bleeding and remove patients' long-term fears regarding the risk of rebleeding.

Keywords Gastric variceal bleeding · Histoacryl · Vascular anatomy · Lipiodol Fluoroscopic observation

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34.1 Introduction

Gastric varices (GV) are often seen in patients with portal hypertension. Although GV are associated with a lower risk of bleeding than esophageal varices (EV), bleeding GV are severe and potentially life-threatening complications [1]. Endoscopic injection sclerotherapy using conventional sclerosants and endoscopic variceal ligation have been widely accepted as treatments for bleeding EV, both for the management of active bleeding and the prevention of recurrent bleeding over the long term [2, 3]. However, in the case of bleeding GV, such endoscopic therapies yield poor control of bleeding and are associated with a high frequency of severe complications [4, 5].

In contrast to standard sclerosants, the tissue adhesive butyl cyanoacrylate (cyanoacrylate glue) polymerizes immediately and induces vascular obliteration on contact with blood. The endoscopic intravascular injection of cyanoacrylate glue was originally proposed by Soehendra et al. in 1986 as a therapeutic option for large bleeding esophagogastric varices [6]. Subsequent studies have suggested that this method might be useful for achieving GV obliteration, and it has been successfully employed for the treatment of GV bleeding worldwide [7, 8]. However, there are still some controversies concerning the optimal technique, and little information is available about the long-term effects of such treatment and the most appropriate management strategies for special types of GV in the gastric cardia and gastric body.

We have conducted endoscopic obliteration with cyanoacrylate glue (Histoacryl®; Braun Melsungen, Germany) for GV bleeding since 1992 [9] based on evaluations of gastric vascular anatomy [10] and have used this technique to save the lives of patients with GV bleeding [9, 11]. To perform this treatment safely and effectively, Histoacryl diluted with 5% Lipiodol (1:1) should be carefully injected into the GV under fluoroscopic guidance while taking the vascular anatomy of the GV into account. This paper mainly describes the technique we employ for the treatment of GV.

34.2 Gastric Vascular Anatomy

According to evaluations of GV anatomy performed with color Doppler endoscopic ultrasonography (CDEUS), varicography, and three-dimensional computed tomography (3D-CT), we consider that the anatomy of GV can be broadly divided into two types: type 1 (Fig. 34.1a), in which the vascular anatomy of the GV consists of a single varicose vessel of almost the same diameter as the inflow/outflow vein without any noticeable ramifications, and type 2 (Fig. 34.1b), in which the vascular anatomy of the GV consists of multiple varicose vessels with complex connecting ramifications [9–11]. Associations have been detected among the endoscopic features, locations, and vascular anatomy of GV. Type 1 is the most common type of GV, although it is found almost exclusively in cases of so-called isolated GV (86%), whereas type 2 is generally encountered in special cases of GV in which EV extend

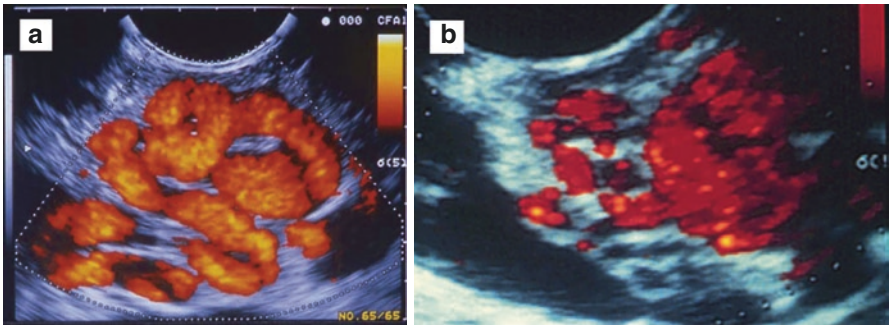

Fig. 34.1 (**a**) CDEUS image of a type 1 GV shows only one inflow/outflow vein and one varicose vessel without ramifications. (**b**) CDEUS image of a type 2 GV shows multiple varicose vessels connected to one another with complex ramifications

into the gastric cardia and body (91%) [10]. The endoscopic injection of Histoacryl should be carried out in a manner that takes the vascular anatomy of the GV into consideration.

34.3 Treatment Procedure

The procedure is visualized using a forward-view videoendoscope (Olympus Optical Co., Ltd., Tokyo, Japan), and a 23-gauge needle (Top Co., Ltd., Japan) is used for the injections. Most procedures require a retroflexed view for visualization and puncture. Before the intravascular puncture procedure, 1 mL of Histoacryl is drawn up into an ordinary 2.5-mL plastic syringe and diluted with 5% Lipiodol (1:1) (producing the Histoacryl mixture) to lengthen the cyanoacrylate polymer and allow fluoroscopic monitoring. The 23-gauge needle should be rinsed with distilled water or 50% glucose before and after the injection.

In patients with bleeding GV, an attempt should be made to puncture the GV as near to the bleeding site as possible. If it is impossible to precisely puncture the target varices because of massive bleeding, or if no Histoacryl has been prepared, e.g., in cases involving emergent endoscopy, the short-term use of a balloon or endoscopic clips to achieve temporary hemostasis is recommended. Once the bleeding has completely stopped, i.e., after approximately 6 h, the Histoacryl should be injected into the GV at the bleeding site, which will be readily recognizable as it will be covered with clotted blood and fibrin. The exact position of the needle relative to the planned GV puncture site should be checked before the injection procedure. The intravascular puncturing of large varices is easy. However, paravascular puncturing causes mucosal swelling. When Histoacryl is injected into the gastric muscular layer, blood might spurt from the puncture site after the needle is pulled out. Deep puncturing should be avoided.Therefore, superficial puncturing is recommended for small GV. The flow of the Histoacryl mixture can be monitored

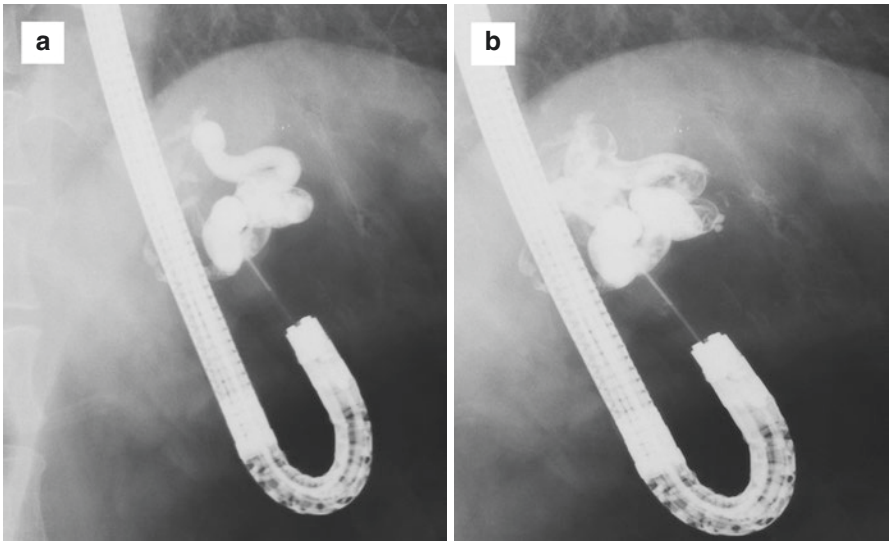

Fig. 34.2 X-ray varicography images obtained in a representative patient during the endoscopic injection of a mixture of Histoacryl and Lipiodol. The GV, which consisted of a single varicose vessel, was completely obstructed via two injections of a mixture of Histoacryl and Lipiodol. (**a**) X-ray images obtained during the second injection. The injection was halted when the mixture of Histoacryl and Lipiodol filled the region extending from the puncture site to the juxta-variceal portion of the outflow vein. (**b**) X-ray images obtained during the first injection. The injection was halted when the mixture of Histoacryl and Lipiodol filled the region extending from the puncture site to the juxta-variceal portion of the inflow vein

fluoroscopically during the injection, and the injection should be continued until the Histoacryl mixture has filled the GV and the juxta-variceal portions of their inflow/outflow veins.

The first injection should be halted when the Histoacryl mixture starts to move from the puncture site to the juxta-variceal portion of the outflow veins (Fig 34.2a), after which a second injection is performed at the same or a different site to occlude the inflow veins (Fig 34.2b). Most GV consist of a single varicose vessel and can be completely obstructed via two injections of the Histoacryl mixture. In fact, some small GV can be obstructed with a single injection. The adequacy of the GV obliteration can be judged based on the shape of the Histoacryl mixture cast. In the case of large type 2 GV, the Histoacryl mixture should be injected into both the main and small varices and any complex connecting ramifications.

34.4 Case Reports

Case 1 This case involved a 54-year-old female patient with decompensated alcoholic liver cirrhosis. At the previous hospital, she underwent endoscopy for anemia, and the endoscopist found blood spurting from a small fundal varix (Fig. 34.3a) and

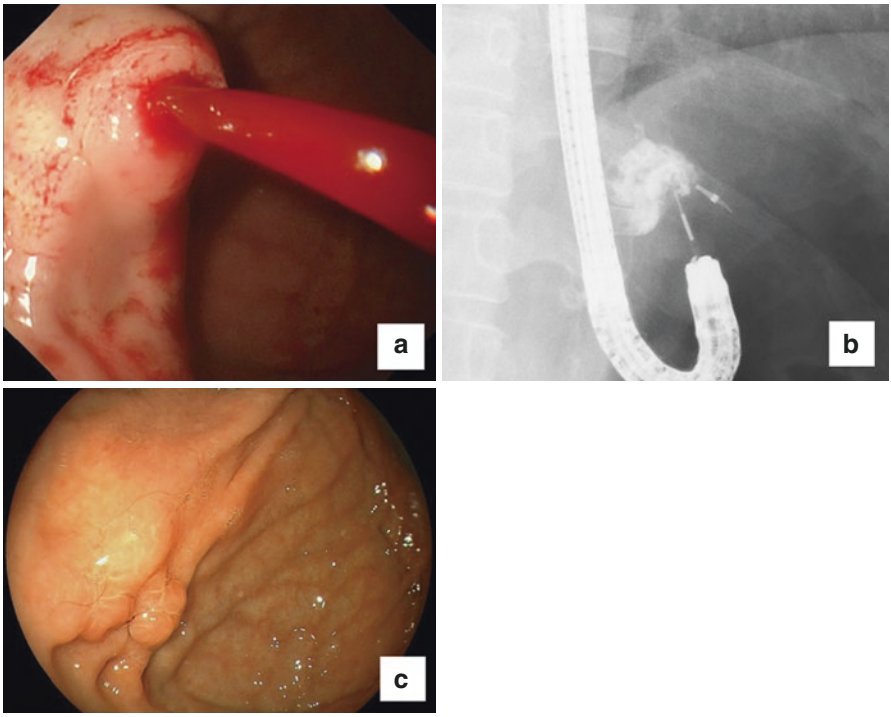

Fig. 34.3 (**a**) Endoscopic appearance of blood spurting from a small fundal varix. (**b**) X-ray varicography showing that the varicose vein has been completely occluded after two endoscopic injections of a mixture of Histoacryl and Lipiodol. (**c**) Endoscopic image obtained at 6 postoperative months showing a completely eradicated GV

immediately subjected the bleeding site to endoscopic clipping. The bleeding was temporarily arrested. The patient received a 4-unit blood transfusion and was referred to our hospital. At our hospital, two endoscopic intravascular injections of 1.5 mL and 1.0 mL, respectively, of the Histoacryl mixture were administered near the clipping site (Fig. 34.3b). The GV was completely eradicated after 6 months (Fig. 34.3c), and since then there has been no further variceal bleeding.

Case 2 A 72-year-old female patient with liver cirrhosis of unknown cause was admitted after producing bloody stools. She had previously undergone endoscopic obliteration with Histoacryl for large GV. Emergent endoscopy revealed blood oozing from the GV, which had been almost completely obliterated. Endoscopic clipping was not effective to stop the bleeding (Fig. 34.4a); therefore it was arrested with a Sengstaken-Blakemore tube. After 6 h, i.e., after the bleeding stopped, 1 mL of the Histoacryl mixture was injected endoscopically into the rupture site, which was covered with a blood clot, under fluoroscopic observation. The remaining small varicose vessels and the associated ramification were fully obstructed with the Histoacryl mixture (Fig. 34.4b), and the bleeding stopped immediately (Fig. 34.4c). No recurrent bleeding has occurred since.

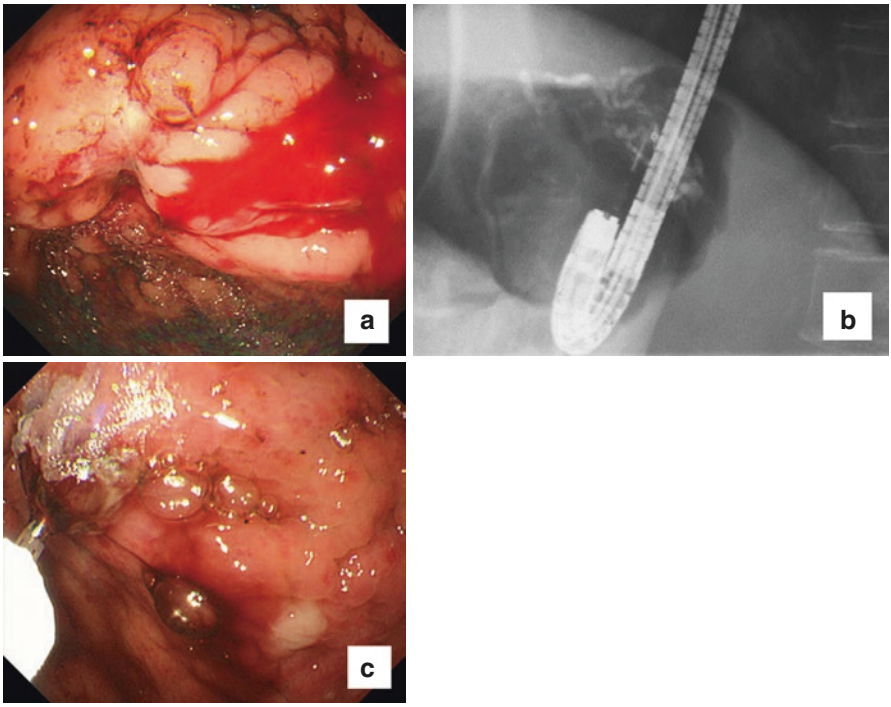

Fig. 34.4 (**a**) Image obtained during emergent endoscopy showing blood oozing from the remaining small varices. The bleeding was arrested with a Sengstaken-Blakemore tube. (**b**) Varicography showing that the small varicose veins and the remaining ramification has been completely filled with a mixture of Histoacryl and Lipiodol. (**c**) Endoscopic image showing that the bleeding has arrested just after the injection of the mixture of Histoacryl and Lipiodol

34.5 Discussion

Regarding our long-term results of endoscopic obliteration with Histoacryl, the primary hemostasis success rate was 95.8% among 71 patients with GV bleeding [11]. This primary hemostasis rate was comparable to or better than those of 90–96% described in other reports [8, 12]. Nine patients (two patients with type 1 GV and seven patients with type 2 GV) developed recurrent GV bleeding over the 17-year study period [11]. Most cases of recurrent GV bleeding were due to incomplete obliteration and occurred within 1 year of the primary hemostasis. The so-called isolated GV, i.e., those with type 1 vascular anatomy (the most common type of GV), were easily obstructed via one or two injections of Histoacryl, indicating that the condition is associated with a very low long-term risk of recurrent bleeding. In the patients with type 2 GV, such as the patient in Case 2, the residual small varicose vessels left after the endoscopic obliteration were found to be associated with a risk of recurrent bleeding. In general, the recurrent bleeding was not severe and could be controlled via repeated endoscopic injections of Histoacryl. However, in a few

patients who had very complex vascular anatomies and had developed collateral vein systems, complete obliteration of the GV could not be achieved [11]. In the patients who respond poorly to re-injection with Histoacryl, non-endoscopic techniques, such as surgical procedures or transjugular intrahepatic portosystemic shunts, are effective alternatives. During a long survey performed at our institution, the main causes of death among patients who underwent endoscopic obliteration for GV were shown to be liver failure, followed by hepatocellular carcinoma, as was found in previous studies [8, 12]. The median survival time of all patients who underwent endoscopic obliteration for GV bleeding was 5.5 years, and the 1-year, 10-year, and 15-year cumulative survival rates of such patients were 76%, 28%, and 12%, respectively.

The overall safety of Histoacryl injection is generally good [5–11]. The injection of an excessive amount of Histoacryl can result in the migration of the injected material after intravasal injections and local tissue necrosis after paravasal injections. Histoacryl should be diluted with 5% Lipiodol (1:1) to lengthen the Histoacryl polymer and allow fluoroscopic monitoring of the intravariceal injections and the extent of the occlusion induced by the injected Histoacryl. The amount of Histoacryl injected should be based on the amount required to fill the GV. If the Histoacryl mixture alone is used to fill the GV, then a large amount of the mixture will be required. As Histoacryl diluted with Lipiodol does not polymerize immediately on contact with blood, the subsequent injection of 50% glucose could help to spread the Histoacryl mixture, which would reduce the amount of Histoacryl required to obstruct the GV. After the injection of 50% glucose, the Histoacryl mixture induces complete vascular obliteration.

To avoid complications, the speed of the Histoacryl injection is important. A slow rate of injection can result in the Histoacryl mixture being displaced by blood flow before it has polymerized in the GV. Thus, rapid injections are recommended, especially in cases involving GV of greater than 10 mm in diameter [11, 13]. However, the subsequent injection of the 50% glucose should be conducted slowly as injecting it rapidly would increase the risk of the Histoacryl mixture being pushed out from the GV and into the inflow/outflow varicose vein, which is known as ectopic embolization. In previous studies, the leakage of a large amount of Histoacryl into muscular tissue caused severe complications, such as gastric wall necrosis and retroperitoneal abscesses. These complications were refractory to conservative treatment and needed to be treated surgically to prevent them from becoming life-threatening [11, 13]. To avoid severe complications developing, accurate intravariceal injections of Histoacryl should be administered at few puncture sites. In addition, the fluoroscopic monitoring of the injection process is very important for reducing the risk of complications and ensuring that GV are completely obliterated.

In conclusion, the complete endoscopic obliteration of GV with Histoacryl under fluoroscopic guidance can rapidly save patients from life-threatening GV bleeding and remove patients' long-term fears regarding the risk of recurrent bleeding. Assessments of variceal anatomy can provide clinically useful information that might aid the development of improved treatment strategies for the patients with GV.

References

1. Watanabe K, Kimura K, Matsutani E, et al. Portal hemodynamics in patients with gastric varices. A study in 230 patients with esophageal and/or gastric varices using portal vein catheterization. Gastroenterology. 1988;95:434–40.
2. Iwase H, Suga S, Schimada M, et al. Eleven-year survey and efficacy of endoscopic injection sclerotherapy using 2% sodium tetradecyl sulfate and contrast medium. J Clin Gastroenterol. 1996;22:58–65.
3. Hon MC, Lin HC, Kuo BIT, et al. The rebleeding course and long-term outcome of esophageal variceal hemorrhage after ligation: comparison with sclerotherapy. Scand J Gastroenterol. 1999;11:1071–6.
4. Goff JS. Endoscopic sclerotherapy for esophageal and gastric varices: safety and efficacy. Endoscopy. 1994;26:483–5.
5. Stiegmn GV. Elastic band ligation of esophageal and gastric varices. Advanced therapeutic endoscopy. New York: Raven Press; 1994. p. 95–103.
6. Soehendra N, Nam VC, Grimn H, et al. Endoscopic obliteration of large oesophageal gastric varices with bucrylate. Endoscopy. 1986;18:25–6.
7. Kind R, Gugkielmn A, Rodella L, et al. Bucrylate treatment of bleeding gastric varices: a 12 year's experience. Endoscopy. 2000;32:512–9.
8. Huang YH, Yeh HZ, Chen GH, et al. Endoscopic treatment of bleeding gastric varices by N-butyl-2-cyanoacrylate (Histoacryl) injection: long-term efficacy and safety. Gastrointest Endosc. 2000;52:160–7.
9. Iwase H, Suga S, Morise K, et al. Color Doppler endoscopic sonography for the evaluation of gastric varices and endoscopic obliteration with cyanoacrylate glue. Gastrointest Endsc. 1995;41:150–4.
10. Iwase H, Maeda O, Shimada M, et al. Endoscopic ablation with cyanoacrylate glue for isolated gastric variceal bleeding. Gastrointest Endsc. 2001;53:585–92.
11. Iwase H, Shimada M, Tsuzuki T, et al. Long-term results of endoscopic obliteration with cyanoacrylate glue for gastric fundal variceal bleeding: a 17-year experience. JJPH. 2011;17:137–44.
12. Kind R, Gugkielmn A, Rodella L, et al. Bucrylate treatment of bleeding gastric varices: a year' experience. Endoscopy. 2000;32:512–9.
13. Seewald S, Stiram PVJ, Naga M, et al. Cyanoacrylate glue in gastric variceal bleeding. Endoscopy. 2002;34:926–32.