Endoscopic Treatment of Boerhaave Syndrome Using Polyglycolic Acid Sheets and Fibrin Glue: A Report of Two Cases

Yumiko Ishikawa¹, Takashi Tagami¹, Hayato Hirashima², Reo Fukuda¹, Yuuta Moroe¹ and Kyoko Unemoto¹

¹Department of Emergency and Critical Care Medicine, Nippon Medical School Tama Nagayama Hospital, Tokyo, Japan ²Department of Gastroenterology, Utsunomiya Memorial Hospital, Tochigi, Japan

Boerhaave syndrome, the spontaneous perforation of the esophagus, is an emergency, life-threatening condition. Current endoscopic treatment options include clipping and stenting, but the use of polygly-colic acid (PGA) sheets for treating the condition has not been reported. In recent years, PGA sheets have been used after endoscopic submucosal dissection to prevent perforations and stricture formation in patients treated for early-stage carcinoma. We report the cases of two patients with Boerhaave syndrome who were successfully treated using PGA sheets. The present clinical outcomes suggest that the use of PGA sheets is feasible and safe for treating patients with Boerhaave syndrome, and that they may be another treatment option. (J Nippon Med Sch 2017; 84: 241–245)

Key words: Boerhaave syndrome, esophageal perforation, polyglycolic acid (PGA) sheet, fibrin glue, endoscopic treatment

Introduction

Boerhaave syndrome, the spontaneous perforation of the esophagus, is an emergency, life-threatening condition with a high mortality rate. Accurate diagnosis, definitive interventional treatment, and perioperative intensive care management are required for patients experiencing this syndrome¹. The gold standard treatment is surgical repair²⁻⁴. However, such highly invasive surgery may not be the preferred option for some patients, especially elderly individuals with hemodynamic and/or respiratory instability. Additionally, exposing the ruptured site of the fragile esophagus is also sometimes difficult. Moreover, strictures and dehiscence of the ruptured suture site often occur postoperatively. Thus, to overcome these surgeryrelated problems, endoscopic treatment (e.g., closure of the ruptured site using clips or stents) may be considered^{1,5,6}.

Throughout recent decades, improvements have occurred in the treatment of early-stage esophageal carcinoma, using endoscopic submucosal dissection (ESD). A novel and effective approach has been reported to involve the use of polyglycolic acid (PGA) sheets, in combination with ESD; promising outcomes have been observed⁷⁻¹¹. Several reports have suggested that the use of an endoscopic tissue-shielding method, involving PGA sheets and fibrin glue, may prevent delayed perforations and stenosis after ESD.

Successful endoscopic treatment of Boerhaave syndrome, involving clipping or stenting, has been recently reported¹²⁻¹⁸, but reports regarding the use of PGA sheets for the treatment of this condition have not been published. Here, we present the cases of two patients with Boerhaave syndrome who were successfully treated, endoscopically, with PGA sheets and fibrin glue, without primary suturing of the ruptured site, during treatment.

Case Report

Case 1

A 64-year-old man (height, 170 cm; weight, 80 kg) was transferred to our university hospital because of chest pain. The patient's chief complaint was sudden-onset severe chest pain that followed alcohol consumption and vomiting; he also reported cold sweats. His blood pressure (88/40 mmHg), pulse rate (70 beats/min, regular),

Correspondence to Takashi Tagami, Department of Emergency and Critical Care Medicine, Nippon Medical School Tama Nagayama Hospital, 1–7–1 Nagayama, Tama, Tokyo 206–8512, Japan

E-mail: t-tagami@nms.ac.jp

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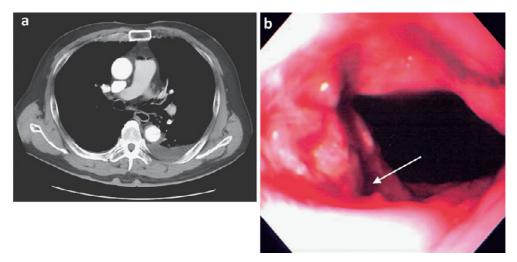


Fig. 1 (a) Computed tomography of Patient 1 shows pneumomediastinum with plural effusion.(b): Endoscopic image of the lacerated left posterior wall of the esophagogastric junction (arrow).

respiratory rate (23 breaths/min), and laboratory findings were unremarkable. Computed tomography revealed pneumomediastinum and pleural effusion (**Fig. 1a**), and endoscopy demonstrated a laceration in the left posterior wall of his esophagogastric junction (**Fig. 1b**). Based on the above findings, the patient was diagnosed with Boerhaave syndrome.

Because of the presence of a large amount of contaminated pleural effusion, a thoracotomy was performed. There was leakage of gastric fluid, with large amounts of saburra and hemothorax. During lesion exteriorization, we noted that the patient's esophagus was very fragile and that primary suturing was not feasible. Thus, we irrigated the pleural cavity and inserted drainage tubes at the anterior and posterior areas of the lesion and at the pulmonary apex. After obtaining written informed consent from the patient's family (he also provided deferred informed consent as he recovered consciousness), we endoscopically covered the laceration with a PGA sheet, after the thoracotomy.

The endoscopic treatment involved the following steps. First, we gripped a 100×50 -mm PGA sheet (Neoveil, Gunze, Kyoto, Japan) with a pair of grasping forceps at the distal end of the endoscope, moistened the sheet with normal saline, and wrapped it around the endoscope (**Fig. 2a and 2B**). After the end of the endoscope passed the wound, we advanced the grasping forceps through the overtube, released the grip, and placed the PGA sheet over the wound (**Fig. 2c**). Next, we fixed the distal part of the PGA sheet to normal tissue with a clip (**Fig. 2d**), partially withdrew the endoscope to cover the wound with the PGA sheet, and fixed the proximal end of the

PGA sheet to normal tissue with another clip (**Fig. 3a and 3b**). Finally, we sprayed fibrin glue (Beriplast P Combi-Set Tissue Adhesion, CSL Behring, King of Prussia, PA, USA) through a spray tube, followed by thrombin through another spray tube (**Fig. 3c and 3d**).

The following day, endoscopy showed that the PGA sheet remained attached to the wound. The patient was discharged from our hospital, without complications, 47 days after receiving critical care treatment and rehabilitation. After 123 days, outpatient endoscopy revealed that the wound had healed and that the PGA sheet had been absorbed.

Case 2

A 68-year-old man (height, 165 cm; weight, 57 kg) was transferred to our hospital due to sudden-onset chest pain after alcohol intake and vomiting. The patient was taking two kinds of antithrombotic agents (cilostazol and ethyl icosapentate) due to inoperable left subclavian artery stenosis. His vital signs indicated a blood pressure of 142/64 mmHg; a radial pulse of 110 beats/min, regular; and a respiratory rate of 28 breaths/min; the laboratory findings were unremarkable. Similar to the previous case, computed tomography showed the presence of pneumomediastinum and endoscopy revealed a laceration at the esophagogastric junction.

This patient was treated in the same manner as the first patient. During the thoracotomy, the patient demonstrated a hemorrhagic tendency, probably due to his use of antithrombotic agents, during the exteriorization of the esophageal lesion. Again, primary suturing was not feasible; thus, we irrigated the pleural cavity, and placed three drainage tubes before completing the thoracotomy.

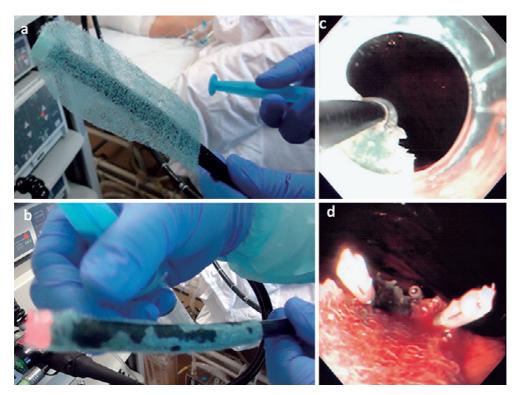


Fig. 2 (a) A 100×50-mm polyglycolic acid (PGA) sheet. (b) The PGA sheet was wrapped around the endoscope after moistening it with normal saline. (c) After the end of the endoscope was advanced past the wound, the grasping forceps were advanced slightly through the overtube, the grip was released, and the PGA sheet was placed over the wound. (d) The distal part of the PGA sheet was fixed to normal tissue using a clip.

After obtaining written informed consent from his family (the patient also provided deferred consent during recovery), endoscopic treatment to cover the laceration with a PGA sheet was performed.

During the patient's hospital stay, his condition was complicated by deep thrombophlebitis that required anticoagulation. The patient was discharged home, without complication, 72 days after intensive treatment and longterm rehabilitation. After 144 days, outpatient endoscopy confirmed that the wound had healed and that the PGA sheet had been absorbed (**Fig. 4**).

Discussion

The outcomes of these two cases suggest that the endoscopic placement of PGA sheets may be a feasible and safe treatment option for patients with Boerhaave syndrome. Because the PGA sheets are flexible and can easily cover the lesion, they may overcome some of the surgery-related problems associated with other treatment options.

The standard treatment for Boerhaave syndrome remains surgical treatment and primary closure of the lesion. However, recent studies have suggested that endoscopic treatments, such as clipping and stenting, may be acceptable alternatives¹²⁻¹⁸. Indeed, endoscopic treatment may be particularly useful for high-risk patients and those with comorbidities that limit their tolerance of surgery1. Randomized trials have not been conducted to directly compare endoscopic therapy with surgery for the treatment of Boerhaave syndrome, but observational studies suggest that a significant number of patients undergoing endoscopic therapy required reintervention. In one systematic review that described 340 patients with esophageal perforations, endoscopic stenting had a success rate of 81%, but endoscopic reintervention was required in 58 (17%) and surgical reintervention was required in 33 (10%) patients¹³. Another retrospective study compared the clinical outcomes of 20 patients who underwent surgery with those of 13 patients who underwent endoscopic stenting for the management of Boerhaave syndrome6. No differences in morbidity or intensive care unit/hospital stays were found between the groups, but 11 of the 13 patients undergoing endoscopic stenting required additional operative interventions⁶.

PGA sheets are reinforcing materials that are hydrolyzed, in situ, within 15 weeks after shielding. In the

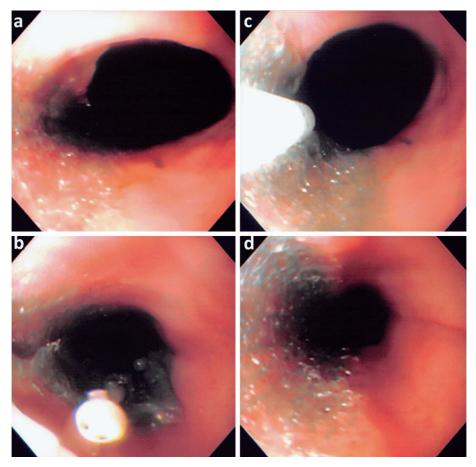


Fig. 3 (a) The wound was covered with a polyglycolic acid (PGA) sheet. (b) The proximal part of the PGA sheet was fixed to normal tissue using a clip. (c) Fibrin glue was applied through a spray tube. (d) The laceration was covered with the PGA sheet.

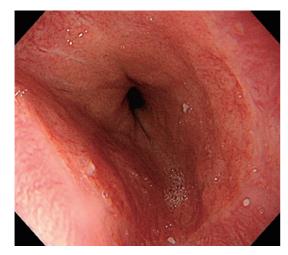


Fig. 4 Case 2: Endoscopy showed the healed wound and the absence of the (adsorbed) polyglycolic acid sheet.

field of gastrointestinal endoscopy, they are used after ESD to prevent strictures and perforations⁷⁻¹¹. Based on the studies of Takimoto et al.^{7,8}, we devised an endoscopic treatment that incorporated the use of PGA sheets

and fibrin glue to provide a treatment that is simpler and safer than other gastrointestinal endoscopic treatments.

Each endoscopic treatment method has advantages and disadvantages. Although clipping is easy to perform, it only covers approximately 1.5 cm of the lesion, and it cannot be adjusted based on the lesion's size or location¹⁹. Although stents can cover larger wounds than clipping, their placement in nonstrictured lumens is associated with significant rates of stent migration, resulting in technical and clinical failures. In addition, endoscopic intervention for anastomotic leaks is associated with further disruption of the anastomosis and with other potential complications, including perforation, bleeding, and stricture formation¹³. PGA sheets are flexible and can cover wounds of different sizes, are easy to replace, and are absorbable, leading to fewer complications than may be associated with the other techniques. If a patient shows signs of clinical deterioration after endoscopic treatment, surgical treatment should be performed immediately; however, the presence of clips and stents may pose problems during surgery, unlike PGA sheets.

We encountered two patients with Boerhaave syndrome who were successfully treated using PGA sheets, without primary suturing of the ruptured site. Further studies are required to confirm our findings and to optimize the treatment protocol for Boerhaave syndrome (e.g., surgical or endoscopic treatment). We suggest using PGA sheets to treat patients with Boerhaave syndrome if they have a high surgical risk or have comorbidities that minimize their tolerance of surgery.

In conclusion, endoscopic therapy using PGA sheets may be considered a treatment option for Boerhaave syndrome. The use of PGA sheets during endoscopic therapy is relatively safe and can be easily performed in combination with surgical drainage of the pleural cavity. Further studies are required to confirm our results.

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Conflict of Interest: The authors declare no conflicts of interest pertaining to this article.

References

- Lazar G Jr, Paszt A, Simonka Z, Barsony A, Abraham S, Horvath G: A successful strategy for surgical treatment of Boerhaave's syndrome. Surg Endosc 2011; 25: 3613–3619.
- Carrott PW Jr, Low DE: Advances in the management of esophageal perforation. Thorac Surg Clin 2011; 21: 541– 555.
- Connelly CL, Lamb PJ, Paterson-Brown S: Outcomes following Boerhaave's syndrome. Ann R Coll Surg Engl 2013; 95: 557–560.
- Shinozuka E, Nomura T, Miyashita M, Makino H, Okawa K, Hagiwara N, Shigehara K, Akagi I, Shioda Y, Uchida E: Successful treatment of a spontaneous esophageal rupture in an elderly patient: a case report. J Nippon Med Sch 2010; 77: 338–341.
- Keeling WB, Miller DL, Lam GT, Kilgo P, Miller JI, Mansour KA, Force SD: Low mortality after treatment for esophageal perforation: a single-center experience. Ann Thorac Surg 2010; 90: 1669–1673; discussion 1673.
- Schweigert M, Beattie R, Solymosi N, Booth K, Dubecz A, Muir A, Moskorz K, Stadlhuber RJ, Ofner D, McGuigan J, Stein HJ: Endoscopic stent insertion versus primary operative management for spontaneous rupture of the esophagus (Boerhaave syndrome): an international study comparing the outcome. Am Surg 2013; 79: 634–640.
- Takimoto K, Toyonaga T, Matsuyama K: Endoscopic tissue shielding to prevent delayed perforation associated with endoscopic submucosal dissection for duodenal neoplasms. Endoscopy 2012; 44 (Suppl 2 UCTN): E414–415.
- 8. Takimoto K, Imai Y, Matsuyama K: Endoscopic tissue

shielding method with polyglycolic acid sheets and fibrin glue to prevent delayed perforation after duodenal endoscopic submucosal dissection. Dig Endosc 2014; 26 (Suppl 2): 46–49.

- Tsuji Y, Ohata K, Gunji T, Shozushima M, Hamanaka J, Ohno A, Ito T, Yamamichi N, Fujishiro M, Matsuhashi N, Koike K: Endoscopic tissue shielding method with polyglycolic acid sheets and fibrin glue to cover wounds after colorectal endoscopic submucosal dissection (with video). Gastrointest Endosc 2014; 79: 151–155.
- Iizuka T, Kikuchi D, Yamada A, Hoteya S, Kajiyama Y, Kaise M: Polyglycolic acid sheet application to prevent esophageal stricture after endoscopic submucosal dissection for esophageal squamous cell carcinoma. Endoscopy 2015; 47: 341–344.
- 11. Doyama H, Tominaga K, Yoshida N, Takemura K, Yamada S: Endoscopic tissue shielding with polyglycolic acid sheets, fibrin glue and clips to prevent delayed perforation after duodenal endoscopic resection. Dig Endosc 2014; 26 (Suppl 2): 41–45.
- Harries K, Masoud A, Brown TH, Richards DG: Endoscopic placement of fibrin sealant as a treatment for a long-standing Boerhaave's fistula. Dis Esophagus 2004; 17: 348–350.
- Dasari BV, Neely D, Kennedy A, Spence G, Rice P, Mackle E, Epanomeritakis E: The role of esophageal stents in the management of esophageal anastomotic leaks and benign esophageal perforations. Ann Surg 2014; 259: 852–860.
- 14. Laukoetter MG, Mennigen R, Neumann PA, Dhayat S, Horst G, Palmes D, Senninger N, Vowinkel T: Successful closure of defects in the upper gastrointestinal tract by endoscopic vacuum therapy (EVT): a prospective cohort study. Surg Endosc 2016.
- 15. Kobara H, Mori H, Rafiq K, Fujihara S, Nishiyama N, Kato K, Oryu M, Tani J, Miyoshi H, Masaki T: Successful endoscopic treatment of Boerhaave syndrome using an over-the-scope clip. Endoscopy 2014; 46: E82–E83.
- 16. Scharl M, Stanek N, Kroger A, Bauerfeind P, Gubler C: Successful treatment of a proximal esophageal rupture with a luminal sponge. Endoscopy 2015; 47 (Suppl 1 UCTN): E293–E294.
- Dickinson KJ, Buttar N, Wong Kee Song LM, Gostout CJ, Cassivi SD, Allen MS, Nichols FC, Shen KR, Wigle DA, Blackmon SH: Utility of endoscopic therapy in the management of Boerhaave syndrome. Endosc Int Open 2016; 4: E1146–E1150.
- Swinnen J, Eisendrath P, Rigaux J, Kahegeshe L, Lemmers A, Le Moine O, Deviere J: Self-expandable metal stents for the treatment of benign upper GI leaks and perforations. Gastrointest Endosc 2011; 73: 890–899.
- 19. Ramhamadany E, Mohamed S, Jaunoo S, Baker T, Mannath J, Harding J, Menon V: A delayed presentation of Boerhaave's syndrome with mediastinitis managed using the over-the-scope clip. J Surg Case Rep 2013; 2013.

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