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CASE REPORT

Successful treatment of an esophageal perforation that occurred during endoscopic submucosal dissection for esophageal cancer using polyglycolic acid sheets and fibrin glue

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Abstract

A 74-year-old female, who was diagnosed with superficial esophageal cancer, underwent endoscopic submucosal dissection (ESD) at another hospital, but a perforation occurred during the procedure. The perforation was closed with endoscopic clips, and the ESD was halted. The patient was referred to our hospital, and ESD was retried. There was severe fibrosis around the lesion, and injections into the submucosal layer were difficult. In addition, it was not possible to identify the submucosal layer, and making an oral-side incision caused a large perforation along the incision line. As continuing the submucosal dissection with an endoknife was considered difficult, the lesion was finally resected with hybrid ESD using a snare. The perforation was closed using polyglycolic acid (PGA) sheets and fibrin glue. Endoscopy performed 6 days later showed that the defect had been closed, and no contrast leakage was detected. Follow-up endoscopy conducted 3 months after the ESD showed ulcer healing at the dissection site and scar formation, but no residual tumor or esophageal stricture was noted. Our experience suggests that the use of PGA sheets with fibrin glue is a feasible, safe, and effective way of treating large esophageal perforations during ESD.

Keywords Endoscopic submucosal dissection · Perforation · Polyglycolic acid sheet

Introduction

Endoscopic submucosal dissection (ESD) is a standard treatment for early esophageal cancer [1, 2]. However, the potential complications of ESD include bleeding, intraoperative/delayed perforation and postoperative stricture [3]. The frequency of esophageal perforation during ESD was reported to be as low as about 5% [4], but such complications can be serious. Perforations are usually caused by excessive coagulation or cutting of the muscle layer. The optimal treatment option for esophageal perforation depends on the location and size of the perforation and the clinical status of the patient. In some cases, surgical interventions are required, but they are associated with high morbidity and mortality rates [5]. Some cases can be treated using endoscopic treatments, such as with conventional clips, the over-the-scope clipping (OTSC) system, or with clips and detachable snares [6, 7]. On the other hand, bioabsorbable polyglycolic acid (PGA) sheets (Neoveil; Gunze Co., Kyoto, Japan), which are commonly used in the surgical field, have also recently been used in endoscopic techniques for the closure of perforations and the prevention of postoperative bleeding and perforations [8, 9]. However, there have been few reports about the use of PGA sheets and fibrin glue to treat esophageal perforations. We experienced a case in which an esophageal perforation occurred during ESD and

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was successfully treated using PGA sheets and fibrin glue. We describe this case here.

Case report

A 74-year-old female underwent esophagogastroduodenoscopy (EGD) for screening, which resulted in a diagnosis of superficial esophageal cancer in the middle thoracic esophagus. Macroscopically, the lesion was classified as type 0–IIb and was about 4 cm in diameter. A biopsy conducted at a previous hospital revealed an intraepithelial neoplasm. ESD was performed at the institution, but the esophagus was perforated when the first mucosal incision was made and partial submucosal dissection was carried out on the oral side. The perforation was closed with endoclips, and the ESD was stopped. Computed tomography (CT) showed mediastinal emphysema. The patient was treated with non-surgical conservative management. Then, she was referred to our hospital to undergo ESD. The pretreatment EGD showed a macroscopic type 0–IIb lesion, together with a scar, and it was suspected that the lesion did not extend beyond the epithelial layer (Fig. 1). ESD was performed using a 1.5-mm Flush knife BTS (DK2620J-BS15S; FTS, Tokyo, Japan) and a VIO 300D (ERBE Elektromedizin, GmbH, Tubingen, Germany) as the electrical power source. It was difficult to administer submucosal injections due to the severe fibrosis that had developed around the previous scar, and the submucosal and muscle layers could not be clearly identified. We tried to make shallow incisions where possible, but the incisions caused a large perforation along the incision line (Fig. 2b). As further dissection was considered difficult, we decided to conduct a hybrid ESD procedure using a snare (Olympus SD-210U-25). Although this resulted in the resection being performed in a piecemeal manner, the lesion was completely resected endoscopically. The perforation measured about 30 × 30 mm in size (Fig. 2c, d). There was no obvious subcutaneous emphysema, and the patient's vital signs were stable. The muscle defect was too large to close

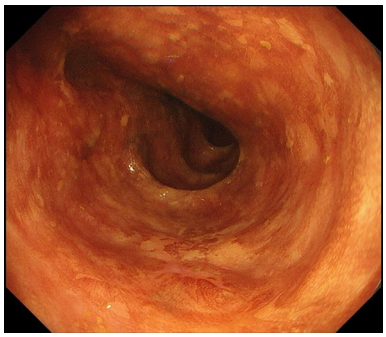

Fig. 1 Esophagogastroduodenoscopy (EGD) performed before endoscopic submucosal dissection (ESD). A lesion oriented in the 6 o'clock direction was seen at the site of a previous scar

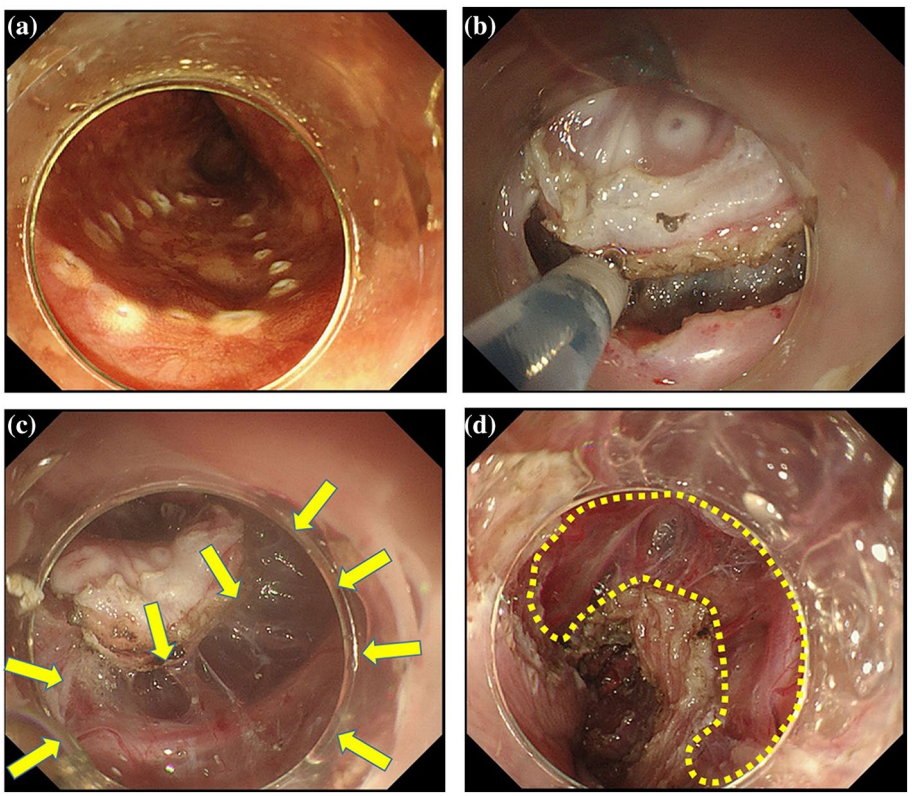

Fig. 2 ESD for esophageal cancer. **a** A line indicating the lesion's margins is shown. **b, c** Perforation occurred during a mucosal incision due to the fibrosis in the submucosal and muscle layers (yellow arrows). **d** After the ESD, the perforated area (yellow dotted line) measured 30 mm in diameter

using simple clips or the OTSC system, so we decided to employ a shielding technique involving the use of PGA sheets and fibrin glue.

The PGA sheets were cut into 10 × 10-mm pieces, and the fibrin glue (Beriplast P Combi-Set; CSL Behring Pharma, Tokyo, Japan) was prepared. A piece of PGA sheet was held with biopsy forceps at the tip of the endoscope, which had a transparent hood, and was transported to the muscle defect through an overtube. This process was repeated until the defect was covered. After the lesion had been sufficiently covered with PGA sheets, solution A of the fibrin glue (fibrinogen) was applied to the PGA sheets using a spray tube, and then solution B (thrombin) was sprayed onto the sheets with another spray tube. The defect was completely covered with PGA sheets (Fig. 3). The time spent covering the defect, from the delivery of the PGA sheets to the completion of the fibrin glue application, was 30 min.

A CT scan obtained just after the ESD showed mediastinal emphysema around the esophagus (Fig. 4).

After the procedure, the patient was subjected to fasting, parenteral nutrition for 6 days, and intravenous antibiotics (ampicillin sodium/sulbactam sodium) for 7 days. She had a fever of 38 °C and complained of mild chest pain the day after the ESD, but it resolved within a day. The patient's C-reactive protein level was elevated (5.77 mg/dl) at 2 days after the perforation, but it subsequently decreased gradually. Her white blood cell count did not increase. CT performed 3 days after the perforation showed that the amount of mediastinal emphysema around the esophagus had reduced.

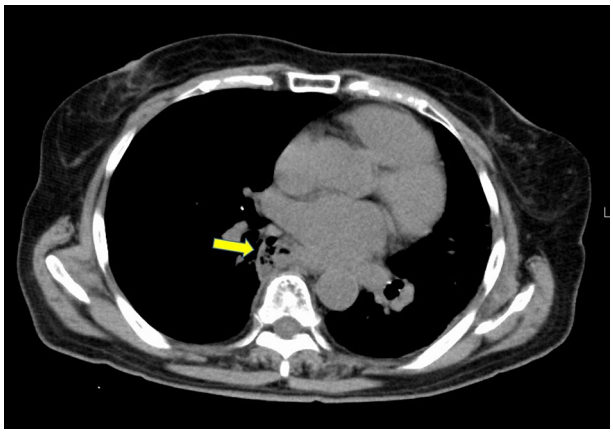

Fig. 4 Computed tomography (CT) performed just after the ESD. Mediastinal emphysema was seen around the esophagus (yellow arrow)

EGD conducted on day 6 revealed that the PGA sheets were still covering the perforation, and there was no contrast leakage (Fig. 5). After starting oral intake, the patient's general condition remained stable, and she was discharged on postoperative day 13.

A pathological examination revealed squamous cell carcinoma in situ with non-assessable horizontal and vertical

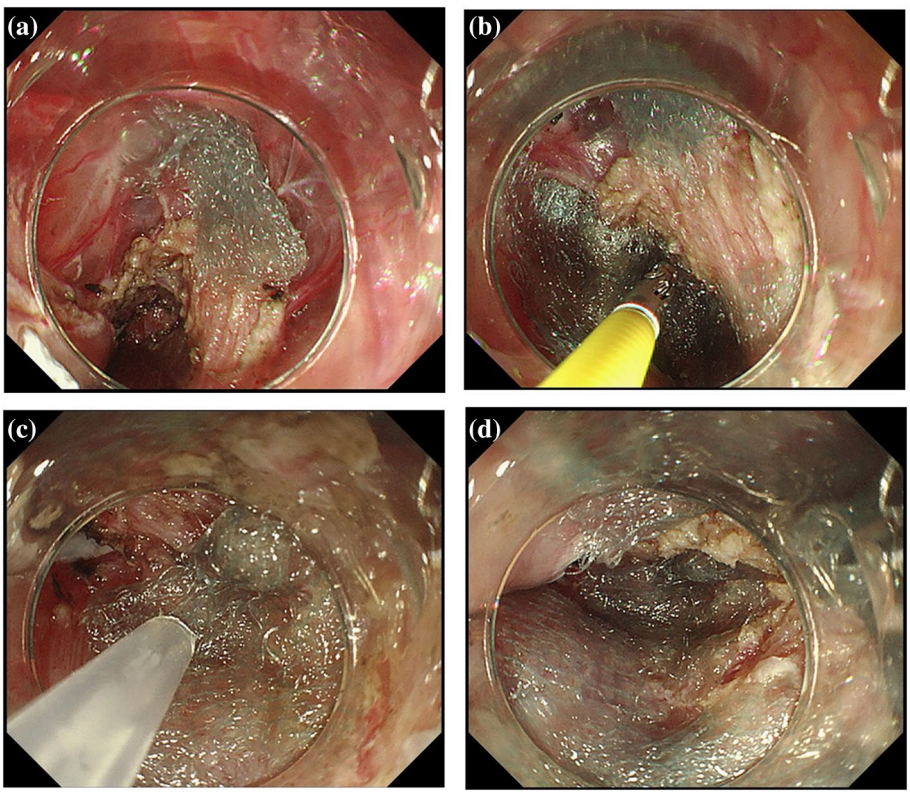

Fig. 3 An endoscopic tissue-shielding method involving the use of polyglycolic acid (PGA) sheets and fibrin glue. **a** The PGA sheets were delivered and attached to the muscle defect using biopsy forceps. **b** The muscle defect was filled with pieces of PGA sheet. **c** Fibrin glue was sprayed through a tube to fix the sheets in place. **d** The muscle defect was completely covered by the PGA sheets and fibrin glue

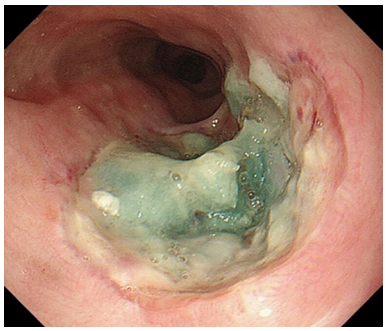

Fig. 5 Endoscopic view at 6 days after the ESD. The PGA sheets were still attached to the base of the defect

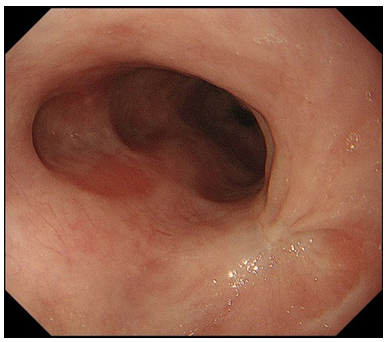

Fig. 6 Follow-up EGD performed at 3 months after the ESD. Ulcer healing and scar formation were observed, but no residual tumor or esophageal stricture was detected

resection margins. The follow-up EGD conducted 3 months after the ESD showed ulcer healing and scar formation, but no residual esophageal tumor or stricture was detected (Fig. 6).

Discussion

In Japan, ESD is widely performed for superficial esophageal neoplasms, and its usefulness is well recognized [1]. However, esophageal perforation can occur as an adverse event of ESD [3]. Such perforations can cause various conditions, from fevers and chest pain to mediastinitis and septic shock. The potential treatments for esophageal perforation include conservative treatment with fasting and antibiotics, endoscopic closure, and surgery, and the optimal treatment is chosen depending on the size and location of the defect, the time between the occurrence and detection of the perforation in cases of delayed perforation, and the patient's condition. Among the various treatments, endoscopic closure with simple clips and the OTSC system are the most common approaches. However, Zhong et al. suggested that conventional endoscopic clips can be used when the diameter of the defect is < 10 mm, but it is difficult to completely close larger perforations with them [10]. Ono et al. reported that the OTSC system was useful for closing a large perforation, which occurred during balloon dilation for esophageal stricture after esophageal ESD [11]. However, this device seems to be difficult to use, especially when the defect is quite wide, because it results in imperfect grasping of the defect [12]. Furthermore, the use of the OTSC system to close large defects carries a risk of esophageal stricture. In the present case, the perforation was quite large (30×30 mm) and was located in a region with a narrow lumen, and fibrosis, which had been caused by a previous ESD procedure, was noted around the lesion. Therefore, it was considered that grasping the edges of the defect with the OTSC system would have been difficult, and there was also a concern that an esophageal stricture might develop. Tanaka et al. reported that the use of detachable snares with clips was effective in closing an esophageal muscle defect caused by a diverticulum found during ESD [13]. However, this method is also considered to be difficult to employ in cases involving large esophageal defects and carries a risk of stricture.

On the other hand, we previously reported that the PGA sheet-based filling and shielding technique was successful at closing a delayed perforation that occurred after duodenal ESD [14].

In the current case, the use of PGA sheets in combination with fibrin glue led to the successful closure of a large esophageal perforation within a week.

The use of PGA sheets in combination with fibrin glue has healing effects, as the sheets serve as scaffolds for tissue regeneration, and the regenerated tissue fills and covers any mucosal defects. The PGA sheets are gradually absorbed within about 15 weeks. This shielding method has some advantages in that it can be used in any gastrointestinal region, and it can be applied to cases involving large defects. Furthermore, it has been used in the surgical field for a long time, and its safety is guaranteed [15, 16].

We consider that large esophageal perforations that cannot be closed with conventional clips or the OTSC system are indicated for treatment using PGA sheets. Furthermore, although closing a large perforation would cause a postoperative stricture in the narrow esophageal lumen, PGA sheets cover, rather than close, the perforated area, and so the risk of narrowing the esophageal lumen seems low. Recently, it was reported that PGA sheets are useful for reducing the risk of postoperative stricture after esophageal ESD, which supports our opinion [17].

Conversely, the main disadvantages of the PGA sheet-based technique are that it must be possible for the PGA sheets to stay in place for a long time without being dislodged, and at present the cost of using PGA sheets with fibrin glue to treat gastrointestinal perforations is not covered by the Japanese national medical insurance system.

Furthermore, it cannot be used to treat patients who are allergic to PGA sheets, and the feasibility and usefulness of this approach for treating defects accompanied by infections and/or bleeding remain to be clarified.

However, when large esophageal perforations are encountered, attaching PGA sheets with fibrin glue is worth trying because it can help to close defects without invasive surgery or postoperative stricture.

In conclusion, endoscopic therapy involving the use of PGA sheets in combination with fibrin glue is considered to be useful for closing large esophageal defects.

Compliance with ethical standards

Conflict of interest None of the authors have any conflicts of interest that are relevant to the content of this article.

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