Successful treatment of enterocutaneous fistula after esophagectomy with scopolamine ointment and negative pressure wound therapy: a case report

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Abstract

Background: Despite improved surgical techniques and perioperative management, anastomotic leakage (AL) after esophageal cancer surgery remains a potential complication. In most cases, spontaneous healing upon proper drainage is observed, but sometimes, AL results in intractable enterocutaneous fistulas. We here report a case of intractable enterocutaneous fistula caused by post-esophagectomy AL and successfully treated by scopolamine ointment and negative pressure wound therapy (NPWT).

Case presentation: A 77-year-old man underwent thoracoscopic subtotal esophagectomy with 3-field lymph node dissection, followed by gastric tube reconstruction through the posterior mediastinal route. On the 6th postoperative day, AL was identified, forming an enterocutaneous fistula. Initially, conservative treatment was performed, but the fistula failed to close. We hypothesized that the substantial amount of exudate might be hampering fistula closure. Scopolamine ointment was used to reduce the amount of fluid. NPWT was also initiated to promote wound healing. Approximately 3 weeks after the beginning of the treatment, the fistula closed; oral intake became possible, and the patient was discharged from the hospital without any symptoms.

Conclusions: The combination of scopolamine ointment and NPWT may be regarded as one effective treatment option for intractable enterocutaneous fistula due to AL after esophagectomy.

Keywords: Intractable enterocutaneous fistula, Esophagectomy, Scopolamine ointment, Negative pressure wound therapy

Background

Anastomotic leakage (AL) is one of the major complications of esophageal cancer surgery, with a frequency of 13.3% according to the Japanese National Clinical Database [1]. In most cases, spontaneous healing is observed after conservative treatment, which may include fasting and proper drainage; however, intractable enterocutaneous fistulas sometimes develop. Large amounts of fistula discharge significantly reduce the patient’s quality of life and prolong the fasting period and hospitalization.

Negative pressure wound therapy (NPWT) is a relatively new treatment, which promotes healing by sealing the wound surface [2]. The use of NPWT for enterocutaneous fistula due to post-esophagectomy AL has rarely been reported. Here, we report a case of postoperative fistula successfully managed by a combination of scopolamine ointment and NPWT.
**Case presentation**

A 77-year-old man underwent esophagectomy for thoracic esophageal cancer with 3-field lymph node dissection, followed by gastric tube reconstruction through the posterior mediastinal route. The reconstruction was performed in the cervical region with end-to-side anastomosis using an automatic anastomotic device. Eventually, the length of the residual esophagus was about 3 cm. On the 6th postoperative day (POD), redness was observed around the cervical wound. The wound was partially opened, and AL discharge was observed. Conservative treatment, including fasting, drainage of defective granulation, and tube feeding, was initiated; however, a large amount of exudate continued to come out, producing an enterocutaneous fistula. On the 29th and 43rd POD, we attempted to close the fistula by suturing, but it soon broke apart. On the 57th POD, we injected Dermabond® into the fistula, but to no avail. On the 58th POD, because it is considered that the stenosis of the anastomosis is an obstacle to the healing of the fistula, endoscopic balloon bougie to enlarge the size of anastomosis was performed (Fig. 1a, b). However, the exudate was never reduced. Therefore, we speculated that the large amount of exudate incessantly flowing out might be obstructing fistula closure. First, we aimed to reduce the flow through the fistula using scopolamine ointment. On the 61st POD, a small amount of scopolamine ointment was applied near the papillary process in the posterior auricle twice a day (Fig. 2). In Japan, transdermal scopolamine is not commercially available, and therefore, it was prepared in our hospital; its use was approved by the Ethics Review Committee in our hospital for off-label use. Although there was concern about anticholinergic side effects, only mild thirst was recognized. Simultaneously, NPWT was initiated to promote wound healing (Fig. 3a, b). A vacuum-assisted closure treatment system (KCI International, San Antonio, TX, USA) was used as a negative pressure maintenance device, and the polyurethane foam was replaced every 72 h. The negative pressure was appropriately adjusted to 100 to 150 mmHg. Sometimes, the negative pressure stopped. This issue was addressed by adjusting the suction pressure and appropriately improving the shape of the polyurethane foam. Gradually, good granulation appeared, and the fistula shrank (Fig. 3c). Approximately 3 weeks after the beginning of the treatment, the fistula had closed, and oral intake was possible (Fig. 3d). The patient was discharged from the hospital on the 97th POD with no symptoms.

**Discussion**

Enterocutaneous fistulas complicating esophageal cancer surgery can become intractable due to substantial exudate, which constantly exposes the surrounding skin to strong irritation and impairs granulogenesis. Also, a large amount of fistula exudate causes considerable pain [3, 4]. For intractable enterocutaneous fistulas arising due to AL, a minimally invasive approach should be considered first. Therefore, surgical treatments such as...
Pedicled myocutaneous flap filling [5] are not among the first-choice treatments. The usefulness of covered stents for fistula closure after esophagectomy has been reported [6, 7]. However, in this case, since the anastomosis was located in the neck, endoscopic placement of the stent was not suitable. Although over-the-scope clip system was reported as one of the treatment options for anastomotic fistula [8], it was technically difficult to grasp all layers of the digestive tract and was abandoned. Intrathecal injection of fibrin glue or cyanoacrylate has been reported as useful treatment for intractable fistulas [9, 10]. The mechanism of action of fibrin glue involves fibroblasts invading and proliferating in the fibrin matrix adhering to the tissue, resulting in tissue repair with angiogenesis. However, it takes several minutes for fibrin to form a stable cross-link and adhere to the tissue, and the adhesion and fixation are weak. Therefore, this method appeared unsuitable for this case, where exudate was constantly emerging, and the pressure was high. Cyanoacrylate preparations have the advantages of quick and high-strength adhesion [11], and so we attempted to close the fistula using Dermabond®, which, however, proved ineffective.

As the excessive exudate was suspected to be one of the causes of delayed wound healing, we first aimed to reduce the amount of exudate. Although drug therapy options include the use of anticholinergic drugs, both oral and intravenous administration may lead to adverse events such as blurred vision, miosis, palpitation, hot flushes, dizziness, and constipation. Meanwhile, scopolamine is known to be transdermally absorbed [12]. Regarding skin permeability, the posterior part of the ear shows high skin permeability. In the USA, a scopolamine patch is an anticholinergic preparation approved for prevention of motion sickness and is commercially available [13]. Scopolamine patches have also been reported to suppress saliva production in cancer patients [14]. In Japan, such patches are not commercially available, and so one was prepared in our hospital in addition to a hydrophilic ointment so that the concentration of scopolamine hydrobromide hydrate was 5%. In our case, from the day of application, the amount of saliva decreased to about half, and only a slight degree of mouth dryness was observed.

NPWT is a physical therapy in which a negative pressure is continuously or intermittently applied to a wound in a closed environment to promote the formation of granulation tissue, adjust the wound bed, and hence facilitate wound healing. It is widely used for acute wounds, such as those that cannot be closed temporarily; open wounds on amputated limbs; and chronic wounds such as pressure ulcers and diabetic foot ulcers [15–17]. Endoscopic vacuum-assisted closure treatment is increasingly used for intrathoracic leakage after esophagectomy [18]. On the other hand, there have been few reports of percutaneous NPWT for management of enterocutaneous fistula due to AL after esophagectomy [19]. We speculated that NPWT would be fully applicable to postoperative enterocutaneous fistulas, such as the one in the present case, and would fit the criterion of a minimally invasive approach. It is also thought that a synergistic effect was obtained in the process of fistula closure by using scopolamine ointment in combination. The reduction in the exudate enabled protection of the

![Fig. 3](image-url). a Appearance of the cervical wound on the 61st POD. Exudate constantly emerging from the fistula caused peripheral dermatitis. b NPWT was initiated for continuous aspiration of exudate and skin protection. c Appearance of the cervical wound on the 73rd POD (13th day after NPWT initiation). Granulation is in development, the skin closes in, and the fistula is shrinking. d Appearance of the cervical wound on the 81st POD (21st day after NPWT initiation). The fistula had closed, and no exudate was observed.
Conclusion

The combination of scopolamine ointment and NPWT may be regarded as one effective treatment option for intractable enterocutaneous fistula due to AL after esophagectomy.

Abbreviations

AL: Anastomotic leakage; NPWT: Negative pressure wound therapy; POD: Postoperative day

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Authors’ contributions

SS reported the case and wrote the manuscript. RA, SO, NM, WW, AM, YH, and YN were involved in treating the patient. MS, MS, HS, and KS participated in revising the manuscript critically. All authors declare that they contributed to this article and that they have read and approved the final manuscript.

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Availability of data and materials

The data supporting the conclusions of this article are included within the article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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