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# The treatment for refractory rectovaginal fistula after low anterior resection with estriol, polyglycolic acid sheets and primary closure: A case report

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## ABSTRACT

**INTRODUCTION:** Rectovaginal fistula (RVF) is a refractory complication that occurs after anastomotic leakage following low anterior resection for rectal disease. Due to its refractory nature, RVF is often managed with surgical treatment, such as stoma creation for fecal diversion, closure of the fistula and/or re-anastomosis, rather than conservative therapy.

**PRESENTATION OF CASE:** A 72-year-old woman who underwent laparoscopic low anterior resection developed RVF on post-operative day (POD) 15. Conservative therapy with the administration of estriol and total parenteral nutrition was started. In addition, a polyglycolic acid (PGA) sheet was inserted into the fistula using colonoscopy, and fibrin glue was applied. However, this treatment with the PGA sheet and fibrin glue seemed to be unsuccessful. Therefore, an operation for simple closure of the RVF was performed on POD47. The PGA sheet was then removed, and primary closure of the RVF from both sides of the rectum and vagina was performed. Following re-operation, solid food with low dietary fiber content was started on original POD55 (POD14 after re-operation), and the dietary fiber content was gradually increased. The patient was discharged from the hospital on original POD 83 (re-operation POD42).

**DISCUSSION:** The administration of estrogen might result in increased vaginal compliance, decreased vaginal pH, increased vaginal blood flow and improved lubrication. Therefore, vaginal suture was made possible because the vaginal extensibility was restored.

**CONCLUSION:** Primary closure of the RVF following administration of estriol may be an effective treatment.

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## 1. Introduction

Anastomotic leakage after low anterior resection for rectal cancer is a serious complication, with a recently reported incidence of 9.7%–12.4% [1,2]. Among the female patients, 1.6%–3.0% of the patients experiences rectovaginal fistula (RVF), which is more complicated than other complications and refractory to treatment [3–5].

Due to its refractory nature, RVF is often managed with surgical treatment, such as stoma creation for fecal diversion, closure of the fistula and/or re-anastomosis, rather than conservative therapy [5,6]. However, due to the low incidence and complicated clinical course following various options for treatment, the optimal strategy remains controversial.

We herein report a case of refractory RVF after low anterior resection treated with the administration of estriol, polyglycolic acid (PGA) sheets and primary closure. This work has been reported in line with the SCARE criteria [7].

## 2. Case presentation

A 72-year-old woman was admitted to our hospital with bloody feces. She had a history of dizziness. A diagnosis of rectal cancer (Stage I: T2, N0, M0 according to the TNM classification of the UICC 8th edition) was made, and laparoscopic low anterior resection with D3 lymph node dissection was performed. The tumor was located at the anterior left wall of the lower rectum. Rectal transection and anastomosis were performed using an Endo GIA™ Reinforced Reload with Tri-Staple™Techcnology (Medtonic) and an EEA 25 × 4.8 mm (Medtonic), a circular stapler, using the double-stapling technique, respectively. The operation time was 4 h and 11 min, and blood loss was 15 mL. The operation was uneventful.

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The pathologic diagnosis was Stage I (T2, N0, M0). Liquid food was started on postoperative day (POD) 4. The transanal decompression tube placed during the surgery [1] was removed on POD5. Solid food was started on POD6. The abdominal drain placed near the anastomosis during the surgery was removed on POD7. The patient was discharged from our hospital on POD11 without any complications during the hospital stay.

However, she developed a small amount of bleeding from the vagina on POD14, suffered discharge of feces and gas from the vagina on POD15, and was re-admitted to the hospital on POD16. Her body temperature was 37.0 °C. A physical examination of the abdomen showed no tenderness. Laboratory studies on re-admission were unremarkable, including no elevation of inflammation markers of white blood cell count or C-reactive protein levels. Computed tomography (CT) showed air in the vagina. However, neither free peritoneal air nor abdominal abscess was observed. Enema using amidotrizoic acid confirmed the formation of RVF (Fig. 1a, b). An examination of the vagina confirmed a 3-mm fistula at the posterior right wall of the upper vagina (Fig. 1c). Colonoscopy revealed RVF formation at the anterior right wall of the anastomotic ring (Fig. 2a). Based on these findings, the diagnosis of RVF was made.

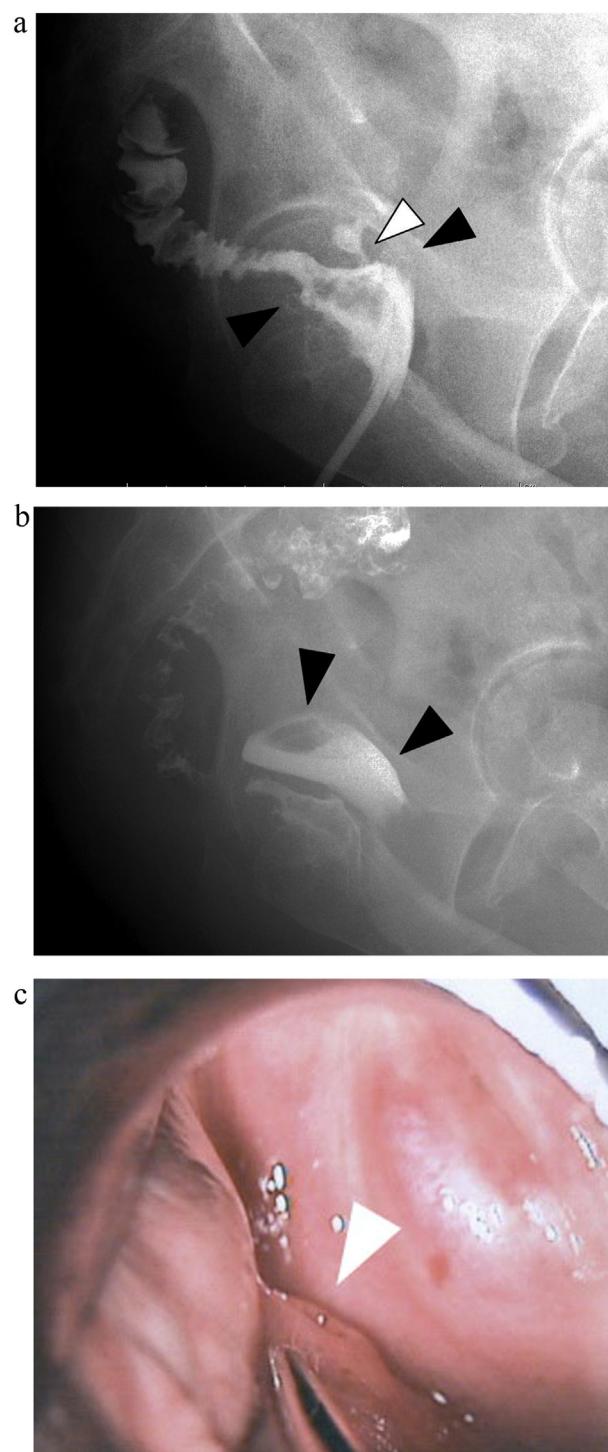
Conservative treatment was initially chosen because the general condition was stable and elevated inflammatory markers were not seen. In addition, abscess formation around the RVF was not detected by CT or enema. The oral intake of liquid and solid food was stopped, and total parenteral nutrition was started.

The clinical course is summarized in Fig. 3. A PGA sheet was inserted into the fistula via colonoscopy, and fibrin glue was applied to close the RVF (Fig. 2b). In addition, estriol (1 mg/day) and chloramphenicol (100 mg/day) were administered into the vagina every day in the hopes of improving the vaginal condition.

After starting the treatment, discharge of feces and gas from the vagina disappeared on POD18. However, colonoscopy showed that the fistula remained on POD26 (Fig. 2c). The RVF was not detected by an enema examination. Thus, liquid and solid food was restarted on POD28 and POD30, respectively. However, a gynecological examination detected slight discharge from the vaginal side of the fistula, so the oral intake of food was stopped again. Colonoscopy still showed no marked change in appearance. Therefore, the old PGA sheet was removed, and a fresh PGA sheet was inserted with the application of fibrin glue after the unhealthy granulation tissue was coagulated on POD35 (Fig. 2d, e). The administration of estriol and chloramphenicol to the vagina was stopped, and the oral administration of estriol (2 mg/day) was started.

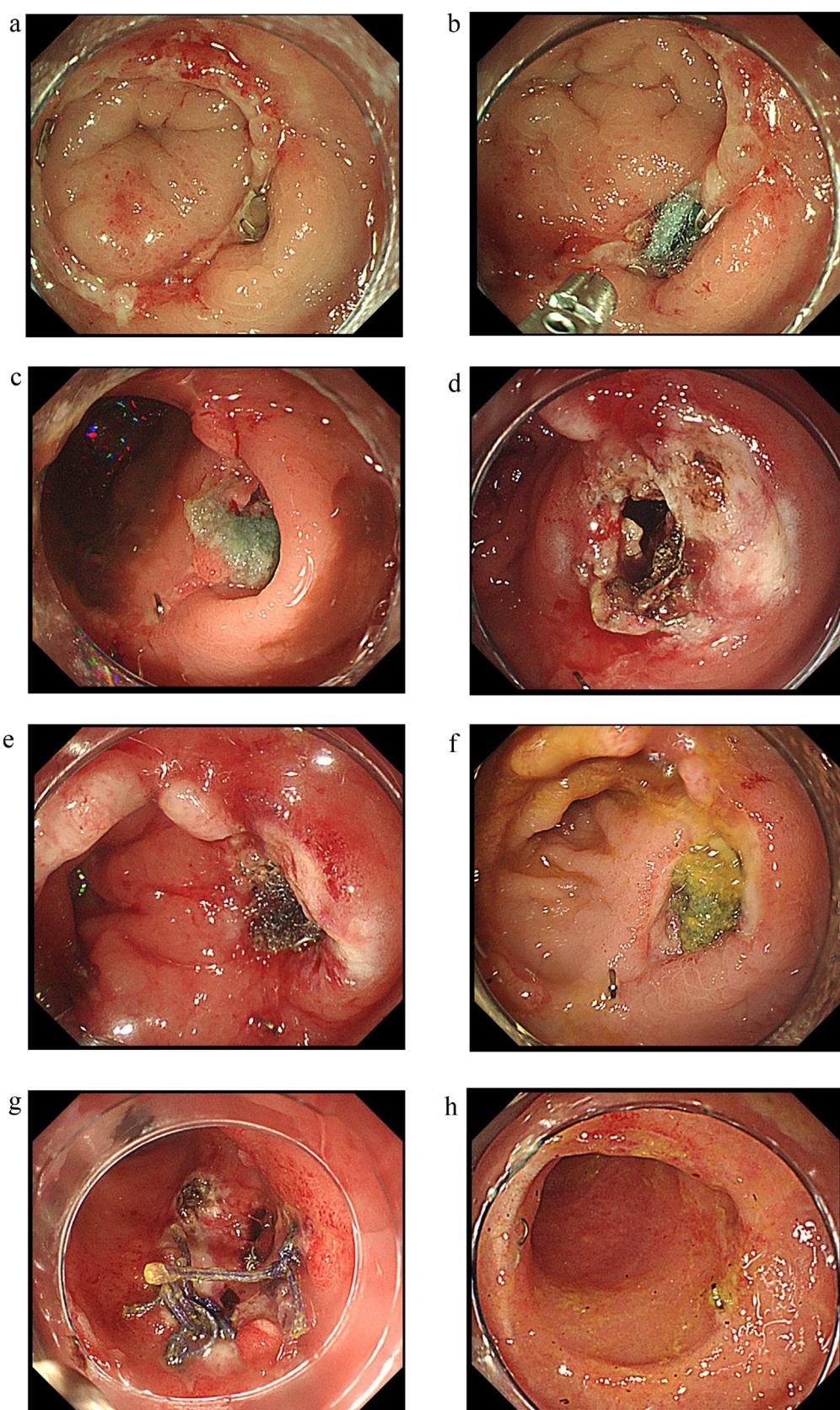
The fistula at the rectal side showed ulceration and still remained on POD42 (Fig. 2f). Therefore, freeze-dried coagulation factor XIII (FXIII) derived from human plasma was administered for 5 days to improve the wound healing and facilitate closure of the fistula, even if the FXIII activity remained in the normal range (82%). Treatment using a PGA sheet with fibrin glue seemed unsuccessful. Therefore, an operation for simple closure of the RVF was performed on POD47.

The PGA sheet was removed, and primary closure of the RVF was performed. From both sides of the rectum and vagina, primary closure of the fistula with interrupted suture incorporation throughout all layers using 3–0 Vicryl was done. Following re-operation, an enema examination from the rectal side detected no fistula on original POD53 (POD6 after re-operation). Although colonoscopy showed the collapse of the sutures at the rectal side and revealed a small fistula on original POD54 (re-operation POD7) (Fig. 2g), an examination from the vagina seemed to show a cured fistula. Therefore, liquid food was re-started on original POD56 (re-operation POD9). Solid food with a low dietary fiber content was started on original POD55 (re-operation POD14), with the dietary fiber content gradually increased. A normal diet was started on

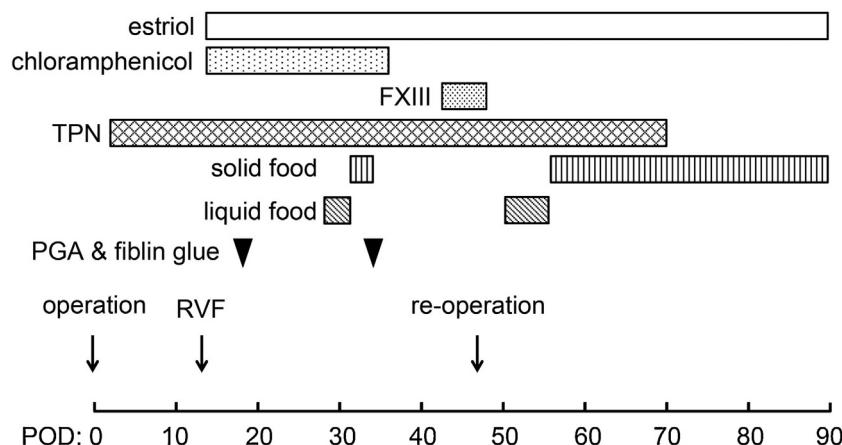


**Fig. 1.** Rectovaginal fistula. Enema demonstrates anastomotic leakage (white arrowhead) at the anastomotic site (black arrow) (a), with leakage later seen from the vagina (b: black arrowhead). A vaginal examination shows a 3-mm fistula (c).

original POD77 (re-operation POD36), and the patient was discharged from the hospital on original POD 83 (re-operation POD42). After starting meal intake, magnesium oxide and Daikenchuto, a traditional herbal medicine, were administered to ensure soft defecation two to three times a day. Colonoscopy on original POD90 (re-operation POD49) showed that the RVF was completely closed (Fig. 2h). No recurrence of RVF or rectal cancer was seen at six months after the initial operation.



**Fig. 2.** Colonoscopy during treatment. Rectovaginal formation at the anterior right wall of the anastomotic ring (a). A polyglycolic acid sheet was inserted to the fistula, and fibrin glue was applied on post-operative date (POD) 18 (b). The fistula remained on POD26 (c). The removal of the old polyglycolic acid sheet, coagulation of the unhealthy granulation tissue (d), insertion of a fresh polyglycolic acid sheet and re-application of fibrin glue were performed on POD35 (e). The fistula shows ulceration on POD42 (f). Colonoscopy shows the collapse of the sutures at the rectal side and reveals small fistula on POD54 (POD7 after re-operation) (g). RVF was cured on POD90 (POD49 after re-operation) (h).



**Fig. 3.** The summary of the clinical course. FXIII: freeze-dried coagulation factor XIII, TPN: total parenteral nutrition, PGA: polyglycolic acid, RVF: rectovaginal fistula, POD: postoperative date.

### 3. Discussion

RVF is a refractory complication that occurs after anastomotic leakage following low anterior resection for rectal disease. Due to its refractory nature, it can cause long-term fasting and hospitalization, fecal diversion with colostomy or ileostomy and/or additional surgical treatment.

Regarding the treatment strategy, Woo et al. analyzed 18 patients with RVF after low anterior resection [5]. In their study, different types of procedures were compared, including redo-coloanal anastomosis, diverting stoma, primary repair and conservative treatment. The individual success rates of redo-coloanal anastomosis, diverting stoma, primary repair and conservative treatment were 85.7%, 54.5%, 33.3% and 0%, respectively. Among these treatment strategies, the combination of redo-coloanal anastomosis and diverting stoma succeeded in 100% of cases and seemed to be effective. However, the patients needed to undergo additional abdominal surgery. Schloericke et al. reported the efficacy of the transperitoneal omentum flap after local fistulectomy [6]. However, 89% of patients also needed to receive ileostomy. Surgical treatments of re-laparotomy and/or stoma creation seemed to be effective and have high success rates. However, these procedures could be excessive and overly invasive.

In the present study, we initially chose conservative therapy with placement of the PGA sheets and application of fibrin glue at the RVF from the rectal side. A PGA sheet is a bio-absorbable suture reinforcement material recently reported to be effective for the endoscopic management of gastrointestinal leakage and perforation [8]. In rectal surgery, PGA has been used to reinforce staple lines and was reported to potentially be effective for reducing anastomotic leakage [9,10]. Therefore, we expected a PGA sheet with fibrin glue to be effective for treating RVF, even though there have been no previous reports of its application for anastomotic leakage after rectal surgery. However, this approach was ultimately not successful. In the future, we need to re-consider the effective application of PGA sheets, e.g. placement over the fistula, inserted or filling the fistula. In addition, successful treatment with this approach has only been previously reported for the upper gastrointestinal tract [8]. Therefore, the blood flow in the tissue and capability of wound healing in each organ might also be relevant.

In our case, we performed both transrectal and transvaginal approaches for the closure of the RVF, as this procedure is relatively minimally invasive. As a result, primary closure via the transvaginal approach was successful. We administered estriol vaginally or orally. Estriol is a steroid hormone, specifically a type of estrogen [11]. Estrogen deficiency occurs beyond menopause

and disrupts the physiological response, such as muscle relaxation, vasocongestion and lubrication of the vagina. The administration of estrogen results in increased vaginal compliance, decreased vaginal pH, increased vaginal blood flow and improved lubrication [12]. Therefore, vaginal suture was made possible because the vaginal extensibility was restored. Indeed, the vaginal wall had been thick and tight before the treatment of RVF due to inflammation, but it was restored to a nearly normal condition by treatment. In addition, it is reported that the administration of estrogen increased the number of periurethral vessels and resulted in an increased blood flow [13]. Thus, the administration of the estriol might also promote healing around the fistula and perineum by increasing blood flow. A previous report also described a case in which RVF caused by pessary was successfully treated with only estrogen cream [14], and RVF after low anterior resection was also treated with estriol in Japanese article [15]. However, closure from the transrectal approach was unsuccessful because the closure site was eventually disrupted, possibly caused by vulnerable granulation of the fistula and surrounding rectal tissue due to multiple colonoscopic treatments and consequent chronic inflammation. The efficiency of endoscopic closure by clipping for fistulae has been also reported [16]. This treatment seemed to be effective for relatively small fistulae. However, the size of the RVF in our case was about 3 mm, which was relatively large for clipping. In addition, the unhealthy granulation tissue seemed to be vulnerable and difficult to close using clipping.

The etiology of the RVF in this case was speculated to be anastomotic leakage caused by early post-operative diarrhea. The initial post-operative course after low anterior resection was uneventful, except for post-operative watery diarrhea seven times on POD5. We previously reported that early post-operative diarrhea was an independent risk factor for anastomotic leakage after low anterior resection [1]. This might influence the clinical course and post-operative complications. Another reported potential etiology of RVF is the inclusion of the vaginal wall in the stapled anastomosis [17]. However, when we reviewed the operative video after the procedure, the rectal stump and stapled anastomosis were not found to include the vaginal wall.

### 4. Conclusion

We performed treatment for a refractory RVF after low anterior resection with estriol, PGA sheets and primary closure. Colonoscopic treatment using PGA sheets with fibrin glue should be re-considered with regard to the usage and ingenuity. The administration of estriol might aid in the treatment of RVF.

## Conflicts of interest

The authors declare that they have no competing interests.

## Funding

None.

## Ethical approval

This case report is not research study. That is not applicable in this case report. The case report is exempt from ethical approval.

## Consent

Informed broad consent and written informed consent for images were obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

## Author contribution

All the authors contributed to diagnose and treat the patient. Masatsugu Hiraki contributed in drafting the manuscript. Masatsugu Hiraki and Toshiya Tanaka edited the manuscript. Toshiya Tanaka and Kenji Kitahara supervised and made the final approval of the manuscript. All authors read and approved the final manuscript.

## Registration of research studies

This case report is not research study. That is not applicable in this case report.

## Guarantor

Dr. Toshiya Tanaka.

## Provenance and peer review

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