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### Abbreviations

EMR	Endoscopic mucosal resection
ESD	Endoscopic submucosal dissection
GI	Gastrointestinal
LST	Laterally spreading tumor
NBI	Narrow-band imaging
TAR	Trans anal resection

### 19.1 Case 1

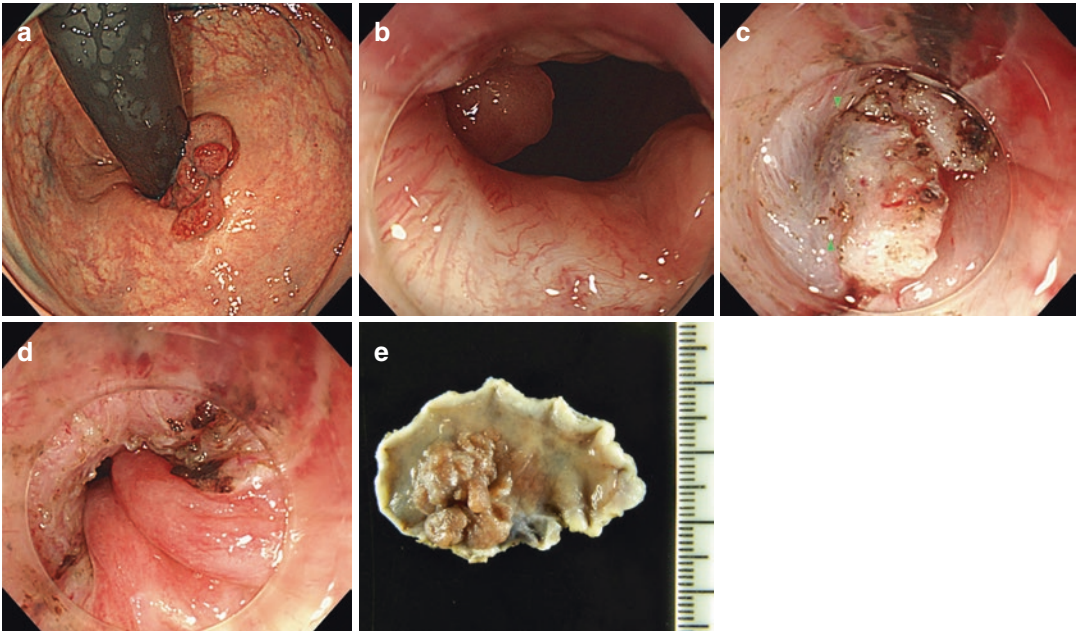
A 67-year-old woman was referred to our hospital for the treatment of an anorectal residual polyp after treatment at another hospital. Trans anal resection (TAR) was performed previously as an initial treatment. The histology showed carcinoma in situ with positive resection margins. Residual adenoma was detected at the surveillance colonoscopy, which was performed 2 years after the initial treatment, and EMR using snare and hot biopsies were attempted. However, residual adenoma was observed at the 3-year surveillance colonoscopy. A colonoscopy performed at our center showed a 20 mm polypoid lesion extending to the anal canal as well as multiple surrounding scars (Fig. 19.1a). Magnifying endos-

copy with narrow-band imaging (NBI) showed dilated microvessels with a regular arrangement. Chromoendoscopy with magnification following crystal violet staining revealed a regular blanched pit pattern. The diagnosis was residual adenoma. The lesion extended to the anal canal, and scars were also found at the one-third circumference of the anal canal (Fig. 19.1b). Rectal tumors extending to the dentate line are technically difficult to excise because of their anatomical features, i.e., the narrow space and complex shape of the anal canal, the thin submucosal layer containing fibrotic tissues (termed “musculus submucosae ani”), the rich vasculature of the rectal venous plexus, and the presence of sensory nerves in the anoderm [1]. There is also the theoretical risk of systemic bacteremia because of direct drainage via the venous plexus to the systemic circulation [2]. Moreover, in this case, poor lifting of the lesion after submucosal injection was considered likely due to possible widespread submucosal fibrosis. Thus, we predicted that it would be difficult to remove the residual adenoma by EMR using a snare. Accordingly, we decided to use ESD to achieve complete removal.

#### 19.1.1 ESD Setting

- Endoscope: A gastroscope with a water-jet system (GIF-Q260J; Olympus Medical Systems Corp., Tokyo, Japan)

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**Fig. 19.1** (a) Colonoscopy revealed a 20 mm rectal polyp extending to the anal canal with surrounding multiple scars. (b) There was a widespread scar in the anal canal due to previous trans anal resection. It would have been difficult to make a mucosal incision to create a mucosal flap on the anal side that was far away from the

scar. (c) After a mucosal flap was successfully created on the left side of the lesion at the anal canal, the submucosal layer could be directly visualized using the mucosal flap (green arrowheads). (d) The ulcer bed at the anal canal. (e) The resected specimen

- Device: Dual knife and ITknife nano™ (Olympus)
- Fluid: Hyaluronic acid plus Glycerol (1: 1) tinged with indigo carmine
- Electrosurgical unit: VIO300D (cut mode; Endocut Q 80W effect 3, coagulation mode; SWIFT 60W)
- Coagulation forceps: Coagulaspar (Olympus), SOFT 40W
- Sedation: Midazolam and pethidine
- Other: Carbon dioxide insufflation

### 19.1.2 Technical Problems

The potential technical problems were as follows: (1) poor visualization from the narrow lumen; (2) a possible risk of bleeding due to the presence of rectal venous plexus; (3) pain due to unique innervation; (4) a risk of systemic bacteremia due to the unique vascular supply; (5) the complex shape of the submucosa at the

anal canal; and (6) possible submucosal fibrosis due to previous treatment.

### 19.1.3 ESD Technique Modifications

We modified the ESD procedure as follows: (1) A transparent hood was attached to the tip of the endoscope to improve visualization. (2) A gastroscope was used to improve scope operability in the narrow surgical space. (3) Local injection of 1% lidocaine (100 mg/10 mL) was used prior to ESD to reduce the pain. (4) Prophylactic antibiotics were administered intravenously after ESD. (5) A needle-type knife (dual knife) was used to accurately trace the complex resection line at the anal canal. (6) Indigo carmine was used so that blue-tinged fluid would improve the visualization of the submucosal layer with fibrotic tissue. (7) A highly viscous fluid, hyaluronic acid, was used to create a good cushion. (8) A small-caliber-tip transparent hood (ST

hood, DH-28GR; Fujinon, Japan) was used to make it easy to enter the submucosal layer.

### 19.1.4 ESD Procedure

The key to the success of the ESD procedure is to enter the submucosal layer using a mucosal flap after mucosal incision. Entering into the submucosal layer enables stable endoscope maneuver under direct vision of the resection line. A larger mucosal flap is helpful for treating lesions with fibrosis. In this particular case, creating a large mucosal flap at the distal side of the lesion was considered difficult because wide field submucosal dissection was not feasible in the anal canal. Therefore, we made an initial mucosal incision to create a mucosal flap 10 mm to the left of the tumor. Because there was no scar there, a good submucosal cushion could be created by submucosal injection. After a mucosal flap was created, a mucosal incision was performed around the anal side, and submucosal dissection was started. Using a mucosal flap, the thin submucosal layer could be observed directly as a transparent layer (green arrowheads, Fig. 19.1c). When dissecting thin submucosa with fibrosis, one must use a horizontal approach with ESD knives in order to minimize thermal damage to the muscular layer. Meticulous rotation of the endoscope enabled safe and efficient submucosal dissection with direct visualization of the thin submucosal layer. The anal canal area was carefully dissected, and then circumferential mucosal incision and submucosal dissection were performed in the retroflex position in the remaining area that did not involve the anal canal. Finally, en bloc resection was successfully performed without any complications (Fig 19.1d). The procedure was completed within 2 h. Although the patient did not have pain during or after the procedure, she developed a slight fever (37–38 °C). This resolved 3 days after ESD, and she was discharged without any symptoms. The resected specimen measured 40 × 25 mm, and the lesion within it was 20 × 20 mm (Fig. 19.1e). Histological analysis revealed tubular adenoma with high-grade dysplasia (Vienna classification

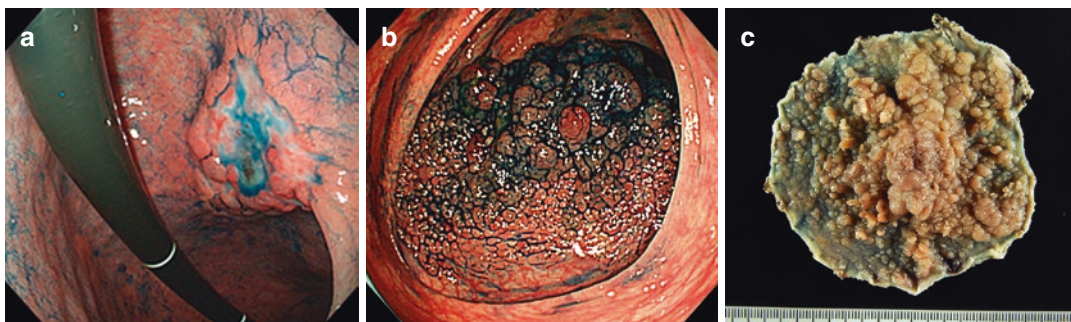
4.1) with negative lateral and vertical margins. A 1-year surveillance colonoscopy showed a flat anorectal scar with no residual adenoma and no stenosis.

## 19.2 Case 2

A 66-year-old woman was referred to our hospital for surgical treatment of advanced gastric cancer that was detected by esophagogastroduodenoscopy after she complained of epigastralgia. Although she had no lower gastrointestinal (GI) symptoms, surgeons recommended that she undergo a colonoscopy, since she had not had one previously. Colonoscopy showed an 80 mm granular-type laterally spreading tumor (LST) at the ascending colon. The LST lesion had a large nodule (>10 mm) at its center with a flat elevation base. Magnified endoscopy with NBI showed a dilated, tortuous microvascular structure, corresponding to Japan NBI Expert Team Classification Type 2A. Magnified chromoendoscopy with crystal violet staining revealed a regular tubular pit, corresponding to the Type IV pit pattern in Kudo's classification. The diagnosis was intramucosal cancer with no submucosal invasion; thus, we recommended ESD as the initial treatment. Open gastrectomy with lymph node dissection was planned for the gastric cancer because it was diagnosed at an advanced stage with positive lymph node metastasis. We performed ESD for the colonic LST (Fig. 19.2).

### 19.2.1 ESD Setting

- Endoscope: An intermediate-length colonoscope with a water-jet system (PCF-Q260J; Olympus)
- Device: Dual knife and ITknife nano™ (Olympus)
- Fluid: Hyaluronic acid plus glycerol (1:1) tinged with indigo carmine
- Electrosurgical unit: VIO300D (cut mode; Endocut Q 80W effect 3, coagulation mode; SWIFT 60W)



**Fig. 19.2** (a) Retroflex gastroscopy showed a 30 mm excavated gastric cancer at the anterior wall of the antrum. (b) An 80-mm laterally spreading mixed nodular granular-type tumor can be seen over a semilunar fold of the

ascending colon. (c) The resected specimen of the laterally spreading tumor suggested en bloc resection with macroscopically tumor-free lateral margins

- Coagulation forceps: Coagulaspar (Olympus), SOFT 40W
- Sedation: Midazolam and pethidine
- Other: Carbon dioxide insufflation

### 19.2.2 Technical Issues

The potential technical issues were as follows: (1) The presence of semilunar folds. (2) The possible presence of thick vessels under the large nodule.

### 19.2.3 ESD Technique Modifications

We modified the ESD procedure as follows: (1) An ITknife nano™ was used for submucosal dissection. (2) A Dual Knife rather than an ITknife nano™ was used to dissect fibrotic tissue.

### 19.2.4 ESD Procedure

Initially, a mixed solution of hyaluronic acid and glycerol was injected submucosally. To confirm that the injection correctly targeted the submucosal layer, we performed a test injection using only a glycerol solution. After confirming adequate submucosal lifting, we then used a syringe with a mixed solution of hyaluronic acid and glycerol. Next, a one-third mucosal incision was made on the anal side using a needle-type knife (Dual

Knife). Two or three additional mucosal incisions allowed us to place the endoscope into the submucosal layer. We then used an ITknife nano™ for submucosal dissection. Repeated submucosal injections helped maintain an adequate submucosal fluid cushion and improved our visualization of the submucosal tissues. When thick vessels could be seen within the submucosal layer, prolonged application of a coagulation current allowed us to dissect the vessels without extensive bleeding [3]. The ITknife nano™ was thus effective for this safe and time-saving procedure. En bloc R0 resection was achieved without any complications. Histological analysis showed an 80-mm intramucosal cancer (Tis) with negative margins.

## 19.3 Discussion

Here we presented two cases: in Case 1, ESD was used as salvage therapy for anorectal residual neoplasms after several previous treatments; in Case 2, ESD was used for the optimal management of a large synchronous colonic LST in a patient with advanced-stage gastric cancer. Case 1 demonstrated the advantages of using ESD rather than trans anal surgical procedures in the anorectal region. TAR can be performed as a local resection method as an alternative to surgery; however, the rate of local recurrence is high and there can be severe complications [4]. In recurrent cases, salvage resection to treat local recurrence would



be increasingly difficult due to severe submucosal fibrosis. Moreover, when the tumor extends into the anal canal, surgical resection would result in the loss of the anus itself (along with anal function), greatly reducing the patient's quality of life. Thus, the overuse of surgery for nonmalignant rectal tumors that extend into the dentate line should be avoided in order to keep medical costs down and to ensure higher quality of life [5, 6]. ESD was not used for anorectal lesions in the past due to considerable technical difficulties during the early phase of development of this technique. However, recent advances in endoscopic equipment and techniques make it possible to now offer ESD to patients with anorectal lesions [7]. In our previous reports, ESD for rectal tumors extending to the dentate line was feasible and showed high rates of complete tumor removal and en bloc resection (95.6%), with a perforation rate was 4.4%. Minor postoperative complications were common, including high-grade fever over 38.0 °C (22%), persistent anal pain (26%), and proctostenosis (2%); however, these were not serious complications.

In the current case, en bloc R0 resection and detailed histological evaluations were achieved by ESD even for a severely scarred lesion that recurred after TAR. The possibility of residual neoplasm development and the subsequent risk of metastasis were completely eliminated by ESD. Thus, curative therapy using ESD for anorectal lesions as an alternative to surgical options would have great value in terms of preserving anal organ function.

Survival has improved for patients with gastrointestinal cancer owing to advances in surgery and adjuvant chemotherapy, but synchronous neoplasms in other parts of the GI tract must also be addressed. In our previous report, patients with gastric cancer showed a twofold greater prevalence of high-risk adenomas than healthy individuals [8]. Screening colonoscopy that is performed in patients with gastric cancer prior to surgery sometimes detects large colorectal neoplasms, as for case 2. In case 2, the large size and the morphology of an 80-mm granular-type LST nodular mixed-type lesion raised the possibility that there could be submucosal invasion. Indeed,

a previous study showed that approximately 19% of granular-type LST nodular mixed-type lesions  $\geq 40$  mm was submucosal invasive cancers [9]. Certain histological findings pertaining to invasion depth, tumor differentiation, tumor budding, lymph-vascular permeation, and margin status, are significant independent risk factors for lymph node metastasis in submucosal invasive colorectal cancer [10]. The histological findings that are linked to lymph node metastasis are difficult to see in specimens that are resected in multiple pieces. In case 2, the surgeon notified us that complete removal of the lesion was necessary and that the histology of the LST needed to be determined prior to gastrectomy to avoid secondary colectomy after gastrectomy. In general, pathological findings related to metastatic risks, such as tumor invasion depth, lymph-vascular permeation, tumor budding, and resection margin, are carefully evaluated for a few weeks. The waiting time prior to pathological reports of the ESD specimen could raise concerns in patients because of the delay prior to the curative gastrectomy. The patient hoped to undergo ESD for her LST without delay. We should plan the ESD within a week after the diagnosis to reduce the waiting time. A time-saving ESD procedure is needed, because we perform many colonoscopies every day. In this context, ESD using the ITknife nano™ is useful for achieving en bloc resection in a shorter period. A definitive pathological assessment helps physicians develop an optimal treatment strategy for patients with two malignancies, i.e., advanced gastric cancer plus superficial colon cancer. Case 2 demonstrated that ESD could be part of an optimal treatment strategy with minimal invasiveness in patients with synchronous cancerous lesions in multiple organs.

These two case reports illustrate how ESD can be used to minimize the use of surgery to treat patients with complex lesions. In case 1, ESD eliminated the need for more extensive surgery by achieving complete en bloc resection at a delicate site. In case 2, ESD minimized the need for the patient to undergo two surgeries, i.e., colectomy and gastrectomy, by eliminating the need for colectomy due to the complete removal and favorable histology of a huge LST.

To summarize, ESD offers a way to minimize the need for invasive treatment in patients with GI cancers. To facilitate and spread the use of ESD, GI endoscopists and surgeons should continue to share their knowledge of this technique and their experiences and results and should discuss the use of this treatment strategy in patients.

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