Endoscopic Submucosal Dissection Improves Bloody Stool Associated with Polypoid Type Mucosal Prolapse Syndrome: A Case Series

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Abstract:
Mucosal prolapse syndrome (MPS) is a benign inflammatory disease of the rectum that causes bloody stool. Endoscopic treatment for MPS has not been established. We herein report a consecutive case series of endoscopic submucosal dissection (ESD) for MPS. There were four cases treated with ESD alone. All lesions were on the dentate line, and all were polypoid. The median procedure time was 77 minutes. No complications were observed. The median observation period was 1,108 days, and bloody stool and endoscopic recurrence of MPS were not observed. ESD for polypoid-type MPS was an effective treatment for improving bloody stool and suppressing endoscopic recurrence.

Key words: endoscopic submucosal dissection, mucosal prolapse syndrome, solitary rectal ulcer syndrome

Introduction
Mucosal prolapse syndrome (MPS) is a benign inflammatory disease characterized by abnormal defecatory habits and histological fibromuscular obliteration of the lamina propria (1). MPS is similar to solitary rectal ulcer syndrome but is distinguished by abnormal bowel habits (1). MPS presents with ulcerated, flat, or polypoid lesions and causes bloody stool and anemia. It may also be associated with cancer. Therefore, MPS is treated when symptoms are present or when cancer is suspected. In particular, 96% of MPS cases occur on the dentate line of rectum above peritoneal reflection (Rb) (2), and a diagnosis is often challenging due to the difficulty differentiating it from cancer (3). Therefore, endoscopic resection is conducted both for a pathological diagnosis and treatment of MPS.

Conservative treatment, such as with laxatives and a high-fiber diet, changes in defecatory habits, and the use of biofeedback, is first attempted to treat symptomatic MPS, but the 3-year recurrence rate of symptoms in patients receiving conservative treatment is as high as 50% (4). In addition, 50% (25-100%) of patients who undergo surgery as additional treatment show recurrence in the long term (5). Although lasers and argon plasma coagulation (APC) treatments have been reported to be minimally invasive (6-8), their long-term efficacy is unknown.

We previously reported a case in which endoscopic submucosal dissection (ESD) showed long-term effectiveness for symptomatic MPS (9). ESD is used for the treatment for early-stage cancer and is widely used worldwide as a minimally invasive treatment in comparison with surgery. We speculate that ESD is effective for the treatment of MPS because of the strong post-ESD scarring that contributes to its long-term efficacy. However, ESD for MPS has been performed in only a few cases, and its efficacy is currently unknown; therefore, we collected cases in which ESD was performed for MPS with bloody stool at our hospital and evaluated its efficacy.

Material and Methods
A total of five cases of MPS involved resection by ESD at Toranomon Hospital between January 2011 and March 2021. After excluding one case in which endoscopic mu-
Table. Characteristics and Outcomes of All Cases.

|                | Case 1          | Case 2          | Case 3          | Case 4          |
|----------------|-----------------|-----------------|-----------------|-----------------|
| Age, years     | 53              | 60              | 71              | 74              |
| Sex            | Male            | Male            | Female          | Male            |
| Abnormal defecatory habits | Long defecation time Straining to defecate | Long defecation time Straining to defecate Anus discomfort | Long defecation time Straining to defecate |
| Hemoglobin level, g/dL | 9.6            | 11.2            | 12.9            | 13.5            |
| Location       | Rb              | Rb              | Rb              | Rb              |
| On the dentate line | Yes            | Yes            | Yes             | Yes             |
| Form           | Polypoid        | Polypoid        | Polypoid        | Polypoid        |
| Anesthesia method | Intravenous and local | Intravenous and local | Intravenous and local | Intravenous and local |
| Procedure time, min | 55              | 74              | 80              | 130             |
| Device         | Dual knife      | Dual knife      | Dual knife      | Dual knife      |
| Scope          | GIF-Q260J       | GIF-H290T       | GIF-Q260J       | GIF-2TQ260M     |
| Diagnosis      | MPS             | MPS             | MPS             | MPS around cancer |
| Lesion size, mm | 42              | 40              | 24              | 30              |
| Delayed bleeding | No            | No              | No              | No              |
| Perforation    | No              | No              | No              | No              |
| Stenosis       | No              | No              | No              | No              |
| Length of stay, days | 5              | 7               | 5               | 6               |
| Defecation guidance | Yes (before ESD) | Yes (after ESD) | Yes (after ESD) | Yes (after ESD) |
| Defecation control | No            | Yes            | No              | No              |
| Outcomes       |                 |                 |                 |                 |
| Bloody stool   | No              | No              | No              | No              |
| Recurrence     | No              | No              | No              | No              |
| Observation period, days | 1,861         | 730            | 1,485           | 349             |
| Follow-up colonoscopy | Almost every year | 2 years after ESD | Every 2 years | 1 year after ESD |

MPS: mucosal prolapse syndrome, ESD: endoscopic submucosal dissection

ESD procedure
ESD for MPS was performed as reported previously (9). We usually performed ESD with a dual knife (KD-650Q; Olympus, Tokyo, Japan) and used glycerol with indigo carmine for submucosal injection. We used a single-channel endoscope (GIF-Q260J or H290T; Olympus) or a two-channel endoscope (GIF-2TQ260M; Olympus). In contrast to conventional ESD, mepivacaine was used for local anesthesia.

Results
Table shows the patient characteristics and outcomes. The four cases included 3 men and 1 woman with a median patient age of 65.5 years old. The median hemoglobin level was 12.1 g/dL, and 1 patient had anemia. All lesions were on the dentate line of the Rb, and all of them were polypoid (Figure). In one case, cancer was found near the MPS and was resected together with the MPS. The median procedure time was 77 minutes. The patients showed no complications. The median length of stay was 5.5 days. The median observation period was 1,108 days, and no bloody stool was observed in the patients. No endoscopic recurrence of MPS was observed in the patients, and all treatment sites showed scarring (Figure).
Case Reports

Case 2

A 60-year-old man was admitted to our hospital with a chief complaint of blood-stained stool. He had a history of abnormal defecatory habits, such as long defecation times, straining to defecate, and anal discomfort. Colonoscopy revealed a 15-mm red-colored polypoid lesion on the rectal dentate line, indicating a neoplastic lesion. Therefore, ESD was performed. The procedure lasted for 55 minutes. The patient was discharged with no complications seven days after the procedure. The pathological findings showed MPS rather than a neoplastic lesion. After ESD, he ceased abnormal defecation habits and used senna to control defecation. However, due to poor defecation control, his medication was changed from senna to Macrogol 4000. For approximately two years after ESD, he showed no recurrence of bloody stool, and the anal discomfort also disappeared. In addition, colonoscopy was performed two years after ESD, and no recurrence of MPS was observed endoscopically.

Case 3

A 71-year-old woman was admitted to our hospital with a chief complaint of blood-stained stool and positive results for fecal occult blood. She had a history of abnormal defecatory habits, such as anal discomfort. Colonoscopy revealed a 15-mm red-colored polypoid lesion on the rectal dentate line. Therefore, ESD was performed for a total biopsy and symptoms. The procedure lasted for 80 minutes. The patient was discharged with no complications five days after the procedure. The pathological findings showed MPS. After ESD, she received defecation guidance and underwent colonoscopy every two years. For approximately four years after ESD, she experienced no recurrence of bloody stool. In addition, no recurrence of MPS was observed endoscopically.

Case 4

A 74-year-old man was admitted to our hospital for removal of a polyp in the rectum. He had a history of abnormal defecatory habits, such as long defecation times and straining to defecate. Colonoscopy revealed two lesions. The first lesion was a 15-mm red-colored polypoid lesion on the rectal dentate line, and the other was a typical elevated tumor near the lesion; a biopsy indicated that the former was MPS, and the latter was cancer. Therefore, ESD was performed simultaneously for the two lesions. The procedure lasted for 130 min. The patient was discharged with no complications six days after the procedure. Pathological findings revealed MPS and Tis carcinoma. After ESD, his abnormal defecation habits disappeared. For approximately one year after ESD, he experienced no recurrence of bloody stool. In addition, colonoscopy was performed one year after ESD, and no recurrence of MPS was observed.

Discussion

In all cases, bloody stool disappeared after ESD, and endoscopic MPS recurrence was not observed. Furthermore, the efficacy was continued for about 3 years, indicating the long-term effectiveness of this technique. This case series indicated that ESD could be a new treatment approach for polypoid-type MPS with bloody stool.

ESD is effective because it primarily eliminates the cause of bleeding, and the scarring formed after ESD suppresses recurrence. Removal of the source of bleeding directly pre-
vented the appearance of bloody stool. Except for surgery, no treatment other than ESD can remove the source of bleeding. ESD also offers the advantages of being less invasive than surgery and allowing the evaluation of resected specimens. Since cancer may occur in patients with MPS (11), the ability to evaluate excised specimens is a major advantage. Therefore, ESD for MPS can be considered a reasonable treatment technique that is minimally invasive and can allow for histological assessments.

Scars were formed after ESD in all cases, and no recurrence of MPS was observed endoscopically. Thus, scarring after ESD may suppress the MPS. Inflammation often spreads deeper than the submucosa during ESD, resulting in strong fibrosis after ESD (12). Therefore, it is speculated that scars with such strong fibrosis prevented mucosal prolapse. Furthermore, we believe that ESD is more effective in suppressing the recurrence of MPS than other endoscopic treatments, such as polypectomy or endoscopic mucosal resection. This is because post-ESD fibrosis is stronger and more extensive than that observed after polypectomy or endoscopic mucosal resection (12). Thus, such patients may not show recurrence of MPS after ESD.

ESD was performed safely with no noticeable complications. Since all lesions were on the dentate line, ESD for MPS may show problems similar to those associated with ESD for rectal tumors extending to the dentate line. First, the dentate line is often accompanied by fibrosis, shows abundant blood flow, and involves hemorrhoids. In particular, in polypoid-type MPS, fibrosis of the lamina propria grows extensively and often extends to the submucosal layer. In addition, there is dilation and proliferation of capillaries associated with mechanical stimulation, while blood vessels are also developing. Therefore, it is difficult to lift the submucosal layer since the lesions are fibrotic and thus performing ESD is associated with a high risk of bleeding due to the abundance of blood vessels. Second, because the lumen is narrow, maneuverability is poor, and good visualization of the resection field cannot be maintained. Therefore, ESD is technically difficult and may take longer than normal rectal ESD. Due to such difficulties, prophylactic hemostasis is carefully performed during incision and dissection. For narrow lumens, a thin therapeutic upper scope, such as a GIF-Q260J or GIF-H290T, has been actively used. Furthermore, a GIF-2TQ260M can often help when the device is poorly grounded to the lesion or the scope cannot approach the lesion during the reversal operation. With such ingenuity, the procedure time for ESD in this case series was reduced to 77 min, compared to the 90-104 min required for the previous procedure on the dentate line (13-15); thus, ESD for MPS may be acceptable.

Of note, this study had several limitations. First, this was a single-center retrospective case series study based on medical records. However, this is the first case series of ESD for MPS, so it is more valuable than previously reported cases. Second, all lesions were on the dentate line of Rb, and all were polypoid. Therefore, the effectiveness of ESD for MPS in other locations and forms is unknown. Third, there is no evidence that ESD is superior to polypectomy or endoscopic mucosal resection in the long-term efficacy. Therefore, further verification will be needed by another study. Finally, one patient had a cancer that was around the MPS, and we could not rule out the bloody stool being associated with bleeding due to the cancer. However, since the tumor was an intramucosal tumor and showed no ulcer or erosion, the possibility of bleeding from the tumor was low.

**Conclusion**

This case series showed a high rate of bloody stool disappearance and a low rate of endoscopic recurrence of MPS after ESD. Thus, ESD may be effective for polypoid-type MPS in the long term and may become a viable new treatment method in the future for polypoid-type MPS with bloody stool.

The authors state that they have no Conflict of Interest (COI).

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