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Clinical features and surgical treatment of inflammatory colorectal polyps in miniature dachshunds: 40 cases (2002–2015)

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Abstract
The medical records of 40 client-owned miniature dachshunds were reviewed to analyze the clinical features of miniature dachshunds with inflammatory colorectal polyps (ICRPs) and to evaluate the therapeutic effects of surgical treatment involving the mucosa-submucosal pull-through technique. All the dogs underwent a physical examination, digital rectal examination, complete blood count, serum chemistry, colonoscopy, endoscopic ultrasound, radiography, abdominal ultrasonography, surgical treatment (with the mucosa-submucosal pull-through technique), and postoperative care, including non-steroidal anti-inflammatory drugs (NSAIDs). Typical clinical signs included hematochezia (100%), tenesmus (75%), and large intestinal diarrhea (70%). Colonoscopies revealed that the lesions were located only in the rectum in 18 cases (45%), involved the descending colon in 21 cases (52.5%), and involved the transverse colon in 1 case (2.5%). Endoscopic ultrasounds showed that the lesions were located within the mucosal layer in all dogs. The mucosa-submucosal pull-through technique was feasible in all cases without intraoperative complications. Short-term complications were observed; however, they rapidly resolved. No long-term complications were noted. Most dogs were prescribed NSAIDs and mesalazine for long-term postoperative medical management. The mortality rate was 0%; the recurrence rate was 12.5%. Our study described the clinical features of ICRPs in miniature dachshunds and revealed that the lesions were located in the mucosa-submucosal layer even in cases of adenocarcinoma. Our findings suggest the mucosa-submucosal pull-through technique improves the prognosis of miniature dachshunds with ICRPs.

Key Words: dog, inflammatory colorectal polyps, miniature dachshund, mucosa-submucosal pull-through technique, postoperative adjuvant therapy

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Introduction

Canine intestinal and anorectal tumors are rare, and they account for approximately 1% of all canine tumors. Colorectal mucosal lesions are also rare; however, adenomatous polyps and carcinomas are frequently observed in cases of canine colorectal mucosal lesions. In particular, miniature dachshunds in Japan are significantly predisposed to the development of multiple inflammatory colorectal inflammatory polyps (ICRPs). However, it is difficult to ascertain the prevalence of ICRPs in dogs elsewhere, as similar reports are not found in other countries. The clinical signs associated with ICRPs include hematochezia, defecation pain, and tenesmus.

ICRPs in miniature dachshunds have been reported to have significantly higher epithelial cell cyclooxygenase-2 (COX-2) positivity than adenomas and adenocarcinomas in other dog breeds. Increased levels of interleukin-8, toll-like receptor expression, and nucleotide-binding oligomerization domain 2 gene mutations have been reported. However, they are not clearly related to the pathogenesis of ICRPs.

In canine cases of ICRPs, colorectal mucosal lesions have the risk of malignant transformation. To remove colorectal mucosal polypoid lesions, either an endoscopic polypectomy or use of the mucosal eversion technique is the treatment of choice; however, those procedures are likely to limit the extent of resected lesions and to result in the incomplete margins associated with local recurrences. For a complete resection in the cases of widespread colorectal lesions, a colorectomy with synchondrotomy or pubic osteotomy is performed. However, those surgical procedures are highly invasive, and are likely to induce severe postoperative pain and complications, including fecal incontinence, dehiscence, and strictures.

The transanal all-layer pull-through technique is more extendable compared to those procedures. This technique carries significant risk, though, of postoperative complications, and the range of colorectal resectability is limited. In case of the local invasion in the mucosal layer, the mucosa-submucosal pull-through technique is thought to be effective. The technique may also enable the resection of the longer colorectal lumen and reduce the incidence of complications. After the surgical removal of ICRPs, underlying colitis may induce recurrence. Adjunct medical management of the underlying colitis causing the polyps is also essential. However, there is little information on the effective treatment of ICRPs in dogs, especially in miniature dachshunds.

We hypothesized that the mucosa-submucosal pull-through technique and subsequent medical management would improve the prognosis of miniature dachshunds with ICRPs. Therefore, this retrospective study aimed to analyze the clinical features and therapeutic outcomes of ICRPs in miniature dachshunds, and to evaluate the effects of the surgical mucosa-submucosal pull-through technique and postoperative medical management with anti-inflammatory drugs for the treatment of ICRPs.

Materials and Methods

Animals: This study was a retrospective design. The medical records of 40 miniature dachshunds with ICRPs that underwent the mucosa-submucosal pull-through technique at the Animal Medical Center of Nihon University between October 2002 and November 2015 were reviewed. An evaluation of the ICRPs was performed using colonoscopy, endoscopic ultrasound (EUS), and histopathological analysis of endoscopic biopsy samples. In the EUS findings, the degree of vertical infiltration of lesions was classified by 3 stages as mucosal layer, submucosal layer and muscularis propria. All dogs underwent the mucosa-submucosal pull-through technique for ICRPs removal, as mentioned in the previous report.
Anesthesia and Analgesia: A dose of 0.04 mg/kg atropine sulfate (Mitsubishi Tanabe Pharma Co., Osaka, Japan) was subcutaneously administered, followed by intravenous injection of 0.1 mg/kg midazolam (Dormicum; Astellas Pharma Inc., Tokyo, Japan) and 0.1 ml/kg fentanyl citrate-droperidol (Thalamonal; Daiichi-Sankyo Propharma Co., Ltd., Tokyo, Japan). General anesthesia was induced with propofol (Mylan; Mylan Seiyaku Ltd., Tokyo, Japan), then endotracheal intubation was performed. Each dog was mechanically ventilated with a mixture of isoflurane (IsoFlo; Zoetis Japan, Tokyo, Japan) and oxygen. For analgesia, intra- and postoperative continuous drip infusions of remifentanil (5–40 μg/kg/hr) (Ultiva; Janssen Pharmaceutical K.K. Tokyo, Japan) and pre- and postoperative intramuscular injections of morphine hydrochloride (0.3 mg/kg each dose) (Takeda Pharmaceutical Co Ltd. Osaka, Japan) were used. In addition, non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed for postoperative analgesia and anti-inflammatory medical management.

Mucosa-submucosal pull-through technique: For preoperative preparation, all dogs fasted for 24 hr and received enemas. According to the modification of previous surgical techniques, each dog was placed in the perineal position (Fig. 1). Double-stay sutures were placed in the mucosa-submucosal layer in the dorsal, ventral, left, and right directions (Fig. 2). An incision was made between the double-stay sutures using Mayo or Metzenbaum scissors (Fig. 3). The inner-stay sutures were retracted, and the dissection between the muscular and mucosa-submucosal layers was performed using bipolar electrocautery and cotton swabs and/or gauze (Fig. 4). The affected mucosa-submucosal layer was fully isolated to check the mucosal surface after the longitudinal incision of the isolated layer. All visible polypoid lesions were included in the isolated layer. However, if the polypoid lesions were widely spread, only main polypoid lesions were included in the isolated layer to prevent postoperative complications such as dehiscence and strictures. A dorsal-side interrupted suture was placed with 4-0 poliglecaprone 25 (MONOCRYL; Johnson & Johnson, NJ, USA) or polydioxanone (PDS*II; Johnson & Johnson, NJ, USA) monofilament suture material for anastomosis between the isolated (oral side) and
distal mucosa-submucosal layers (aborad side), followed by left- and right-side interrupted anastomosis sutures. These three anastomosis sutures in the orad, left, and right directions were also used as stay sutures, and the isolated layer was resected (Fig. 5). The orad and aborad mucosa-submucosal layers were anastomosed using the interrupted-suture pattern (Fig. 6).

Histopathological diagnosis: The resected lesions were fixed in 10% neutral buffered formalin, embedded in paraffin, and used for histopathological review of the diagnoses. In
the histopathological findings, the vertical infiltration of lesions into the mucosal or mucosa-submucosal layer was evaluated and recorded in each dog. In addition, the vertical and horizontal surgical margins were evaluated. The histopathological findings were compared with the EUS findings in each dog.

**Postoperative management:** All dogs’ diets were monitored after surgery, and each received anti-inflammatory medical management. For short-term (<1 month) postoperative medical treatment, 1–5 ml/head of lactulose (Kowa pharmaceutical Co. Ltd., Tokyo, Japan) was orally administered every 12 hr. NSAIDs, 5 mg/kg of firocoxib (Previcox; Boehringer Ingelheim Animal Health Japan Co., Ltd. Tokyo, Japan), or 4.4 mg/kg of carprofen (Rimadyl; Zoetis Japan, Tokyo, Japan) was also orally administered every 24 hr. In addition, 10–20 mg/kg of mesalazine (Fuji Pharma Co. Ltd., Tokyo, Japan) and 10–15 mg/kg of metronidazole (Flagyl; Shionogi & Co. Ltd., Osaka, Japan) were prescribed every 12 hr. As needed, the dogs underwent the oral administrations of NSAIDs and mesalazine, and were evaluated by physical, blood, and radiological examinations and colonoscopies as a long-term postoperative management. Recurrences were defined in case that the clinical manifestation with suspicious of ICRPs and colonoscopy findings of ICRPs were observed, and a second surgical procedure was proposed.

**Statistical analysis:** The chi-square test was used to compare EUS findings and histopathological examinations, as well as the relationship between horizontal or vertical infiltration of lesions and the recurrence. A P value less than 0.05 was considered statistically significant.

**Results**

The mucosa-submucosal pull-through techniques for miniature dachshunds with ICRPs were performed in 40 dogs. All dogs underwent a physical examination, a digital rectal examination, complete blood count, serum chemistry including C-reactive protein (CRP), radiography, and abdominal ultrasonography. There were 22 males (14 neutered) and 18 females (10 spayed) included in the study. The median age of the dogs was 9.55 years (range, 2–15 years). The median body weight was 5.47 kg (range, 2.25–8.70 kg). Typical clinical signs included hematochezia (40/40 cases, 100%), tenesmus (30/40 cases, 75%), and large-intestinal diarrhea (28/40 cases, 70%). None of the dogs displayed lethargy, weakness, or ataxia. In all cases, the polypoid lesions were palpable via digital rectal examination. Preoperative medical management, including the administration of prednisolone (14/40 cases, 35%), did not resolve all clinical signs. Blood tests revealed increased levels of CRP (17/40 cases, 42.5%), leukocytosis (10/40 cases, 25%), hypoalbuminemia (9/40 cases, 22.5%), and anemia (3/40 cases, 7.5%) (Table 1). Typical clinical signs included hematochezia (40/40 cases, 100%), tenesmus (30/40 cases, 75%), and large-intestinal diarrhea (28/40 cases, 70%). None of the dogs displayed lethargy, weakness, or ataxia. In all cases, the polypoid lesions were palpable via digital rectal examination. Preoperative medical management, including the administration of prednisolone (14/40 cases, 35%), did not resolve all clinical signs. Blood tests revealed increased levels of CRP (17/40 cases, 42.5%), leukocytosis (10/40 cases, 25%), hypoalbuminemia (9/40 cases, 22.5%), and anemia (3/40 cases, 7.5%) (Table 1).

All 10 of the leukocytosis cases involved neutrophil dominance (Median rate, 89%; range, 76–93%). No metastatic lesions were identified on radiographs or abdominal ultrasounds. A median of 28 days (range, 11–178 days) before surgery, a colonoscopy and EUS were performed. Colonoscopies revealed extensive inflammatory polypoid lesions, identified as

| Table 1. Date of complete blood count and serum chemistry |
|---------------------------------------------|----------------|----------------|----------------|----------------|----------------|
| Total protein (g/dL)                        | Reference 5.2-8.2 | Median 6.5 | Range 5.1-7.3 | Below (%) 1 (2.5) | Above (%) 0 (0) |
| Albumin (g/dL)                              | 2.7-3.8 | 2.95 | 2.0-3.9 | 9 (22.5) | 1 (2.5) |
| C-reactive protein (mg/dL)                  | 0.0-0.99 | 0.58 | 0.0-12.0 | - | 17 (42.5) |
| WBC (μL)                                    | 6,000-17,000 | 10,150 | 4,300-220,000 | 3 (7.5) | 10 (25) |
| Hematocrit (%)                              | 37.0-55.0 | 49 | 23.5-57.0 | 3 (7.5) | 3 (7.5) |
INFLAMMATORY COLORECTAL POLYPS IN DOGS

Partial (3/40 cases, 8%), semi-circular (7/40 cases, 18%), or ringing (30/40 cases, 75%) the circumference of the colorectal region. The lesions were localized only in the rectum in 18 cases (45%), involved the descending colon in 21 cases (52.5%), and involved the transverse colon in 1 case (2.5%). Except for 2 cases in which detailed EUS findings concerning location were not recorded, EUS showed that all lesions were localized in the mucosal layer (35/38 cases, 92.1%) (Fig. 7) and mucosa-submucosal layer (3/38 cases, 7.9%) (Fig. 8). The histopathological diagnosis of endoscopic biopsy samples included inflammatory polyps (28/40 cases, 70%), adenocarcinoma (7/40 cases, 17.5%), inflammation (3/40 cases, 7.5%), and adenoma (2/40 cases, 5%).

The mucosa-submucosal pull-through technique was feasible in all cases without intraoperative complications. The visible polypoid lesions were resected from the rectum to the descending colon in 39 dogs (97.5%) and to the transverse colon in 1 dog (2.5%). The median length of the resected layer was 7.5 cm (range, 3.1–12.2 cm). Minor short-term postoperative complications included anastomotic strictures, hematochezia, and tenesmus in all dogs; however, they were resolved in less than 2 months with postoperative medical management. None of the dogs had postoperative fecal incontinence.

The histopathological diagnoses of the excisional biopsies were inflammatory polyps in all cases. Adenocarcinomas (10/40 cases, 25%), adenomas (1/40 cases, 2.5%), and ulcers (1/40 cases, 2.5%) also occurred. The lesions infiltrated the mucosal layer in 37 cases (92.5%) (Fig. 9) and the submucosal layer in 3 cases (7.5%) (Fig. 10). In 38 cases with available EUS results, the infiltration of lesions in the histopathological examination was significantly correlated with the EUS findings ($P = 0.000084$). There was not a significant relationship between submucosal infiltration of lesions and recurrences ($P = 0.50$). In the horizontal margins of the resected lesions, microscopic lesions were detected in 17 cases (42.5%). In 3 cases of those 17 cases, the lesions included adenocarcinomas. There was not a significant relationship between horizontal infiltration of lesions and recurrences ($P = 0.07$). Seven cases were diagnosed differently according to the endoscopic biopsy samples and the
excisional samples (7/40 cases, 17.5%) (Table 2).

For the short-term postoperative management, all dogs underwent the following medical treatment: lactulose (40/40 cases, 100%), NSAIDs (36/40 cases, 90%), mesalazine (36/40 cases, 90%) and metronidazole (29/40 cases, 72.5%). For the long-term medical treatment, NSAIDs (33/40 cases, 82.5%) and mesalazin (33/40 cases, 82.5%) were continued for a median of 123 days (range, 32–1,838 days) and 148 days (range, 34–2,352 days), respectively. For cases in which the NSAIDs had little effect on continuous minor clinical signs, 1 mg/kg of prednisolone was prescribed every 24 hr in place of the NSAIDs (2/40 cases, 5%). The median follow-up period was 118 days (range, 13–2,638 days). The mortality rate was 0%, and the recurrence rate was 12.5% (5/40 cases).

The histopathological diagnosis was adenocarcinoma in 3 of the recurrent cases; however, no infiltrations of adenocarcinomas were detected in the submucosal layer. Of the recurrent cases, 3 continued medical management and 2 discontinued medical management at the time of recurrence. The prognosis of the 3 dogs that continued treatment was good after a second surgery using the mucosa-submucosal pull-through technique (2 cases) or a colectomy under the celiotomy (1 case). Of the 3 dogs that underwent a second surgery, 1 had septic peritonitis after the mucosa-submucosal pull-through technique. The dog was cured by intravenous injections of 30 mg/kg of fosfomycin (FOSMICIN-S; Meiji Seika Pharma Co., Ltd., Tokyo, Japan) and 5 mg/kg imipenem/cilastatin (Tienam; MSD K.K., Tokyo, Japan) every 12 hr for 4 weeks. The prognosis of the 2 dogs that did not undergo the second surgery is unknown due to the discontinuation of

### Table 2. The list of diagnoses differently according to the endoscopic biopsy samples and the excisional samples

<table>
<thead>
<tr>
<th>Case</th>
<th>Endoscopic biopsy sample</th>
<th>Excisional sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inflammation</td>
<td>Inflammatory polyps</td>
</tr>
<tr>
<td>2</td>
<td>Inflammation</td>
<td>Inflammatory polyps</td>
</tr>
<tr>
<td>3</td>
<td>Inflammation</td>
<td>Inflammatory polyps + Ulcer</td>
</tr>
<tr>
<td>4</td>
<td>Inflammatory polyps</td>
<td>Inflammatory polyps + Adenoma</td>
</tr>
<tr>
<td>5</td>
<td>Inflammatory polyps</td>
<td>Inflammatory polyps + Adenocarcinoma</td>
</tr>
<tr>
<td>6</td>
<td>Adenoma</td>
<td>Inflammatory polyps + Adenocarcinoma</td>
</tr>
<tr>
<td>7</td>
<td>Adenoma</td>
<td>Inflammatory polyps + Adenocarcinoma</td>
</tr>
</tbody>
</table>
follow-up examinations. (Table 3).

**Discussion**

In this study, we assessed the clinical features and surgical treatment of ICRPs in miniature dachshunds. We found that ICRPs were located within the mucosa-submucosal layer, even in cases involving adenocarcinomas and that EUS is useful for identifying the location of lesions. Moreover, the mucosa-submucosal pull-through technique improved the prognosis of miniature dachshunds with ICRPs without intraoperative complications.

In the previous study, ICRPs typically occurred in middle-aged miniature dachshunds and primarily caused hematochezia and tenesmus\(^{20}\). In our study, tumor infiltration of the muscularis propria and metastases to the lymph nodes or other distant organs did not occur, even in cases involving adenocarcinomas.

More than half of the cases involved leukocytosis or increased levels of CRP with suspicion of colorectal inflammation. Only 1 dog showed excessive neutrophilia (white blood cell count: 220,000/μl; neutrophils: 199,100/μl), as in a previous case report of neutrophilia (neutrophils: 86,000/μl) in a dog with a rectal tumor\(^{16}\). In the previous report, neutrophilia was thought to be due to granulocyte colony-stimulating factor released from the rectal tumor. In our case, the white blood cell count decreased to 26,100/μl 2 months after surgery. Thus, the lesions in our case were thought to induce the neutrophilia. In addition, several cases had hypoalbuminemia and anemia associated with diarrhea and hematochezia, which seemed to be the cause of inflammation. Therefore, preoperative blood tests were considered necessary.

For preoperative diagnosis, all polyp samples obtained with endoscopic guidance received histopathological examination. In 7 cases, the histopathological diagnosis of the resected samples differed from that of the endoscopic samples. Surgical samples were more likely to be histopathologically diagnosed as malignant than endoscopic samples. This difference may be due to the sample volume. Therefore, even when the histopathological diagnosis of an endoscopic biopsy is benign, there is still a chance that resected lesions are malignant.

Results of endoscopic examinations had the impact on the diagnosis and treatment of choice. Endoscopy can reveal the mucosal distribution of polyps and inflammation in the colorectal area but
cannot clarify the infiltration of the muscularis propria. However, EUS in combination with endoscopy can determine the location of rectal polypoid lesions. All dogs in our study underwent surgical treatment after undergoing EUS to determine lesion location. At that time, no infiltration of the muscularis propria was observed by either EUS or histopathological examination of the resected lesions. For cases in which the ICRPs infiltrate the muscularis propria, the full-thickness pull-through technique should be used. In the previous study, the locations of lesions according to EUS findings were confirmed by histopathological examination of resected lesions in 92% of the affected dogs. In our study, EUS findings were confirmed by histopathological examination in 94.7% of dogs. Therefore, EUS is useful for preoperative planning, especially for the selection of the appropriate surgical procedure.

In the previous study, clinical signs improved after medical treatment in 80% (20/25) of miniature dachshunds with ICRPs, but gross lesions disappeared or markedly regressed in only 40% (10/25) of the cases. In our study, surgical treatment improved the clinical signs in all cases, and the main visible lesions could be removed in all cases. These findings suggest that the mucosa-submucosal pull-through technique may have a higher therapeutic effect on ICRPs in miniature dachshunds. In the previous report, the postoperative morbidity of the full-thickness pull-through technique for the treatment of colorectal carcinoma in dogs was 18%. In addition, 9% of dogs experienced long-term fecal incontinence. In another study of rectal tumors, 78.4% of dogs developed postsurgical complications after the rectal pull-through operation, including fecal incontinence, diarrhea, tenesmus and stricture formation. In that study, 31% of the dogs developed permanent fecal incontinence. In the previous report of miniature dachshunds with ICRPs, 3 dogs were treated using the full-thickness pull-through technique, and 1 had irreversible dyschezia, hematochezia, and fecal incontinence. In our study, minor short-term postoperative complications occurred, but they were rapidly resolved. The mucosa-submucosal pull-through technique produced few serious complications when compared to the full-thickness pull-through technique. Therefore, we suggest the mucosa-submucosal pull-through technique should be the treatment of choice for dogs failing to improve with medical management in which ICRPs are located in the mucosa-submucosal layers.

In human medicine, chronic inflammation is a primary factor of carcinogenesis, and inflammatory conditions develop before malignant transformation in some types of cancer. Previous studies have demonstrated that mutations of the tumor-suppressor gene p53 are often observed in tissues of patients with colitis, and the adenoma-carcinoma sequence theory of malignant transformation from intestinal polyp to adenocarcinoma due to various gene mutations including p53 is widely recognized. In addition, patients with ulcerative colitis and Crohn’s disease have been reported to be at a high risk of colorectal cancer. Aspirin and other NSAIDs, including selective or nonselective COX-2 inhibitors, are useful for preventing colon carcinogenesis. Although the etiology of ICRPs in miniature dachshunds is still unknown, colitis may be the underlying cause of ICRPs and promote gradual carcinogenesis. A higher expression of COX-2 in the tissue samples of miniature dachshunds with ICRPs has been reported. In addition, the previous report indicated clinical signs and polypoid lesions were alleviated by piroxicam in a dog with a rectal tumor. We expected that recurrences would be due to underlying colitis even in cases that underwent complete resection of the polyps and tumors. In our study, NSAIDs and salicylic acid derivatives were prescribed as postoperative adjuvant therapy for the inhibition of colitis, and the recurrence rate was 12.5%. After the resection of lesions, underlying colitis might cause the polypoid formation. Therefore, postoperative
adjuvant therapy may be essential for the improvement of outcomes in dogs with ICRPs. Further randomized controlled clinical trials are needed to establish the optimal postoperative medical treatment.

Recurrence was unrelated to the infiltration of lesions into the submucosal layer, and the horizontal surgical margins were not significantly correlated with the recurrence. However, the horizontal surgical margins were dirty in 4 recurrent cases. Of those 4 cases, 2 had adenocarcinomas. The disease-free time without clinical signs in the 2 recurrent cases with ICRPs including adenocarcinomas was shorter than that of the 2 recurrent cases without adenocarcinomas. Therefore, specific methods for the intraoperative identification of lesions may be required to prevent the recurrences in dogs with ICRPs including adenocarcinomas. In addition, the long-term continuation of ICRPs was thought to not only lead to the spread of lesions, but also malignant transformation. Therefore, early surgical intervention has the potential to reduce the recurrences.

In conclusion, our study described the clinical features of ICRPs in miniature dachshunds. The lesions were located within the mucosa-submucosal layer, even in cases involving adenocarcinomas. EUS is useful for the clarification of lesion location. The mucosa-submucosal pull-through technique might improve the prognosis of miniature dachshunds with ICRPs. Postoperative medical management may be essential to prevent the recurrences.

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References