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Title	Clinical features and surgical treatment of inflammatory colorectal polyps in miniature dachshunds: 40 cases (2002-2015)
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Citation	Japanese Journal of Veterinary Research, 67(2), 173-183
Issue Date	2019-05
DOI	10.14943/jjvr.67.2.173
Doc URL	http://hdl.handle.net/2115/74798
Туре	bulletin (data paper)
File Information	p173-183 Kazushi Asano.pdf



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REGULAR PAPER

Regional Study

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

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Received for publication, July 24, 2018; accepted, December 24, 2018

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 tumors⁶. Colorectal mucosal lesions are also rare; however, adenomatous polyps and carcinomas are frequently observed in cases of canine colorectal mucosal lesions^{2,25}. In particular, miniature dachshunds in Japan are significantly predisposed to the development of multiple inflammatory colorectal inflammatory polyps (ICRPs)²⁰. 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 tenesmus²⁰.

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 breeds²⁴⁾. Increased levels of interleukin-8, tolllike receptor expression, and nucleotide-binding oligomerization domain 2 gene mutations have been reported. However, they are not clearly related to the pathogenesis of ICRPs^{13,14,23)}.

In canine cases of ICRPs, colorectal mucosal lesions have the risk of malignant transformation²⁵⁾. To remove colorectal mucosal polypoid lesions, either an endoscopic polypectomy^{3,12)} or use of the mucosal eversion technique⁴⁾ 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^{1,5)}. 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 procedures¹⁹. 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 technique²²⁾ 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 dachshunds²⁰⁾.

We hypothesized that the mucosa-submucosal pull-though 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 mucosasubmucosal 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 propria¹⁰⁾. All dogs underwent the mucosa-submucosal pull-through technique for ICRPs removal, as mentioned in the previous report²²⁾.

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 citratedroperidol (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 antiinflammatory 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 techniques²²⁾, 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 innerstay 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



Fig. 1. The dogs' position during surgery. Each dog was placed in the perineal position after aseptic preparation.



Fig. 2. Placement of stay sutures. The mucosasubmucosal layers were retracted from the anus using DeBakey forceps and stay sutures. After visualization of the polyps, double-stay sutures were placed in the mucosa-submucosal layer at the distal level of the lesions in the dorsal, ventral, left, and right directions.

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 (orad side) and

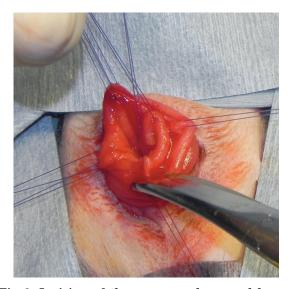


Fig. 3. Incision of the mucosa-submucosal layers for isolation. The incision between the double-stay sutures was made using Mayo or Metzenbaum scissors.

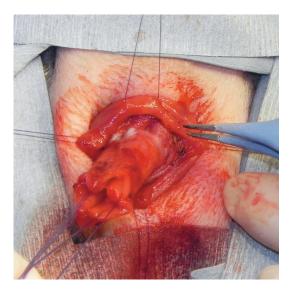


Fig. 4. Retraction of the mucosa-submucosal layer. The inner stay sutures were retracted, and the dissection between the muscular and mucosa-submucosal layers was performed using bipolar electrocautery, cotton swabs, and/or gauze.

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).

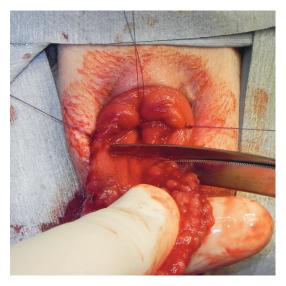


Fig. 5. Resection of the mucosa-submucosal layer, including the lesions. The affected mucosasubmucosal layer was fully isolated with the recognition of lesion distribution in the distal mucosa-submucosal tube. Three sutures were placed in the dorsal, left, and right directions to oppose the orad non-lesional mucosasubmucosal layer with the aborad non-lesional mucosasubmucosal layer; the affected layer was then resected.

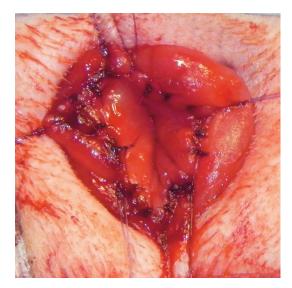


Fig. 6. Anastomosis of the orad and aborad non-lesional layers. The orad and aborad mucosasubmucosal layers were anastomosed with the interrupted suture pattern using 4-0 poliglecaprone 25 or polydioxanone monofilament suture materials.

Histopathological diagnosis: The resected lesions were fixed in 10% neutral buffered formalin, embedded in paraffin, and used for histopathological review of the diagnoses. In

	Reference	Median	Range	Below (%)	Above (%)
Total protein (g/dL)	5.2 - 8.2	6.5	5.1 - 7.3	1(2.5)	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)

Table 1. Date of complete blood count and serum chemistry

the histopathological findings, the vertical infiltration of lesions into the mucosal or mucosasubmucosal layer was evaluated and recorded in each dog. In addition, the vertical and horizontal surgical margins were evaluated. The histopahological findings were compared with the EUS findings in each dog.

Postoperative management: All dogs' diets were monitored after surgery, and each received antiinflammatory medical management. For shortterm (<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 largeintestinal 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

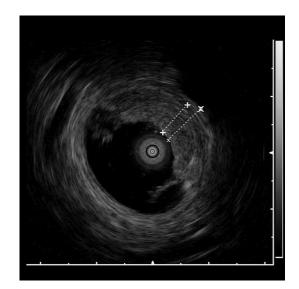


Fig. 7. Endoscopic ultrasound finding of localized mucosal lesion. In this dog, the lesion was located in the mucosal layer, and the submucosal interface was intact. The histopathological diagnosis was inflammatory colorectal polyps.

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,

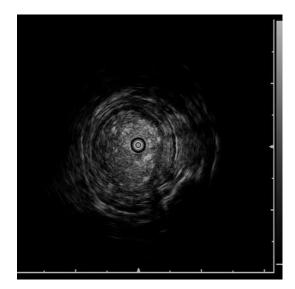


Fig. 8. Endoscopic ultrasound finding of submucosal infiltrating lesion. In this dog, the mucosa-submucosal layers were thickened, whereas the muscularis layer was intact. The histopathological diagnosis was inflammatory colorectal polyps including the adenocarcinoma.

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

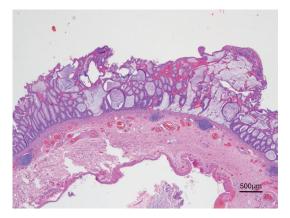


Fig. 9. Histopathological findings of inflammatory colorectal polyps. The mucosa-submucosal layer was resected. The lesion was located within the mucosal layer.

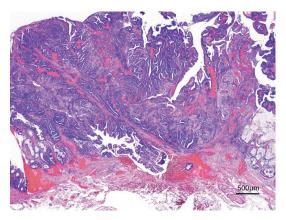


Fig. 10. Histopathological findings of adenocarcinoma. The lesion infiltrated the submucosal layer in this dog.

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

Case	Endoscopic biopsy sample	Excisional sample
1	Inflammation	Inflammatory polyps
2	Inflammation	Inflammatory polyps
3	Inflammation	Inflammatory polyps $+$ Ulcer
4	Inflammatory polyps	Inflammatory polyps $+$ Adenoma
5	Inflammatory polyps	${\rm Inflammatory\ polyps} + {\rm Adenocarcinoma}$
6	Adenoma	${\rm Inflammatory\ polyps} + {\rm Adenocarcinoma}$
7	Adenoma	Inflammatory polyps + Adenocarcinoma

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

Case signalment*	Diagnosis	Horizontal/ Vertical surgical marigins	Vertical infiltration	DF** (months)	Medical management	Outcome	Follow-up (days)
12 y-o, C	Inflammatory polyps	Dirty/ Clean	Mucosal layer	77	Discontinued	Good; no recurrence after the second surgery (open colectomy)	220
8 y-o, F	Inflammatory polyps	Dirty/ Clean	Mucosal layer	47	Continued	Good; no recurrence after the second surgery (mucosa-submucosal pull-through)	311
4 y-o, M	Adenocarcinoma	Clean/ Clean	Mucosal layer	19	Discontinued	Good; no recurrence after the second surgery (mucosa-submucosal pull-through)	727
9 y-o, M	Adenocarcinoma	Dirty/ Clean	Mucosal layer	2	Continued	Out of follow-up after the recurrence	-
12 y-o, F	Adenocarcinoma	Dirty/ Clean	Mucosal layer	2	Continued	Out of follow-up after the recurrence	-

Table 3. Summary of five recurrence cases

*y-o: year-old, C: castrated male, M: male, F: female, **DFI: Desease-free interval

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 mucosasubmucosal 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 tenesmus²⁰⁾. 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: $86,000/\mu$ l) in a dog with a rectal tumor¹⁶⁾. 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 $26,100/\mu$ l 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 lesions¹⁰⁾. 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 $dogs^{10}$. 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 cases²⁰⁾. 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 pullthrough technique for the treatment of colorectal carcinoma in dogs was 18%¹⁸⁾. In addition, 9% of dogs experienced long-term fecal incontinence¹⁸⁾. 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 formation¹⁹⁾. In that study, 31% of the dogs developed permanent fecal incontinence¹⁹⁾. In the previous report of miniature dachshunds with ICRPs, 3 dogs were treated using the fullthickness pull-through technique, and 1 had irreversible dyschezia, hematochezia, and fecal

incontinence²⁰⁾. 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 primary factor of carcinogenesis, and а inflammatory conditions develop before malignant transformation in some types of $cancer^{17}$. demonstrated that Previous studies have 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^{8,11)}. In addition, patients with ulcerative colitis and Crohn's disease have been reported to be at a high risk of colorectal cancer^{7,9)}. Aspirin and other NSAIDs, including selective or nonselective COX-2 inhibitors, are useful for preventing colon carcinogenesis¹⁵⁾. Although the etiology of ICRPs in miniature dachshunds is still unknown, colitis may be the underlying cause of ICRPs and promote gradual carcinogenesis²¹⁾. A higher expression of COX-2 in the tissue samples of miniature dachshunds with ICRPs has been reported²⁴⁾. In addition, the previous report indicated clinical signs and polypoid lesions were alleviated by piroxicam in a dog with a rectal tumor¹⁶⁾. 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 surgical horizontal 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 longterm 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 features of ICRPs in miniature clinical 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 mucosasubmucosal pull-through technique might improve the prognosis of miniature dachshunds with ICRPs. Postoperative medical management may be essential to prevent the recurrences.

Acknowledgments

The authors would like to thank Dr. Orie Yoshida, Dr. Gentoku Iida, and Dr. Yumiko Kagawa for their technical assistance.

References

- Allen SW, Crowell WA. Ventral approach to the pelvic canal in the female dog. Vet Surg 20, 118-121, 1991
- Church EM, Mehlhaff CJ, Patnaik AK. Colorectal adenocarcinoma in dogs: 78 cases (1973–1984). J Am Vet Med Assoc 191, 727–730, 1987
- 3) Coleman KA, Berent AC, Weisse CW. Endoscopic mucosal resection and snare polypectomy for treatment of a colorectal polypoid adenoma in a dog. J Am Vet Med Assoc 244, 1435-1440, 2014
- 4) Danova NA, Robles-Emanuelli JC. Bjorling DE. Surgical excision of primary canine rectal tumors by an anal approach in twentythree dogs. Vet Surg 35, 337-340, 2006
- Davies JV, Read, HM. Sagittal pubic osteotomy in the investigation and treatment of intrapelvic neoplasia in the dog. J Small Anim Pract 31, 123-130, 1990
- 6) Dobson JM, Samuel S, Milstein H, Rogers K, Wood JL. Canine neoplasia in the UK: estimates of incidence rates from a population of insured dogs. J Small Anim Pract 43, 240–246, 2002
- Eaden JA, Abram KR. Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48, 526-535, 2001
- Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell 61, 759-767, 1990
- 9) Gillen CD, Walmsley RS, Prior P, Andrews HA, Allan RN. Ulcerative colitis and Crohn's disease: a comparison of the colorectal cancer risk in extensive colitis. Gut 35, 1590–1592, 1994
- 10) Hayashi K, Okanishi H, Kagawa Y, Asano K, Watari T. The role of endoscopic ultrasound in the evaluation of rectal polypoid lesions in 25 dogs. Jpn J Vet Res 60, 185–189, 2012
- 11) Hussain SP, Amstad P, Raja K, Ambs S, Nagashima M, Bennett WP, Shields PG, Ham AJ, Swenberg JA, Marrogi AJ, Harris CC. Increased p53 mutation load in noncancerous colon tissue from ulcerative colitis: a cancerprone chronic inflammatory disease. Cancer Res 60, 3333-3337, 2000
- 12) Igarashi H, Ohno K, Ohmi A, Tsukamoto A, Nakashima K, Fujino Y, Uchida K, Tsujimoto H. Polypoid adenomas secondary to inflammatory colorectal polyps in 2 miniature dachshunds. J Vet Med Sci 75, 535-538, 2013

- Igarashi H, Ohno K, Maeda S, Kanemoto H, Fukushima K, Uchida K, Tsujimoto H. Expression profiling of pattern recognition receptors and selected cytokines in miniature dachshunds with inflammatory colorectal polyps. Vet Immunol Immunopathol 159, 1-10, 2014
- 14) Igarashi H, Ohno K, Uchida E, Fujiwara-Igarashi A, Kanemoto H, Fukushima K, Uchida K, Tsujimoto H. Polymorphisms of nucleotide-binding oligomerization domain 2 (NOD2) gene in miniature dachshunds with inflammatory colorectal polyps. Vet Immunol Immunopathol 164, 160–169, 2015
- 15) Jänne PA, Mayer RJ. Chemoprevention of colorectal cancer. N Engl J Med 29, 1960– 1968, 2000
- 16) Knottenbelt CM, Simpson JW, Chandler ML. Neutrophilic leucocytosis in a dog with a rectal tumour. J Small Anim Pract 41, 457– 460, 2000
- Mantovani A, Allavena P, Sica A, Balkwill F. Cancer-related inflammation. Nature 454, 436-444, 2008
- 18) Morello E, Martano M, Squassino C, Iussich S, Caccamo R, Sammartano F, Zabarino S, Bellino C, Pisani G, Buracco P. Transanal pull-through rectal amputation for treatment of colorectal carcinoma in 11 dogs. Vet Surg 37, 420-426, 2008
- 19) Nucci DJ, Liptak JM, Selmic LE, Culp WT, Durant AM, Worley D, Maritato KC, Thomson M, Annoni M, Singh A, Matz B, Benson J, Buracco P. Complications and outcomes following rectal pull-through surgery in dogs with rectal masses: 74 cases (2000–2013). J Am Vet Med Assoc 245, 684–695, 2014
- 20) Ohmi A, Tsukamoto A, Ohno K, Uchida K,

Nishimura R, Fukushima K, Takahashi M, Nakashima K, Fujino Y, Tsujimoto H. A retrospective study of inflammatory colorectal polyps in miniature dachshunds. J Vet Med Sci 74, 59–64, 2012

- 21) Saito T, Chambers JK, Nakashima K, Uchida E, Ohno K, Tsujimoto H, Uchida K, Nakayama H. Histopathologic Features of Colorectal Adenoma and Adenocarcinoma Developing Within Inflammatory Polyps in Miniature Dachshunds. Vet Pathol 55, 654–662, 2018
- 22) Shida T, Maruo T, Suga K, Kawamura H, Takeda H, Sugiyama H, Ishikawa T, Inoue A, Yamada T, Ito T, Madarame H, Kayanuma H, Suganuma T. Rectal mucosal pull-through surgical technique for canine rectal multiple tumor. Jpn J Vet Anesth Surg 39, 11–16, 2008
- 23) Tamura Y, Ohta H, Torisu S, Yuki M, Yokoyama N, Murakami M, Lim SY, Osuga T, Morishita K, Nakamura K, Yamasaki M, Takiguchi M. Markedly increased expression of interleukin-8 in the colorectal mucosa of inflammatory colorectal polyps in miniature dachshunds. Vet Immunol Immunopathol 156, 32-42, 2013
- 24) Uchida E, Chambers JK, Nakashima K, Saito T, Ohno K, Tsujimoto H, Nakayama H, Uchida K. Pathologic features of colorectal inflammatory polyps in miniature dachshunds. Vet Pathol 53, 833-839, 2016
- 25) Valerius KD, Powers BE, McPherron MA, Hutchison JM, Mann FA, Withrow SJ. Adenomatous polyps and carcinoma in situ of the canine colon and rectum: 34 cases (1982–1994). J Am Anim Hosp Assoc 33, 156–160, 1997