A Retrospective Study of Inflammatory Colorectal Polyps in Miniature Dachshunds

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ABSTRACT: Medical records of dogs with colorectal polyps were retrospectively reviewed, and clinical presentation of inflammatory colorectal polyps in miniature dachshunds was evaluated. Of 33 dogs found to have colorectal polyps, miniature dachshunds were markedly over-represented with 16 dogs (48%), of which 12 (75%) were found to have inflammatory polyps. Multiple polyps localized between the rectum and the descending colon was the most common finding in miniature dachshunds with inflammatory polyps. Twenty dogs (80%) out of 25 miniature dachshunds with inflammatory colorectal polyps responded to immunosuppressive therapy using prednisolone and cyclosporine. The results of this study indicate that miniature dachshunds are predisposed to develop inflammatory colorectal multiple polyps, for which immunosuppressive therapy may be a treatment option.

KEY WORDS: immunosuppressive therapy, inflammatory colorectal polyps, miniature dachshund.


Polyps are an abnormal growth of tissue arising from the mucosa, including neoplasms and inflammatory polyps. In dogs, colorectal polyps are relatively common in the gastrointestinal tract. These polyps can be single or multiple and are most often located in the distal rectum, causing the common clinical signs of hematochezia or tenesmus. In previous reports, many colorectal polyps in dogs were found to be derived from neoplasms, with adenomatous polyps and adenocarcinoma being most frequently represented [11, 25, 32, 33]. Adenomatous polyps and adenocarcinoma are observed as solitary masses in the rectum, and most polyps appear as friable, lobulated, sessile, or pedunculated lesions on the mucosa. Surgical resection has been recommended in dogs as treatment for colorectal polyps [2, 5, 21]. Endoscopic treatment for adenomatous polyps [7, 10] and piroxicam for tubulopapillary polyps [15] have been reported as alternative therapies for colorectal neoplasms. On the contrary, inflammatory colorectal polyps are rare, and few reports have described the clinical features of inflammatory colorectal polyps [33]. In humans, inflammatory colorectal polyps or polypoid lesions occur in association with inflammatory bowel disease (IBD) and other inflammatory diseases of the colon such as ischemic or infective colitis [3, 17, 24]. These masses form mainly due to extensive mucosal damage and healing processes, rather than infiltration of inflammatory cells. The polyps formed from infiltration of inflammatory cells, which could be termed “true” inflammatory polyps, seem to be relatively rare in humans. This study was conducted on the basis of two objectives. First, we retrospectively investigated dogs with colorectal polyps to characterize the prevalence and clinical features of the disease in Japan. Second, we reviewed the clinical presentation and treatment response of cases with inflammatory colorectal multiple polyps in miniature dachshunds, which were markedly over-represented in our study.

MATERIALS AND METHODS

Retrospective study of colorectal polyps in dogs: We reviewed the medical records of 33 dogs found to have colorectal polyps at the Veterinary Medical Center of the University of Tokyo (VMC-UT) between April 2006 and March 2009. The breed, age, gender, form of polyp, and histopathological diagnosis were investigated. Polyps were classified as solitary or multiple on the basis of their gross appearance. In all cases, biopsy samples were obtained by endoscopy or full-thickness surgical excision. Biopsy samples were fixed with neutral-buffered formalin, routinely processed, and embedded in paraffin. Sections were cut and stained with hematoxylin and eosin. To characterize the differences between miniature dachshunds and the other breeds of dogs, the dogs were classified into the miniature dachshund (MD) group or non-MD group (breeds other than miniature dachshund). Signalment, gross appearance, and histopathological diagnoses of polyps between each group were compared. Chi-square tests and Fisher’s exact tests were used to determine association between categorical variables. Mann-Whitney U tests were used to compare...
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numerical values. Values of $P<0.05$ were considered significant. The statistical analysis was performed by commercial statistical software (JMP 5.0.1; SAS Institute, Cary, NC, U.S.A.).

Clinical features and treatment response of inflammatory colorectal polyps in miniature dachshunds: Thirty miniature dachshunds with inflammatory colorectal polyps at the VMC-UT between April 2006 and March 2011 were retrospectively investigated. Age, gender, form of polyps, histopathological diagnosis, treatment, and therapeutic outcome were investigated. Polyps were classified as solitary or multiple on the basis of their gross appearance. In all cases, biopsy samples were obtained by endoscopy or full-thickness surgical excision. Biopsy samples were fixed with neutral-buffered formalin, routinely processed, and embedded in paraffin. Sections were cut and stained with hematoxylin and eosin. Diagnosis of inflammatory polyps was defined as non-neoplastic polyloid lesion of proliferating mucosa with no atypism, accompanied by significant inflammatory cell infiltration.

RESULTS

Retrospective study of colorectal polyps in dogs: Between April 2006 and March 2009, a total of 7988 dogs, including 1126 miniature dachshunds, were referred to the VMC-UT. Of those, 33 dogs were found to have colorectal polyps, representing an incidence of colorectal polyps of 0.4%. The median age of the dogs was 10.2 years (range, 3.7–17.2 years). Of the 33 dogs, 26 were male (4 castrated), and 7 were female (5 spayed). These 33 dogs consisted of 31 pure breeds and 2 mixed breeds. The most frequently observed breed of dogs with colorectal polyps was the miniature dachshund (n=16, 48%). The odds ratio was calculated as 5.80 ($P<0.001$). Other breeds included golden retriever (n=2), Chihuahua (n=2), Labrador retriever (n=2), American cocker spaniel (n=1), Welsh corgi (n=1), Shih tzu (n=1), Shetland sheepdog (n=1), German shepherd (n=1), Toy poodle (n=1), Beagle (n=1), Brussels griffon (n=1), and Maltese (n=1). Of the 33 dogs, 15 (46%) had inflammatory polyps, 10 (30%) had benign tumors, and 8 (24%) had malignant tumors. Tumor types were adenomatous polyp (n=7), adenocarcinoma (n=6), leiomyoma (n=2), plasmacytoma (n=1), lymphoma (n=1), and leiomyosarcoma (n=1) (Table 1). The gross appearances of polyps in 15 cases were solitary (5 malignant tumors, 8 benign tumors, and 2 inflammatory polyps), whereas the other 18 cases had multiple polyps (3 malignant tumors, 2 benign tumors, and 13 inflammatory polyps).

The 33 dogs were divided into 2 groups: MD group (n=16) and non-MD group (n=17). The MD group included 12 male dogs (2 castrated) and 4 female dogs (3 spayed). The median age was 8.6 years (range, 4.1–12.7 years). The non-MD group included 14 male dogs (3 castrated) and 3 female dogs (2 spayed). The median age of these dogs was 11.0 years (range, 3.7–17.2 years). There was no significant difference in gender or age between the groups ($P=0.688$ and 0.054, respectively). In the MD group, only 3 cases had solitary polyps and 13 cases had multiple lesions. In contrast, 12 dogs in the non-MD group had a solitary mass and 5 dogs had multiple polyps. The dogs in the MD group had a significantly higher tendency to develop multiple polyps ($P<0.001$). Of the dogs in the MD group, 12 (75%) had inflammatory polyps, 3 had benign tumors (19%), and 1 dog had a malignant tumor (6%). Diagnoses for the dogs in the non-MD group were inflammatory polyps in 3 (18%), benign tumors in 7 (41%), and malignant tumors in 7 (41%) cases. The prevalence of inflammatory colorectal polyps was significantly higher in miniature dachshunds than in other breeds ($P<0.001$, Table 2).

Clinical features and treatment response of inflammatory colorectal polyps in miniature dachshunds: The median age of 30 miniature dachshunds with inflammatory colorectal polyps was 9.0 years (range, 6.6–12.7 years). The cases included 22 male dogs (8 castrated) and 8 female dogs (5 spayed). Hematochezia was seen in all dogs. Tenesmus (n=22, 73%) and mucoid feces (n=20, 67%) were relatively common clinical signs. Rectal prolapse was observed in 3 cases. Most dogs presented with multiple polyps (n=27, 90%), with small polyps diffusely spread around the mucosa, whereas only 3 dogs (10%) had a solitary polyp.

| Table 1. Histopathological diagnosis of 33 dogs with colorectal polyps |
|-----------------------------|---|---|---|---|
| Histopathological diagnosis | n |
| Inflammatory polyps         | 15 |
| Benign tumor                |    |
| Adenomatous polyp           | 7  |
| Leiomyoma                   | 2  |
| Plasmacytoma                | 1  |
| Malignant tumor             |    |
| Adenocarcinoma              | 6  |
| Leiomyosarcoma              | 1  |
| Lymphoma                    | 1  |

| Table 2. Comparison of miniature dachshunds (MD) group and non-MD group with regard to diagnosis of polyps |
|---------------------------------|-----|-----|-----|-----|
|                                 | MD group | non-MD group | Odd’s ratio | $P$  |
| All cases                       | 1126     | 6862         | 5.80        | <0.001  |
| Colorectal polyps               | 16       | 17           | 24.63       | <0.001  |
| Inflammatory polyps             | 12       | 3            | 1.74        | 0.5139  |
| Neoplastic polyps               | 4        | 14           | 2.62        | 0.3214  |
| Benign tumor                    | 3        | 7            | 0.87        | 0.7051  |
| Malignant tumor                 | 1        | 7            |             |         |
The polyps were localized at the rectum (n=10, 33%), distal colon (n=3, 10%), or were spread around the colorectal area (n=17, 57%) (Table 3). Histopathological findings of the inflammatory colorectal polyps in miniature dachshunds were proliferative changes of mucosal epithelium without cellular atypia, increased goblet cells with dilated crypts, infiltration of inflammatory cells, edema or hemorrhage of the mucosa, and proliferation of granulomatous tissue, sometimes with osseous metaplasia. Mucosal inflammation consisted of neutrophils, macrophages, eosinophils, lymphocytes, and plasma cells (Fig. 2). In 1 case, severe infiltration of eosinophils into the mucosa was observed.

Of the 30 miniature dachshunds affected with inflammatory colorectal polyps, 25 dogs were treated medically with immunosuppressive drugs, 3 dogs underwent surgery, and the remaining 2 dogs were lost to follow-up. Of the 25 dogs that received immunosuppressive therapy, 5 were treated with prednisolone alone and 20 were treated with combination therapy of prednisolone and cyclosporine. The median dosage of prednisolone at response was 1.6 mg/kg/day (range, 0.6–3.8 mg/kg/day). Cyclosporine was administered at the median dosage of 4.7 mg/kg/day (range, 2.3–8.4 mg/kg/day). Clinical signs were improved in 20 of 25 dogs (80%). In 10 cases, gross lesions of polyps had disappeared or markedly regressed. The dose of prednisolone was reduced gradually by 50% at 2- to 4-week intervals. Eighteen of the 20 dogs with improvement were maintained with low-dose prednisolone with or without cyclosporine. However, recurrence of clinical signs and regrowth of polyps were observed when prednisolone was tapered in the other 2 dogs. Five dogs showed no response to immunosuppressive therapy with prednisolone and cyclosporine.

Some dogs received other additional therapy according to the clinician’s preference. Two dogs were treated with non-steroidal anti-inflammatory drugs before the immunosuppressive therapy. One dog received piroxicam (0.3 mg/kg/day) and the other dog received meloxicam (0.2 mg/kg/day), with no improvement in clinical signs. These two dogs were then treated successfully with prednisolone and cyclosporine, as described above. Another 3 dogs were switched to leflunomide (5 mg/kg/day) instead of cyclosporine because of unsatisfactory clinical results. All 3 dogs responded to the treatment fairly well, with little or no clinical signs. In 8 cases, endoscopic treatment was performed adjunctively with immunosuppressive therapy. In 1 case with a solitary large polyp in the rectum, the polyp was resected with polypectomy, and hematochezia was improved after treatment. The other cases had small polyps diffusely spread around the rectal mucosa, with some comparatively large

![Fig. 1](image-url) Endoscopic findings of inflammatory colorectal polyps in a miniature dachshund. (A) Small round polyps with a white covering are diffusely spread around the mucosa of the descending colon. These polyps are fragile and bleed easily. (B) A large solitary polyp occupying the rectum. The polyp is covered by excess mucus.
polyps in the rectum. As immunosuppressive therapy alone was insufficient or ineffective for those cases, the large polyps were resected with polypectomy and then the small diffuse polyps were coagulated with argon plasma coagulation (APC). All cases showed marked improvement in clinical signs, particularly in 1 case where no clinical signs were observed after therapy. Some dogs required a second treatment due to recurrence of symptoms after the first treatment. There were no complications with these procedures.

Three dogs underwent surgical excision of polyps by the rectal full-thickness pull-through technique. Clinical signs were improved in 2 of the 3 cases, although some temporary complications such as diarrhea and hematochezia were noted. Recurrence was not observed during the study period. However, irreversible dyschezia, hematochezia, and incontinence were observed after surgery in the third dog.

DISCUSSION

In this study, miniature dachshund was the breed most commonly found to have colorectal polyps, accounting for 48% of the cases (odds ratio, 5.80). Furthermore, 75% of dogs in the MD group had inflammatory colorectal polyps, showing statistically higher prevalence of the disease than dogs in the non-MD group. Multiple polyps were more commonly observed in the MD group than non-MD group. The results of the present study suggest that miniature dachshunds in Japan are significantly predisposed to development of multiple inflammatory colorectal polyps. Clinical features of inflammatory colorectal polyps in miniature dachshunds were middle-age onset, male gender predisposition, and multiple polyps localized between the rectum and descending colon. Hematochezia, tenesmus, and mucoid feces associated with the polyps were common symptoms. In almost all cases, the general physical condition of the dog was relatively good. Histologically, polyps consisted of

hyperplastic mucosal epithelium, increased goblet cells with dilated crypts, and cellular infiltration of neutrophils, macrophages or other inflammatory cells.

In the non-MD group, clinical features were similar to those reported in previous studies [11, 25, 32, 33]. Colorectal polyps typically occurred in older, male dogs; adenomatous polyps and adenocarcinoma were frequently observed. Collie, German shepherd and West Highland white terrier have been reported to be the breeds commonly affected by colorectal polyps [11, 25, 32], but our results showed no breed-specific predisposition other than miniature dachshund.

Another feature of inflammatory colorectal polyps in miniature dachshunds was that immunosuppressive therapy with prednisolone and cyclosporine was effective in 80% of the cases. Immunosuppressive therapy has not previously been reported to be effective for colorectal polyps in dogs. In this study, we could not detect any infectious agent or foreign body that could stimulate mucosal inflammation of the colorectum by histopathology. Moreover, some of our cases received empirical treatment such as antibiotics, probiotics, and prescription diet before referral, but showed no clinical improvement. The existence of idiopathic inflammation and the effectiveness of immunosuppressive therapy suggest that certain immunological disturbances, may exist in the disease pathogenesis, although this hypothesis was not further investigated. Based on our results, immunosuppressive therapy may be a treatment option for inflammatory colorectal polyps. Further studies are required to determine the optimal dose of prednisolone and cyclosporine to alleviate clinical signs with minimum risk of side effects. Some dogs were refractory to prednisolone and cyclosporine treatment, but responded well to leflunomide. Leflunomide, which is a relatively new immunosuppressive drug for which few reports are available in dogs [34], is a potent agent and might be a good choice in the management of uncontrollable cases,
although we could not confirm this hypothesis due to the small number cases in this study. Piroxicam has been reported to be an effective agent against rectal tubulopapillary polyps in dogs [15], but was less effective than immunosuppressive therapy in the present study.

Endoscopic treatment was performed in 8 cases and all cases showed satisfying results. In 1 case with a large solitary polyp in the rectum, polypectomy was performed. The other 7 cases were treated with a combination of polypectomy and APC. Polypectomy is useful to resect solitary pedunculated masses, but application of this technique was sometimes difficult in our cases because there were numerous, small, sessile-type polyps. APC is a device for noncontact thermal coagulation of tissue. In humans, APC is applied for treatment of various gastrointestinal conditions, particularly for hemostasis or tumor ablation. Perforation is a severe complication of APC treatment, but complication rates of APC are low compared with other thermal methods of treatment [19, 20]. Since inflammatory colorectal polyps in miniature dachshunds typically develop as small, multiple polyps, endoscopic treatment with APC may be one treatment option for the disease. Further investigation is needed to evaluate proper application of these endoscopic treatments and their long-term prognosis.

The rectal pull-through technique was performed in 3 cases. Some complications, such as tenesmus, fecal incontinence, and rectal bleeding, have been reported in association with this technique. However, these complications are usually moderate and self-limiting, although persistent dysfunction could occur [2, 21]. In our study, one case had irreversible dyschezia. Severe complications would be problematic for surgical resection since this disease is not malignant. To avoid complications, the rectal mucosal pull-through technique may be superior to the full-thickness rectal pull-through technique [27]. Moreover, the rectal full-thickness pull-through technique is limited in its extent of resection because of the colorectal area blood supply. The rectal mucosal pull-through technique, on the other hand, makes it possible to excise longer lesions because it preserves the rectal artery.

One dog in the MD group developed rectal adenoma during the study period. Colorectal inflammatory polyps were first diagnosed in the dog by endoscopy and were treated with oral prednisolone and cyclosporine. Eighteen months after the first diagnosis, a duodenal low-grade lymphoma was found and treated with melphalan (cyclosporine was withdrawn). The colorectal polyps were re-biopsied at the time and re-confirmed to be inflammatory polyps. The dog had achieved complete remission, and chemotherapy was discontinued after 21 months of maintenance therapy. Three months later (3.5 years after the first diagnosis), the polyps became progressively enlarged and hematochezia worsened, so a third biopsy and endoscopic polypectomy was performed. The polyps were diagnosed as adenoma, with neoplastic papillary proliferation of epithelial cells and mild dysplasia. After the procedure, the dog did not experience any more symptoms and recurrence was not observed by 4 months. In humans, the connection between inflammation and tumorigenesis is well-established and has received a great deal of supporting evidence from genetic, pharmacological, and epidemiological data [18, 30]. It is known that 18% of IBD (ulcerative colitis) patients develop colorectal carcinoma within 30 years of disease onset, and >50% of these patients will die from cancer. Chronic inflammation is characterized by the production of proinflammatory cytokines that can induce mutations in oncogenes and tumor suppressor genes, which initiates and promotes cancer development. Administration of immunosuppressive or immunomodulatory drugs is thought to be another cause of tumorigenesis [16]. In veterinary medicine, the relationship between IBD and tumor development is still controversial. Further studies are needed to evaluate the long-term prognosis and possibility of malignant changes to inflammatory polyps in miniature dachshunds.

In humans, several types of the so-called inflammatory polyps occur in IBD and other inflammatory diseases of the colon [3, 17, 24]. Inflammatory pseudopolyps usually occur in ulcerative colitis, and less frequently in Crohn’s disease [8, 9, 12, 29]. The condition is thought to represent regenerating mucosal islands scattered between areas of extensive ulceration. Because the polypoid masses do not actually extend above the level of the mucosa, the term “pseudopolyps” is appropriate. Post-inflammatory polyps are another type of inflammatory polyps, which form due to the mucosal healing process of extensive ulceration. These polyps sometimes become huge and are known as giant inflammatory polyps [6, 13, 26]. The pathogenesis and histopathological features of inflammatory pseudopolyps and post-inflammatory polyps do not coincide with that of the inflammatory polyps of miniature dachshunds in our study.

Cap polyposis in humans is a rare disease characterized by the presence of polyps covered by a “cap” of granulation tissue [4, 22, 31]. Endoscopically, these polyps occur in multiples (1–100 polyps), and are small, reddish, and sessile. The most common sites affected are the sigmoid colon and rectum. Although the etiology of this disease is still unknown, several possible causes have been postulated on its pathogenesis, including a form of IBD, bacterial infection, and mechanical stimulation by stool or mucosal prolapse secondary to abnormal colonic motility [1, 23, 28]. Some investigators have hypothesized that immune stimulation and excess inflammatory reactions may play a role in the pathogenesis of cap polyposis. Various medical treatments have been advocated, including antibiotics, anti-inflammatory agents, and immunomodulators [1, 14, 28]. Polyps associated with cap polyposis are “true” inflammatory polyps and resemble, in gross appearance and histopathological features, the inflammatory polyps we observed in miniature dachshunds. It is interesting that some cases of cap polyposis are reported to respond to anti-inflammatory or immunomodulatory therapy because immunosuppressive therapy seemed to be effective against inflammatory polyps in our study. Although we could not elucidate the relation between these diseases, they may share a common etiology.
To our knowledge, there is no condition in humans that corresponds completely with inflammatory polyps in miniature dachshunds.

In summary, we found miniature dachshund to be the breed most commonly affected by colorectal polyps, particularly inflammatory colorectal multiple polyps, which we hypothesize is unique to a specific population of miniature dachshunds in Japan. In addition to surgical resection, immunosuppressive therapy, such as prednisolone and cyclosporine, or endoscopic treatment may be useful options for disease treatment. To clarify the pathogenesis of the disease, further studies with a larger number of cases are required.

REFERENCES


