

ORIGINAL ARTICLE

## 대장 폴립모양 평활근종에서 내시경 절제술의 유용성

최현호, 조영석<sup>1</sup>, 최수경, 김형근, 김성수, 채현석, 신옥란<sup>2</sup>

가톨릭대학교 의과대학 의정부성모병원 내과, 병원병리과<sup>2</sup>, 서울성모병원 내과<sup>1</sup>

### Clinical Outcomes of Endoscopic Removal in Patients with Colorectal Polypoid Leiomyomas

Hyun Ho Choi, Young-Seok Cho<sup>1</sup>, Soo Kyoung Choi, Hyung-Keun Kim, Sung Soo Kim, Hiun-Suk Chae, and Ok-Ran Shin<sup>2</sup>

Departments of Internal Medicine and Hospital Pathology<sup>2</sup>, Uijeongbu St. Mary's Hospital, Uijeongbu, Department of Internal Medicine, Seoul St. Mary's Hospital<sup>1</sup>, College of Medicine, The Catholic University, Seoul, Korea

**Background/Aims:** Although polypoid leiomyomas in the colon and rectum are rare, they are increasingly detected during colonoscopy. The aim of this study was to evaluate the efficacy and clinical outcomes of endoscopic removal for colorectal polypoid leiomyoma.

**Methods:** Data were retrospectively collected from 22 patients with polypoid leiomyoma arising from the muscularis mucosae in the colon and rectum who underwent endoscopic removal at single referral gastrointestinal endoscopy unit. Colonoscopic findings, endoscopic removal, success rates, complication rates (bleeding or perforation), pathologic characteristics, and recurrence rates were investigated.

**Results:** Most polypoid leiomyomas were small asymptomatic lesions less than 1 cm. The tumors were located predominantly in the left colon. Ten leiomyomas were removed using cold biopsy forceps, and 12 were resected by conventional polypectomy or endoscopic mucosal resection. All tumors arose from or involved the muscularis mucosa. There were no complications, such as bleeding or perforation. No local remnant lesions were found in 19 patients who underwent at least one follow-up colonoscopy.

**Conclusions:** This case series represent cases of small colorectal polypoid leiomyoma that were safely removed endoscopically. An awareness of their endoscopic and clinic-pathological characteristics may provide safe treatment strategy for colonic leiomyomatous tumors of similar size in capable hands. (*Korean J Gastroenterol* 2016;68:179-185)

**Key Words:** Colorectal neoplasms; Colonic polyps; Leiomyoma; Colonoscopy

### INTRODUCTION

Gastrointestinal (GI) smooth muscle tumors are common lesions, primarily of the stomach and small intestine.<sup>1</sup> However, leiomyomas arising in the colon and rectum are rare, only 3% of all alimentary tract leiomyomas.<sup>2</sup> Colonic submucosal lesions, including leiomyomas are usually treat-

ed by surgical resection, because endoscopic resection has a considerably higher perforation risk.<sup>3</sup> However, several case reports have shown that endoscopic resection of small polypoid leiomyomas is feasible.<sup>2,4-13</sup> Since screening colonoscopy for colorectal cancers became widely available, the detection of small polypoid leiomyomas by colonoscopy has increased.<sup>14</sup> In the present study, we evaluated clinicopatho-

Received June 17, 2016. Revised August 3, 2016. Accepted August 18, 2016.

© This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2016. Korean Society of Gastroenterology.

교신저자: 조영석, 06591, 서울시 서초구 반포대로 222, 가톨릭대학교 의과대학 서울성모병원 내과

Correspondence to: Young-Seok Cho, Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea. Tel: +82-2-2258-6021, Fax: +82-2-2258-2038, E-mail: yscho@catholic.ac.kr

Financial support: This work was supported, in part, by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2010-0023295). Conflict of interest: None.

logical characteristics of colorectal polypoid leiomyomas and the efficacy and outcome of endoscopic removal of these lesions.

## SUBJECTS AND METHODS

### 1. Patients

From June 2009 to August 2012, 22 colonic leiomyomas in 22 consecutive patients were removed endoscopically and identified by further pathological examination. We assembled information from the existing medical records of these 22 patients and analyzed it using standard methods. This study protocol was approved by the Institutional Research Ethics Board of our institution (IRB No. UC13RISI0015) and adhered to the Helsinki Declaration. All study subjects provided written informed consent prior the procedure.

### 2. Endoscopic procedure

After preparation with polyethylene electrolyte glycol solution, colonoscopic examinations were performed using standard colonoscopes (CF-H260 series; Olympus, Tokyo, Japan). All detected tumors were removed completely: diminutive lesions less than 5 mm were removed using biopsy forceps and larger lesions by conventional polypectomy or *en bloc* endoscopic mucosal resection (EMR). Three experienced endoscopists performed all endoscopic treatments (YSC, HKK, and HSC; each had experience of more than 2,000 colorectal EMRs). For the EMR procedure, normal saline solution in combination with dilute epinephrine (1 in 10,000) was injected into the submucosa near the tumor through needle forceps. The tumor was captured with a snare device and removed by electrocoagulation with an Endocut Q current (effect 3, cut duration 2 ms, cut interval 1,200 ms) which was generated by a VIO300D electrosurgical unit (ERBE, Tuebingen, Germany).

### 3. Clinical outcome

All specimens were reviewed by pathologists specializing in GI pathology. Hematoxylin and eosin-stained slides were reviewed for each case. The slides were immunohistochemically stained with actin, desmin, CD34 and CD117. Polypoid leiomyoma is characterized by smooth muscle tumors arising from or involved with the muscularis mucosae. Histologic section showed a well-circumscribed proliferation of smooth

muscle fibers with brightly eosinophilic cytoplasm and cigar-shaped nuclei arranged in intersecting fascicles. Polypoid leiomyomas were positive for smooth muscle actin and desmin, and negative for CD34 and CD117. Tumors diagnosed with polypoid leiomyoma were included in the present study.

Complete resection was defined as a lesion-free margin with both the lateral and basal tissues free of pathology. Procedure-related bleeding was defined as bleeding requiring endoscopic and/or radiological hemostasis or transfusions. Perforation was defined as endoscopically observed colonic wall penetration, or a perforation detected after endoscopy by radiologic examination such as abdominopelvic CT. Patients that had a complete resection with endoscopically clear margins were scheduled for re-examination within one year.

## RESULTS

### 1. Patient characteristics

Twenty-two patients were included in this retrospective study. The demographic data are presented in Table 1. There were 18 males and four females with a mean age of 55.7 years (range, 34-82 years). Sixteen of the twenty-two patients (72.7%) underwent colonoscopy for screening of colorectal cancer. Other indications for colonoscopy were as follows: two patients presented with diarrhea, two with rectal bleeding, one with abdominal discomfort, and one with altered bowel habits.

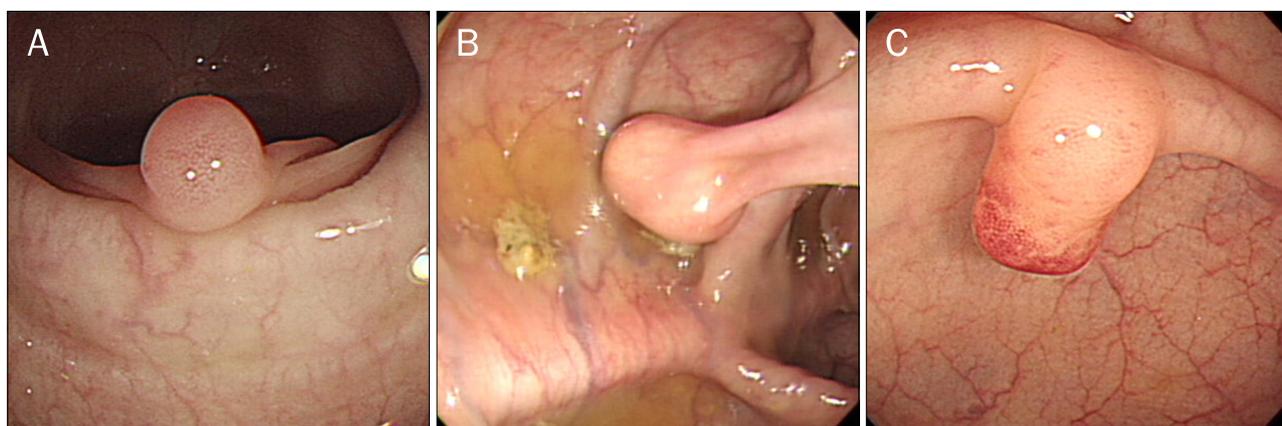
### 2. Clinico-pathologic findings and outcome of endoscopic removal

During colonoscopy, most leiomyomas (n=17, 77.3%) appeared as a glistening, smooth and round sessile polyp (Fig. 1). There were only five pedunculated leiomyomas. Endoscopic diagnoses based on morphologic characteristics were 10 lesions that were leiomyomas, eight adenomatous polyps, two hyperplastic polyps, and two submucosal lipomas. The mean size was 5.82 mm (median, 5 mm; range, 3-13 mm). The lesions were located predominantly in the left colon: two in the rectum, four in the rectosigmoid, six in the sigmoid, four in the descending colon, one in the splenic flexure, two in the transverse colon and three in the ascending colon. Among 22 cases, 10 lesions less than 5 mm were removed using cold biopsy forceps. Twelve cases were resected by conventional poly-

**Table 1.** Patient Demographics and Colonoscopic Findings

Case	Age (yr)	Sex	Location	Morphology	Size (mm)	Indication	Treatment	Other findings	Follow-up (mo)
1	34	M	DC	Sessile	4	Screening	Cold biopsy	None	NED (51)
2	53	M	Rectosigmoid	Sessile	3	Screening	Cold biopsy	None	NED (47)
3	43	M	TC	Sessile	3	Screening	Cold biopsy	None	NED (36)
4	60	M	AC	Pedunculated	13	Screening	EMR	None	NED (45)
5	50	M	Rectosigmoid	Sessile	6	Screening	EMR	2 hyperplastic polyps	NED (40)
6	66	F	TC	Sessile	7	Diarrhea	EMR	None	NED (38)
7	67	M	SC	Sessile	5	Abdominal discomfort	EMR	None	NED (37)
8	49	M	Rectosigmoid	Sessile	4	Screening	Cold biopsy	1 hyperplastic polyp	NA
9	50	F	SC	Sessile	6	Screening	EMR	None	NED (32)
10	62	M	SC	Sessile	8	Screening	EMR	1 adenoma	NED (27)
11	77	F	AC	Sessile	3	Diarrhea	Cold biopsy	3 adenomas; 3 hyperplastic polyps	NED (26)
12	41	M	Rectum	Sessile	3	Screening	Cold biopsy	1 hyperplastic polyp	NED (26)
13	49	M	SC	Sessile	8	Screening	EMR	None	NED (23)
14	60	M	DC	Pedunculated	7	Screening	EMR	2 adenomas	NA
15	66	M	Splenic flexure	Pedunculated	12	Rectal bleeding	EMR	2 adenomas; 1 adenocarcinoma, moderately differentiated	NED (20)
16	82	F	Rectosigmoid	Sessile	3	Altered bowel habits	Cold biopsy	1 adenoma	NA
17	44	M	DC	Pedunculated	7	Screening	EMR	1 adenoma; 1 hyperplastic polyp	NED (19)
18	55	M	SC	Sessile	4	Screening	Cold biopsy	None	NED (17)
19	36	M	SC	Pedunculated	9	Rectal bleeding	EMR	2 adenomas; 1 hyperplastic polyp	NED (15)
20	40	M	AC	Sessile	4	Screening	Cold biopsy	None	NED (15)
21	75	M	DC	Sessile	4	Screening	Cold biopsy	1 adenoma; 1 adenocarcinoma, well differentiated	NED (14)
22	74	M	Rectum	Sessile	5	Screening	EMR	1 adenoma	NED (14)

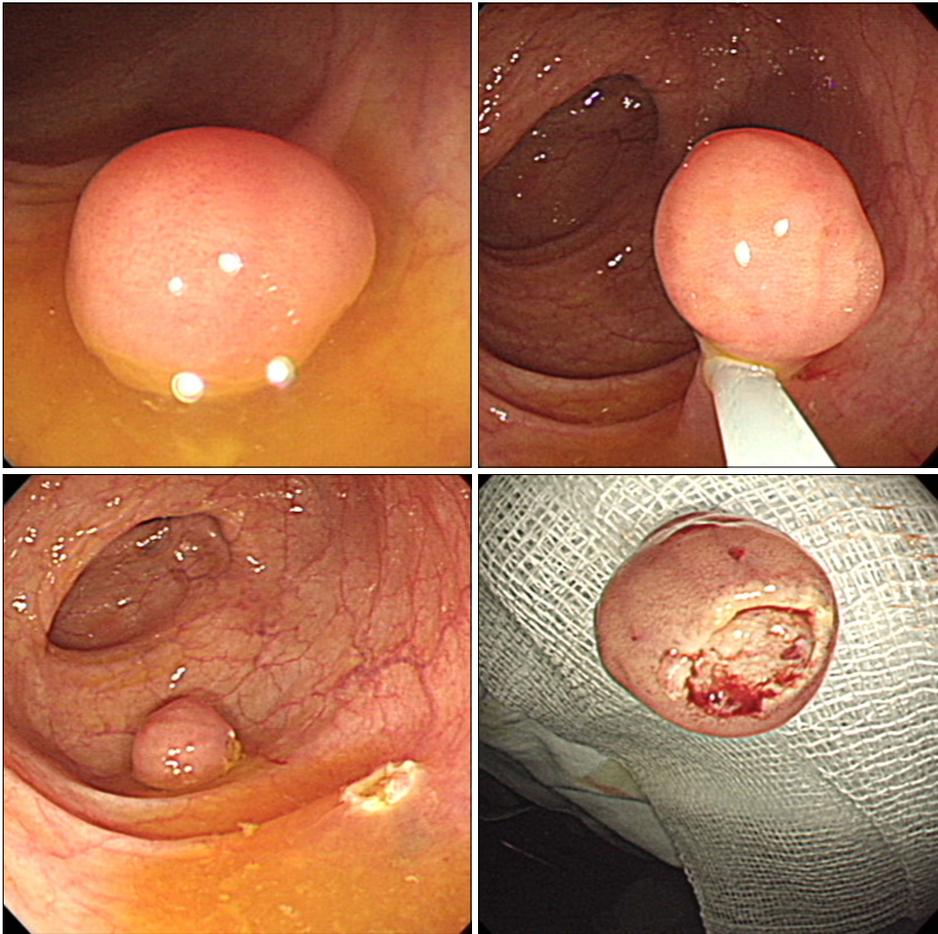
M, male; F, female; DC, descending colon; TC, transverse colon; AC, ascending colon; SC, sigmoid colon; EMR, endoscopic mucosal resection; NED, no evidence of disease; NA, not available.



**Fig. 1.** Colonoscopic findings of polypoid leiomyomas. A typical leiomyoma (approximately 5-mm) presenting as smooth round sessile polyp (A), a 13-mm leiomyoma presenting as pedunculated polyp (B), and a 7-mm leiomyoma resembling a hyperplastic polyp (C).

pectomy or EMR (Fig. 2). Conventional polypectomy or EMR was performed successfully in all 12 patients during a single session. No complications, including perforation and bleeding developed during or after the procedure. With EMR, histologic complete resection was achieved. All tumors were covered by intact colonic mucosa, and mitoses or cellular atypia were not present. Representative histologic section and im-

munohistochemical staining of polypoid leiomyoma were shown in Fig. 3. One advanced colon adenocarcinoma was detected in rectosigmoid region in a patient with leiomyoma in the splenic flexure, which was treated surgically. One intramucosal cancer was found in the rectum of in a patient with leiomyoma in the descending colon, which was treated by EMR. Among 22 patients, 19 underwent at least one later co-



**Fig. 2.** A 12-mm pedunculated leiomyoma removed by endoscopic mucosal resection.

lonoscopy after complete resection of the lesions. The median duration from the procedure to last recorded encounter was 28.5 months (range, 14-51 months). No local remnant lesions were found at the final follow-up examination in 19 patients. Among these patients, 15 have active charts and recent visits at the time of writing, and four with no signs of recurrence have not requested further exams or visits.

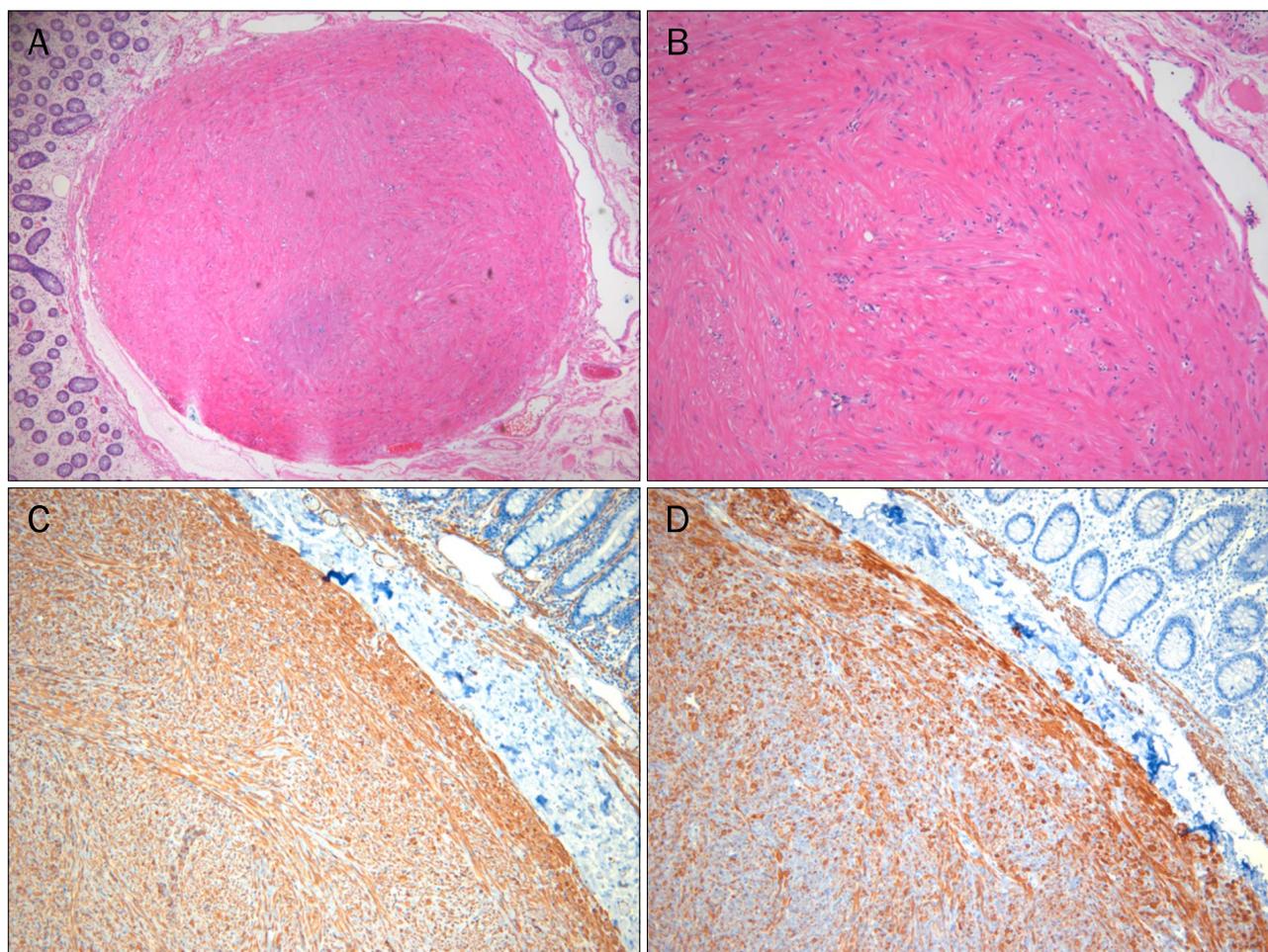
## DISCUSSION

Most GI mesenchymal tumors, previously classified uniformly as smooth muscle tumors, are currently classified GI stromal tumors (GISTs) on the basis of molecular and immunohistochemical characteristics.<sup>15</sup> Typically, leiomyomas are more common in the esophagus, but have occasionally been found in the colon and rectum.<sup>1,16</sup> In the present study, leiomyomas arising from the colon and rectum account for 0.8% of all colon polyps. However, the prevalence may be overestimated because we calculated the prevalence only in

patients who underwent polypectomy.

In a large series involving two referral centers in the United States and Finland over a 29 year study period, Miettinen et al.<sup>17</sup> showed that 88 (16.9%) out of 522 mesenchymal tumors from the colon and rectum were leiomyomas arising from the muscularis mucosae. However, this could be affected by referral bias due to uneven representation of GISTs between two participating centers. Agaimy and Wunsch<sup>14</sup> found 85 (32.4%) true smooth muscle tumors among 262 GI mesenchymal tumors during a 12-year period. In this study, smooth muscle tumors were subclassified into polypoid and intramural tumors based on gross findings and origin (either the muscularis mucosae or proper muscle). Polypoid leiomyomas were the most common smooth muscle tumor (78%, five esophageal and 67 colonic and rectal).

In the present study, there were 22 patients with polypoid leiomyomas of the colon and rectum during a three year period. Polypoid leiomyoma was significantly male predominant (4.5:1), which is higher than findings from Western



**Fig. 3.** Histologic findings (H&E) showing well-circumscribed nodule arising from the muscularis mucosae (A,  $\times 40$ ) composed of well-differentiated smooth muscle cells (B,  $\times 100$ ). On immunohistochemistry, the tumor is positive for smooth muscle actin (C,  $\times 100$ ) and desmin (D,  $\times 100$ ).

studies. Previous studies report somatic deletions in *COL4A5* and *COL4A6* genes, which encode the  $\alpha 5$  and  $\alpha 6$  chain of type IV collagen located in the X-chromosome of both familial and sporadic esophageal leiomyomas.<sup>18,19</sup> These findings may explain the male predominance of leiomyomas, because any deletions involving X-chromosomes are homozygous.<sup>17</sup> Our results showed that non-esophageal polypoid leiomyomas involve mainly rectum and sigmoid colon. This is consistent with a Western study.<sup>14</sup>

In this study, most polypoid leiomyomas were small asymptomatic lesions ( $< 1$  cm), and were detected incidentally during screening colonoscopy, similar to previous reports. Although a small proportion of patients with leiomyoma had symptoms including abdominal discomfort, altered bowel habits, diarrhea, and rectal bleeding, these symptoms are not likely to be lesion-related considering their small size

and location. Leiomyomas larger than 2 cm may cause symptoms such as abdominal pain, constipation, obstruction, anemia or bleeding.<sup>4,11-13</sup> Rarely, small leiomyomas less than 1 cm were reported to cause iron deficiency anemia, which was corrected after endoscopic resection.<sup>10</sup>

Most polypoid leiomyomas of the colon and rectum presented endoscopically as small sessile polyps, with the exception of five pedunculated polyps. Although leiomyomas usually appear as a glistening, smooth, round sessile polyp on colonoscopy, they are occasionally indistinguishable from hyperplastic or adenomatous polyps. Some reports noted that small mucosal lesions, grossly identical to hyperplastic or adenomatous polyps, were diagnosed as leiomyomas following endoscopic resection.<sup>5-8</sup> Leiomyomas originating from the muscularis mucosae are smaller than, and morphologically distinct from, submucosal tumors. In the present

study, polypoid leiomyomas were discovered incidentally during colonoscopy. The lesions were small and had no erosions, ulcers, or yellowish tint. They were clinically diagnosed as adenomatous polyp, and polypectomies were performed.

The diagnosis rate of colorectal leiomyoma has increased with mounting experience of colonoscopy. The accuracy rate of endoscopic diagnosis for leiomyomas based on their morphologic characteristics was 45.5% (10 out of 22 lesions). EUS is helpful in determining therapeutic strategies of GI submucosal tumors, because it can provide valuable information regarding the size, consistency, extension of lesions.<sup>20</sup> However, in our patients, EUS was not performed because most lesions were not considered submucosal tumors. In addition, leiomyoma cannot be easily distinguished from leiomyosarcoma even with EUS.<sup>5</sup> When lesions are larger than 5 cm, surgery is required because of the potential for malignancy.<sup>21</sup>

Histologically, polypoid leiomyomas arising from or limited to the muscularis mucosae are well-circumscribed nodules composed of well-differentiated smooth muscle cells.<sup>22</sup> Immunohistochemically, leiomyomas are positive for  $\alpha$ -smooth muscle actin, muscle specific actin, and desmin, but negative for CD34, CD117 or S100 protein.<sup>23</sup> In this study, no leiomyomas of the muscularis mucosae had the significant atypia that is usually seen in other leiomyomas, such as those of the uterus. Given these results, the possibility of tumor recurrence is likely to be low even with conservative endoscopic resection. Although we cannot rule out the possibility that colorectal leiomyomas of the muscularis mucosae progress to leiomyosarcomas, there is no evidence of malignant transformation.<sup>14,17</sup>

For GI submucosal tumors, complete surgical resection is still considered the most definitive treatment. However, the choice of treatment for colonic submucosal tumors is controversial. To our knowledge, this study is the first endoscopic case series. Our results suggest that polypoid leiomyomas originating from the muscularis mucosae less than 2 cm can be successfully treated with endoscopic resection. Also, lesions less than 5 mm can be removed using cold biopsy forceps without tumor recurrence, similar to adenomatous polyps. When the lesions present as apparent submucosal tumors, EUS should be considered before endoscopic polypectomy. However, surgical resection is recommended in tumors with suspected malignancy. Lee et al.<sup>12</sup> reported that intraluminal colonic leiomyoma as large as 4.5 cm was

successfully resected with skillful colonoscopy manipulation. However, conventional polypectomy or EMR carries higher risk of perforation in tumors with wide-based or extraluminal growth. For such lesions, surgical treatment is mandatory. Emerging evidence indicates that iatrogenic colonic perforation can be managed endoscopically with endoclips, stents, and endoscopic suturing devices,<sup>24,25</sup> but surgery is required in patients with endoscopic closure failure or delayed recognition of perforation.

Although it was easy to evaluate the lesions based on the pathology, this study is limited by its retrospective design and small patient numbers. Colonoscopy might not suffice to evaluate the recurrence of tumor or presence of residual tissue after removal because repeat biopsy was not performed in all patients, and the results cannot be considered representative of all patients with leiomyomatous polyp. A large randomized trial with long term patient surveillance is necessary.

In conclusion, this study suggests that small colorectal polypoid leiomyomas can be treated successfully by endoscopic removal. Endoscopic removal should be considered the potential for malignancy and postpolypectomy complications in patients with leiomyomas. Awareness of the endoscopic and clinicopathological characteristics may provide a safe treatment strategy for colonic leiomyomatous tumors of similar size in capable hands.

## REFERENCES

1. Miettinen M, Furlong M, Sarlomo-Rikala M, Burke A, Sobin LH, Lasota J. Gastrointestinal stromal tumors, intramural leiomyomas, and leiomyosarcomas in the rectum and anus: a clinicopathologic, immunohistochemical, and molecular genetic study of 144 cases. *Am J Surg Pathol* 2001;25:1121-1133.
2. Björnsdóttir H, Björnsson J, Gudjónsson H. Leiomyomatous colonic polyp. *Dig Dis Sci* 1993;38:1945-1947.
3. David SS, Samuel JJ. Pedunculated extraluminal leiomyoma of the sigmoid colon. *J Gastroenterol Hepatol* 1996;11:299-300.
4. Kadakia SC, Kadakia AS, Seargent K. Endoscopic removal of colonic leiomyoma. *J Clin Gastroenterol* 1992;15:59-62.
5. Chow WH, Kwan WK, Ng WF. Endoscopic removal of leiomyoma of the colon. *Hong Kong Med J* 1997;3:325-327.
6. Jovanovic I, Cvejic T, Popović D, Micev M. Endoscopic removal of pedunculated leiomyoma of the sigmoid colon (case report and literature review of diagnostic and treatment options). *Acta Chir Iugosl* 2006;53:87-89.
7. Hirasaki S, Suwaki K, Tada S, Goji T. Pedunculated leiomyomatous polyp (pedunculated leiomyoma) of the transverse colon.

- Intern Med 2010;49:2519-2520.
8. Kemp CD, Arnold CA, Torbenson MS, Stein EM. An unusual polyp: a pedunculated leiomyoma of the sigmoid colon. *Endoscopy* 2011;43 Suppl 2 UCTN:E306-E307.
  9. Han DH, Cheon YK, Cho JY, et al. Pedunculated leiomyoma. *Gastrointest Endosc* 2005;61:429.
  10. Urgesi R, Pastorelli A, Zampaletta C, et al. Obscure-occult bleeding: resolution of unexplained chronic sideropenic anaemia by colonoscopic removal of a colonic leiomyoma. *BMJ Case Rep* 2011. doi: 10.1136/bcr.11.2009.2455.
  11. Ishiguro A, Uno Y, Ishiguro Y, Munakata A. Endoscopic removal of rectal leiomyoma: case report. *Gastrointest Endosc* 1999;50: 433-436.
  12. Lee IL, Tung SY, Lee KF, Chiu CT, Wu CS. Endoscopic resection of a large colonic leiomyoma. *Chang Gung Med J* 2002;25:39-44.
  13. Friedman CJ, Cunningham WN, Sperling MH. Colonoscopic removal of a colonic leiomyoma: report of a case. *Gastrointest Endosc* 1979;25:107-108.
  14. Agaimy A, Wünsch PH. True smooth muscle neoplasms of the gastrointestinal tract: morphological spectrum and classification in a series of 85 cases from a single institute. *Langenbecks Arch Surg* 2007;392:75-81.
  15. Rubin BP, Fletcher JA, Fletcher CD. Molecular insights into the histogenesis and pathogenesis of gastrointestinal stromal tumors. *Int J Surg Pathol* 2000;8:5-10.
  16. Miettinen M, Sarlomo-Rikala M, Sobin LH, Lasota J. Esophageal stromal tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 17 cases and comparison with esophageal leiomyomas and leiomyosarcomas. *Am J Surg Pathol* 2000;24:211-222.
  17. Miettinen M, Sarlomo-Rikala M, Sobin LH. Mesenchymal tumors of muscularis mucosae of colon and rectum are benign leiomyomas that should be separated from gastrointestinal stromal tumors—a clinicopathologic and immunohistochemical study of eighty-eight cases. *Mod Pathol* 2001;14:950-956.
  18. Heidet L, Boye E, Cai Y, et al. Somatic deletion of the 5' ends of both the COL4A5 and COL4A6 genes in a sporadic leiomyoma of the esophagus. *Am J Pathol* 1998;152:673-678.
  19. Ueki Y, Naito I, Oohashi T, et al. Topoisomerase I and II consensus sequences in a 17-kb deletion junction of the COL4A5 and COL4A6 genes and immunohistochemical analysis of esophageal leiomyomatosis associated with Alport syndrome. *Am J Hum Genet* 1998;62:253-261.
  20. Waxman I, Saitoh Y, Raju GS, et al. High-frequency probe EUS-assisted endoscopic mucosal resection: a therapeutic strategy for submucosal tumors of the GI tract. *Gastrointest Endosc* 2002; 55:44-49.
  21. Kusminsky RE, Bailey W. Leiomyomas of the rectum and anal canal: report of six cases and review of the literature. *Dis Colon Rectum* 1977;20:580-599.
  22. Mansoor S, Dolkar T, El-Fanek H. Polyps and polypoid lesions of the colon. *Int J Surg Pathol* 2013;21:215-223.
  23. Matsukuma S, Takeo H, Ohara I, Sakai Y. Endoscopically resected colorectal leiomyomas often containing eosinophilic globules. *Histopathology* 2004;45:302-303.
  24. Velchuru VR, Zawadzki M, Levin AL, et al. Endoclip closure of a large colonic perforation following colonoscopic leiomyoma excision. *JSL* 2013;17:152-155.
  25. Baron TH, Wong Kee Song LM, Zielinski MD, et al. A comprehensive approach to the management of acute endoscopic perforations (with videos). *Gastrointest Endosc* 2012;76:838-859.