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ORIGINAL ARTICLE

Retrospective Study

Endoscopic resection of colorectal granular cell tumors

Iri Take, Qiang Shi, Zhi-Peng Qi, Shi-Lun Cai, Li-Qing Yao, Ping-Hong Zhou, Yun-Shi Zhong

Iri Take, Qiang Shi, Zhi-Peng Qi, Shi-Lun Cai, Li-Qing Yao, Ping-Hong Zhou, Yun-Shi Zhong, Endoscopy Center, Zhongshan Hospital of Fudan University, Shanghai 200032, China

Iri Take, Qiang Shi, Zhi-Peng Qi, Shi-Lun Cai, Li-Qing Yao, Ping-Hong Zhou, Yun-Shi Zhong, Endoscopy Research Institute of Fudan University, Shanghai 200032, China

Author contributions: Take I, Shi Q and Qi ZP contributed equally to this work; Take I and Qi ZP collected the data; Take I analyzed and drafted the manuscript; Shi Q designed and supervised the study; Cai SL, Zhou PH and Yao LQ revised the manuscript for important intellectual content; Yao LQ, Zhou PH and Zhong YS provided administrative support; all authors have read and approved the final version to be published.

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Correspondence to: Yun-Shi Zhong, MD, PhD, Endoscopy Center, Zhongshan Hospital of Fudan University, No 180 Fenglin Road, Shanghai 200032, China. zhongamy2002@126.com
Telephone: +86-13564623481
Fax: +86-21-64041990

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Abstract

AIM: To determine the feasibility and effectiveness of endoscopic resection for the treatment of colorectal granular cell tumors (GCTs).

METHODS: This was a retrospective study performed at a single institution. From January 2008 to April 2015, we examined a total of 11 lesions in 11 patients who were treated by an endoscopic procedure for colorectal GCTs in the Endoscopy Center, Zhongshan Hospital of Fudan University, Shanghai, China. Either endoscopic mucosal resection or endoscopic submucosal dissection (ESD) was performed by three surgeons with expertise in endoscopic treatment. The pre- and post-operative condition and follow-up of these patients were evaluated by colonoscopy and endoscopic ultrasonography (EUS).

RESULTS: Of these 11 lesions, 2 were located in the cecum, 3 were in the ileocecal junction, 5 were in the ascending colon, and 1 was in the rectum. The median maximum diameter of the tumors was 0.81 cm (range 0.4-1.2 cm). The *en bloc* rate was 100%, and the complete resection rate was 90.9% (10/11). Post-operative pathology in one patient showed a tumor

at the cauterization margin. However, during ESD, this lesion was removed *en bloc*, and no tumor tissue was seen in the wound. No perforations or delayed perforations were observed and emergency surgery was not required for complications. All patients were followed up to May 2015, and none had recurrence, metastasis, or complaints of discomfort.

CONCLUSION: Endoscopic treatment performed by endoscopists with sufficient experience appears to be feasible and effective for colorectal GCTs.

Key words: Endoscopic submucosal dissection; Granular cell tumors; Endoscopic mucosal resection; Colorectal

Core tip: Granular cell tumors (GCTs) are asymptomatic and are potentially malignant, which can pose a significant diagnostic and therapeutic challenge for endoscopists. The development of endoscopic techniques has had a marked influence on the diagnosis and treatment of colorectal submucosal tumors. We determined the feasibility and effectiveness of endoscopic resection for the treatment of colorectal GCTs. We conclude that endoscopic resection is safe and effective for treating colorectal GCTs, which allows *en bloc* resection in one visit, with a clear histological diagnosis, provides patients with a greater degree of comfort and leads to a better compliance.

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INTRODUCTION

Granular cell tumor (GCT) is an uncommon, potentially malignant, asymptomatic mesenchymal tumor arising from Schwann cells[1,2]. In the gastrointestinal tract, GCTs often appear as a round, yellowish submucosal nodule covered by normal mucosa during endoscopy[3-5]. The development of endoscopic techniques and immunohistochemical analysis has had a marked influence on the diagnosis and treatment of gastrointestinal tract submucosal tumors (SMT)[6-9]. Recently, there have been many reports on upper gastrointestinal GCTs[3,9-11]; however, there are few studies on colorectal GCTs. The present study was conducted to evaluate the feasibility and effectiveness of endoscopic resection for the treatment of colorectal GCTs.

MATERIALS AND METHODS

Patient information

During a 7-year period between January 1, 2008 and April 30, 2015, a total of 531 colorectal SMTs were treated at the Endoscopy Center of Zhongshan Hospital of Fudan University, Shanghai, China. A computer search of the SMT pathology files was carried out to determine GCTs arising in the colon, and 11 cases were identified. Patient demographics, pathological data and surgery reports were obtained for all cases (Table 1). All the GCTs were discovered incidentally during endoscopy performed as a screening examination or for unrelated indications. All patients were informed about the option of endoscopic surgery and provided written informed consent.

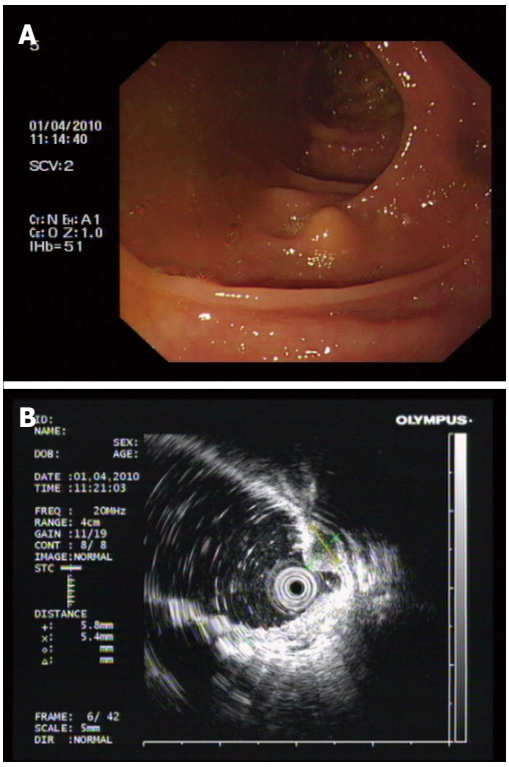

Figure 1 Preoperative examination. A: A 0.8 cm submucosal lesion was observed 60 cm from the anal verge (ascending colon). The mass was sessile, the mucosal surface was smooth, with non-necrotic erosion, and was non-circumferential. B: Ultrasonographic examination revealed a 0.5 cm hypoechoic submucosal lesion without muscularis propria involvement.

Preoperative management

Lesion size, location, color, and surface conditions, with or without ulceration were recorded. Endoscopic ultrasonography (EUS) (Figure 1) was performed to evaluate the depth and echo of the lesion. All patients were asked to finish bowel preparation according to established principles for colorectal surgery.

Endoscopic equipment and accessories

Standard single-accessory-channel endoscopy (GIT-H260; Olympus, Tokyo, Japan), and AQ100 (Aohua, Shanghai, China) were used during the procedures. A short, transparent cap (ND-201–11802; Olympus) was attached to the front of the endoscope to provide a constant endoscopic view and to apply

Table 1 Clinicopathologic features of 11 patients with colorectal granular cell tumors

Patient number	Gender	Age (yr)	Location	Maximum tumor size (cm)	Treatment methods	Length of stay (d)	*En bloc* resection	Margin	S-100
1	F	27	Cecum	1.0	EMR	0	Yes	Negative	+
2	F	33	Ascending colon	0.4	EMR	1	Yes	Negative	++
3	M	42	Ileocecal junction	0.6	EMR	0	Yes	Negative	+
4	M	47	Cecum	0.6	ESD	1	Yes	Negative	++
5	F	51	Ascending colon	0.6	EMR	0	Yes	Negative	+
6	M	49	Rectum	0.8	ESD	1	Yes	Negative	+
7	M	48	Ascending colon	0.7	ESD	2	Yes	Positive	+
8	F	37	Ascending colon	0.8	ESD	1	Yes	Negative	++
9	M	49	Ileocecal junction	1.0	ESD	0	Yes	Negative	++
10	F	45	Ileocecal junction	1.2	ESD	1	Yes	Negative	++
11	M	60	Ascending colon	1.2	ESD	1	Yes	Negative	+++

M: Male; F: Female; EMR: Endoscopic mucosal resection; ESD: Endoscopic submucosal dissection.

tension to the connective tissues during dissection. An IT-knife and/or a hook-knife (KD-611 and KD-620LR; Olympus) was used to dissect the submucosal layer and to peel the tumor. The high-frequency generator used was the HybridKnife system (ERBE, Tuebingen, Germany). Other equipment included injection needles (NM-4L-1), snares (SD-230U-20), hot biopsy forceps (FD-410LR), and clips (HX-610–135) (all from Olympus).

Endoscopic resection

All procedures were performed under general anesthesia by three surgeons with expertise in endoscopic treatment (Zhou PH, Yao LQ and Zhong YS).

Endoscopic mucosal resection procedure

Endoscopic mucosal resection (EMR) procedures were performed in a standardized manner as follows: (1) Marking; marking dots were made approximately 5-10 mm from the lesion by argon plasma coagulation (APC); (2) Submucosal injection; several milliliters of solution (100 mL saline, 5 mL 0.8% indigo carmine, and 1 mL of epinephrine) were injected around the lesion using a 23-gauge disposable needle; (3) Snare resection; an endoloop was used to snare and ligate the lesion with the aid of suction, and then the lesion was completely resected; and (4) Closure; exposed vessels on the artificial ulcer were coagulated with APC or hot biopsy forceps to prevent delayed bleeding, and metallic clips were always used to close the deeply dissected areas.

Endoscopic submucosal dissection procedure

The following steps were used in this procedure (Figure 2): (1) Marking; (2) Submucosal injections were the same as for EMR; (3) Circumferential incision; we used an IT knife or a hook knife to cut the mucosa initially along the marked points; (4) Strip lesions; the submucosal connective tissue beneath the lesion was gradually dissected with the aid of the transparent cap; the above-mentioned solution was injected repeatedly during the dissection when necessary; direct dissection of the submucosal layer was carried out until complete removal was achieved; and (5) Closure was the same as for EMR.

Postoperative management and follow-up

Patients were allowed oral intake from the second day unless serious complications occurred. Antibiotics (second-generation cephalosporins, such as celaclor or cefuroxime) and hemocoagulase injections (ethamsylate or P-aminomethybenzoic acid) were routinely administered after the procedure.

Pathologic evaluation

Tissue specimens were fixed to a plastic foam plate using thin needles along their edges and were then fixed in formalin solution. Processing of the resected specimens and histopathological evaluations were performed after endoscopic resection by highly experienced pathologists. A resection with a tumor-free margin in which both the lateral and basal margins were free of tumor cells was considered a complete resection. A resection in which the tumor extended into the lateral or basal margin or in which the margins were indeterminate due to artificial burn effects was considered an incomplete resection and recommended for surgical intervention.

RESULTS

Of the 11 colorectal GCTs in 11 patients, 2 (18.2%) were located in the cecum, 3 (27.3%) were in the ileocecal junction, 5 (45.4%) were in the ascending colon, and 1 (9.1%) was in the rectum. The median maximum diameter of the tumors was 0.81 cm (range 0.4-1.2 cm).

All patients underwent endoscopic resection, including 4 cases of EMR and 7 cases of endoscopic submucosal dissection (ESD). Each lesion was removed by *en bloc* resection, which was defined as no tumor identified at the resection site by endoscopy. All lesions were submucosal without muscularis layer

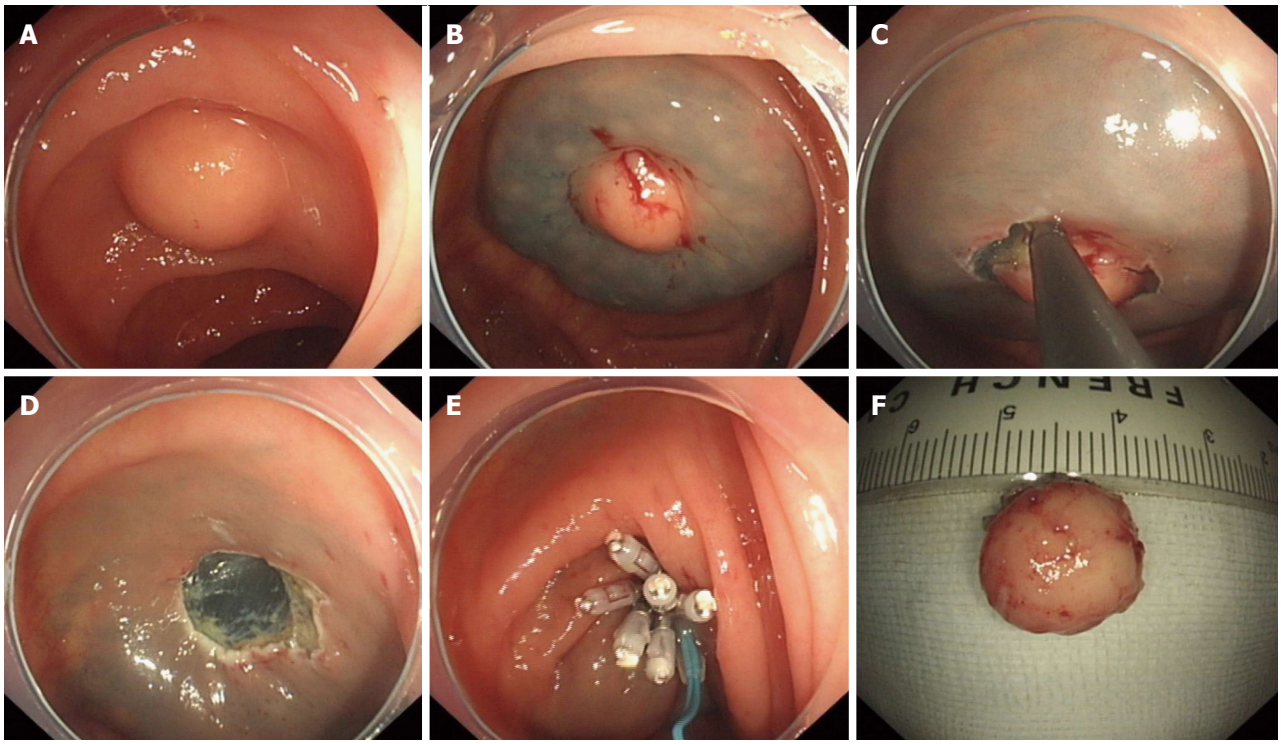

Figure 2 Endoscopic submucosal dissection procedure. A: A 1.0 cm × 1.2 cm hemispherical submucosal lesion which had a hard texture, fixed, smooth surface, was observed in the ileocecal junction; B: Saline solution with a small amount of epinephrine and indigo carmine was injected beneath the lesion, and resulted in good elevation; C: Complete dissection of the lesion after circumferential incision; D: The lesion was completely removed without any bleeding or perforation; E: Purse-string suture with metallic clips and endoloop; F: Dissected specimen was sent for pathologic examination.

invasion. There were 10 (90.9%) complete resections, which were defined as no granular cell tissue seen microscopically at the resection margin. Post-operative pathology of one lesion showed that the tumor was seen at the cauterization margin, indicating incomplete resection. However, during ESD, this lesion was removed *en bloc*, and no tumor tissue was seen in the wound. The patient refused surgery or any other additional treatment after a full discussion with his physician. There was no recurrence in this patient during close follow-up.

The procedures were successful, with no perforations, endoscopically uncontrolled bleeding, or any other severe adverse events requiring emergency surgery. The patients did not experience abdominal pain, abdominal distension, or any sign of peritonitis after endoscopic surgery. All samples were diagnosed as GCTs by hematoxylin and eosin (HE) staining and immunohistochemical (IHC) analysis (Figure 3).

One rectal GCT patient received a follow-up endoscopy one week after ESD. In the examination up to the rectum, wound healing was satisfactory, dry, and no bleeding was seen. In May 2015, all patients were followed up by telephone, and none complained of discomfort, including hematochezia or changed bowel habits. All 11 patients underwent complete colonoscopy up to the ileocecal junction annually after endoscopic treatment and no abnormalities were observed.

DISCUSSION

GCTs often occur in the tongue and the skin, and approximately 1%-8% of GCTs occur in the gastrointestinal tract[2,12], one-third of which occur in the esophagus[3,9,11]. Colorectal GCTs are even rarer. With improvements in endoscopy and IHC, there is the potential for an increase in the identification of GCTs in the gastrointestinal tract. Based on our experience, colorectal GCTs are found more frequently in the ileocecal junction and ascending colon. Of the 11 colorectal GCTs in the present study, 2 (18.2%) were located in the cecum, 3 (27.3%) were in the ileocecal junction, 5 (45.4%) were in the ascending colon, and 1 (9.1%) was in the rectum.

Most GCTs are asymptomatic and are clinically insignificant. However, 1%-3% of all GCTs have malignant potential[13,14], thus it is essential to distinguish them from other benign or malignant lesions. Malignant GCTs are often larger than 5 cm, have an unclear margin with the surrounding tissue, invade fat and/or muscle tissue, and are strongly positive for S-100 and neuron-specific enolase on IHC. Neither biopsies nor EUS can reliably distinguish benign GCTs from malignant GCTs; therefore, GCTs can pose a significant diagnostic and therapeutic challenge for endoscopists.

For asymptomatic and relatively small gastrointestinal SMTs, clinical follow-up is standard care.

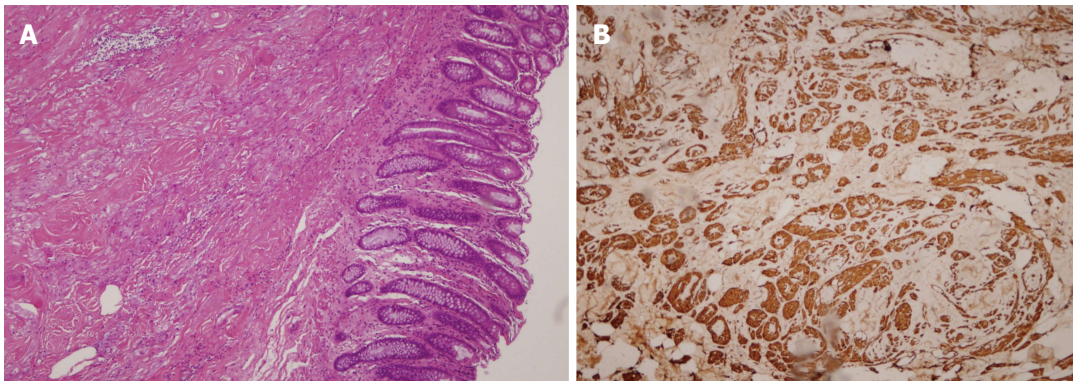

Figure 3 Pathologic findings. A: Infiltrative growth pattern of colorectal granular cell tumor (× 400); B: Tumor cells were strongly positive for cytoplasmic S-100 protein (+++) (× 400).

This usually requires patients to undergo multiple endoscopies, which often leads to noncompliance. Furthermore, histopathological diagnoses of SMTs are unobtainable unless the lesion is removed. Endoscopic resection has the advantage of being a minimally invasive technique, which typically results in a shorter operation time, minor post-operative pain, shorter hospital stay, and lower cost than traditional surgery[15,16]. EMR and ESD are both safe and effective for treating superficial gastrointestinal SMTs[17-19].

All our 11 colorectal GCTs evaluated were submucosal without muscularis layer involvement. In view of our results[17,18,20] and those in other studies[21,22], ESD and EMR are both suitable for GCTs less than 2 cm, as their complication rates and long-term outcomes are equivalent. In the present study, the lesions were approximately 1 cm; and the median maximum diameter of the tumors was 0.81 cm (range 0.4-1.2 cm). Eleven lesions were removed *en bloc* by both ESD and EMR, and the *en bloc* resection rate was 100%. Post-operative pathology showed a complete resection rate of 100% (4/4) for EMR, and 85.7% (6/7) for ESD. None of the patients in the two groups experienced bleeding, perforation, or disease progression. For lesions larger than 1 cm and/or closely related with the muscularis propria, we suggest performing ESD. During excavation, using the knife to dissect the submucosal connective tissue, the complete tumor capsule must be preserved and perforation avoided. Post-operative pathology showed a positive margin in only one patient; however, ESD achieved *en bloc* resection, and no tumor tissue was seen in the wound. The patient refused surgery after a full discussion with his physician. No recurrence was observed in this patient during close follow-up.

The main complication of endoscopic treatment for colorectal SMTs is perforation; this is also the bottleneck which limits endoscopic treatment of colorectal SMTs. With the widespread use of endoscopic full-thickness resection for gastric SMTs and improvements in suturing techniques[7,8,17], colorectal defect repair skills have also significantly improved. Common endoscopic suture methods suitable for colorectal defect repair include: (1) clipping; (2) clipping then strengthening with the endoloop; (3) purse-string suture with metallic clips and endoloop; and (4) interrupted suture with endoloop and metallic clips[23]. Furthermore, we have reported the submucosal tunneling endoscopic resection for the treatment of rectal SMTs[7], which solves the problem of difficulties in complete closure using the endoscopic suture technique. By mastering such techniques, breaking through the bottleneck can lead to expanded indications for endoscopic treatment, and the successful treatment of colorectal SMTs using minimally invasive endoscopic techniques.

Endoscopic resection is a safe, feasible and effective treatment for colorectal GCTs, allows *en bloc* resection in one visit, and a clear histological diagnosis.

In conclusion, endoscopic treatment performed by endoscopists with sufficient experience appears to be feasible and effective for colorectal GCTs.

COMMENTS

Background

Colorectal granular cell tumors (GCTs) are often asymptomatic and potentially malignant. As the tumor grows, patients present with different symptoms depending on the tumor location and size. Diagnosis and management of colorectal GCTs remain challenging.

Research frontiers

Due to the rarity of these tumors, few studies have focused on colorectal GCTs. Therefore, this study described the authors' experience in the diagnosis and surgical treatment of patients with colorectal GCTs.

Innovations and breakthroughs

Based on this study, the use of endoscopy, endoscopic ultrasonography and immunohistochemistry are effective means of diagnosing colorectal GCTs. The authors focused on the treatment of colorectal GCTs by endoscopic resection, which proved to be a feasible and effective treatment.

Applications

Endoscopic resection is a feasible and effective treatment for colorectal GCTs. Future randomized controlled trials comparing endoscopic resection and surgery are needed to address quality of life issues.

Terminology

Endoscopic submucosal dissection and endoscopic mucosal resection are two treatment modalities used for gastrointestinal submucosal tumors.

Peer-review

Early detection and simultaneous removal of colorectal granular cell tumors with endoscopy are safe and effective which provide patients with a greater degree of comfort and lead to a better compliance.

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