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Management of Symptomatic Hamartomatous Polyps in Stomach: Analysis of a Single Center Experience

Jung-Chun Lin[1,2], Tien-Yu Huang[1,2], Yu-Lueng Shih[1,2], Yi-Ming Chang[3], Heng-Cheng Chu[1,2], Wei-Kuo Chang[1,2], Tsai-Yuan Hsieh[1,2], and Peng-Jen Chen[2*]

[1]Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei;
[2]Division of Gastroenterology, Department of Internal Medicine;
[3]Department of Pathology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, Republic of China

Background: No consensus has been reached on the management of gastric hamartomatous polyps, owing to a lack of knowledge of the long-term outcome of after removal of these polyps. **Methods:** A retrospective database review was performed in a tertiary referral hospital between 1995 and 2011. Thirty-two consecutive patients who were diagnosed with gastric hamartomatous polyps were managed by surgical or endoscopic resection. **Results:** Patients developed the disease predominantly in their seventh and eighth decades of life. The tumors were located mostly in the antrum, and the diameter ranged from 5 to 52 mm. In one patient, adenocarcinoma in situ accompanied by gastric hamartomatous polyp was diagnosed by pathologic examination after endoscopic mucosal resection (EMR).There were no significant differences in the rates of technical success, treatment success, complications, or recurrence between surgery and endoscopic excision. The endoscopic excision group had a shorter mean post procedure hospital stay than the surgery group (7.2 vs. 21.4 days, P = 0.002). **Conclusions:** Endoscoipic resection for gastric hamartomatous polyps is an effective procedure and a less-invasive alternative to surgery.

Key words: endoscopic resection, gastric polyp, hamartomatous polyp

INTRODUCTION

Gastric hamartomatous polyps are characterized pathologically as hyperplastic glands lined by foveolar-type epithelia and separated by branching cores of smooth muscle, with atrophy of the deep glandular components.[1-3] Gastric hamartomatous polyps are also called “hamartomatous inverted polyps” in the Japanese literature and “solitary polypoid hamartoma” of the oxyntic mucosa in western countries.[1,2,4-12] Previous reports described gastric hamartomatous polyps based on clinical, endoscopic, radiological and pathologic criteria, and divided them into obstructive[5,8,9,12,13] and hemorrhagic[11] categories. Gastric hamartomatous polyps are difficult to diagnose because the tumor can be inverted into the submucosal layer.[1] Long-term follow-up data on these patients are scanty. Gastric hamartomatous polyps have been reported as paracancerous lesions and are possibly related to gastric cancer.[2,14] Surgical resection is the traditional choice of treatment.[1,12,14] However, two case reports stated that gastric hamartomatous polyps could be treated by endoscopic resection.[2,4] To our knowledge, no prior research has compared the clinical outcomes of endoscopic resection with those of surgical excision in the treatment of gastric hamartomatous polyps. In this study, a series of patients with gastric hamartomatous polyps were reviewed, and their treatment and the long-term outcomes are described.

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*Corresponding author: Peng-Jen Chen, Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, No. 325, Sec 2, Cheng-Gong Road, Taipei 114, Taiwan, Republic of China. Tel: +886-2-87927409; Fax: +886-2-87927139; E-mail: doc12983@gmail.com; endoscopy@ndmctsgh.edu.tw

METHODS

This study retrospectively reviewed patients who were diagnosed with gastric hamartomatous polyps at Tri-Service General Hospital, a medical teaching hospital belonging to the National Defense Medical Center in Taipei, Taiwan, from January 1995 to December 2011. The patients received endoscopy because of their presenting symptoms of gastrointestinal hemorrhage and obstruc-

tion. Endoscopically, only 3 patients could be diagnosed by a forceps biopsy. Other specimens were obtained by endoscopic or surgical excision. The following three inclusion criteria were used to exclude ambiguous cases that might have potentially indicated Peutz-Jeghers syndrome or Cowden's syndrome: 1) availability of complete medical records, a description of clinical presentation, patient information and laboratory values; 2) availability of histological specimens for review; and 3) no family history of polyps in the gastrointestinal tract and a physical examination that did not reveal any mucocutaneous melanin pigmentation. The histological features of the gastric hamartomatous polyps were determined from the original microscopic slides. Diagnosis was confirmed by smooth muscle proliferation, glandular hyperplasia and cystic dilatation in the pathological examination.

Technical success was defined as the ability to remove polyps through either surgical or endoscopic methods. Treatment success was defined as symptomatic relief as shown by complete removal of the polyps on follow-up at 6 weeks. Recurrence was defined as reappearance of polyps after the procedure.

Endoscopic Procedure

Conventional Polypectomy (CP).

Fifteen patients were treated by CP. Neither suction nor a submucosal saline solution injection was performed before snare resection.

Endoscopic mucosal resection (EMR)

EMR was performed through a single-channel endoscope (GIF-240 or GIF-Q260, Olympus Optical Co. Ltd, Tokyo, Japan). A mixture of saline and epinephrine was injected into the submucosal layer beneath the tumor to elevate the lesion,which thereby reduced the risk of perforation and decreased the involvement of the resection margin. Snare resection was performed with the use of a blended electrosurgical current.

Endoscopic submucosal dissection (ESD)

Since 2005, ESD has been usedat the Gastrointestinal Endoscopy Center, Tri-Service General Hospital, to treat gastric mucosal or submucosal tumors. All ESD procedures were performed by a single experienced endoscopist (P.J.C.). After March 2006, ESD methods were applied to manage large gastric hamartomatous polyp(s) (> 20 mm). The ESD procedure was similar to the method used for resecting early gastric cancer through the use of an insulated-tip knife (KD-610L, Olympus Optical Co.).[15-17] The device was a single-channel endoscope (GIF-Q260J, Olympus Optical Co.) with a hood and a high-frequency generator with an automatically-controlled system (VIO 200D; ERBE, Tübingen, Germany). Marking dots were made around the circumference of the lesion. Next, several milliliters of a solution, consisting of glycerol with a small amount of indigo carmine and epinephrine was injected into the submucosa around the lesion in order to lift it off the muscle layer. Thereafter, an incision into the mucosa outside the marking dots was performed to separate the lesion from the surrounding nonneoplastic mucosa. The submucosal connective tissue just beneath the lesion was then gradually dissected from the muscle layer by the insulated-tip knife.

Statistical analysis

Comparison of continuous variables between two groups was performed using Student's t test of independent samples for normally distributed variables and the Mann Whitney U test for non-normal distribution. Multiple groups were compared via analysis of variance. The chi-square test and Fisher’s exact test were used to compare discrete variables between groups. All statistical analysis was performed with SPSS 15.0 for Windows, and a P value < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

Table 1 shows the characteristics of the 32 patients with gastric hamartomatous polyp(s). All patients were diagnosed in adulthood, with a peak incidence in the seventh and eighth decades of life. They were categorized the gastrointestinal hemorrhage group and the obstruction group, according to their presenting symptoms. Upper gastrointestinal hemorrhage secondary to gastric hamartomatous polyps occurred in 16 cases; 14 patients presented with melena and two of them had acute profuse bleeding with either hematemesis or coffee-ground emesis. The majority of them (69%) had a hemoglobin value of < 11 g/dl, and 46% required transfusions. Five patients in this group presented with iron-deficiency anemia. Sixteen patients presented with symptoms of gastrointestinal obstruction. Approximately one-third of them had symptoms of abdominal pain in the epigastric region.

All patients underwent endoscopic or surgical resection during the 17-year study period. Seven patients from the surgery arm of the study were treated for polyps which were either actively or persistently hemorrhaging,

Table 1 Clinical Data from 32 Patients with Gastric Hamartomatous Polyp(s)

Case	*Age/ Gender*	*S/ S*	*Location*	*Polyp features*	*Polyp size (cm)*	*Ulceration*	*Disease*	*Treatment*	*Complica-tions*	*Recurrence*
1	38/M	B	L	without stalk	2.5	+	Cirrhosis, HCVD, Schizophrenia, DM, Biliary stone(s)	SR; EMR for recurrence	-	+
2	58/M	B	M	with stalk	3	+	BPH	CP	-	-
3	74/M	O	M	with stalk	3.5	+	HCVD, Lung cancer, Adrenal tumor, Rectal adenocarcinoma	EMR	-	-
4	65/F	O	L	with stalk	2.6	-	DM, HCVD, Dyslipidemia, CAD	ESD, EMR	-	-
5	57/F	O	L	with stalk	1	+	Cirrhosis, DM, HCVD	ESD	-	+
6	80/M	B	L	without stalk	1	+	CAD, Af, VHD, CRF	CP	-	-
7	43/M	B	L	without stalk	4	-	Dyslipidemia	STG with B-I anastomosis; ESD for recurrence	-	+
8	72/M	B	L	without stalk	0.5	+	Cirrhosis, DM, HCVD, GERD, CAD	CP	-	+
9	77/F	O	L	with stalk	2	-	Biliary stone(s), Status post cholecystectomy, DM, CAD	ESD	-	-
10	69/F	B	M	with stalk	1.5	-	Cirrhosis, HCC, DM, HCVD	SR	UTI	-
11	53/F	B	L	without stalk	2	+	CRF, Cirrhosis, HCVD	CP	-	Lost follow up
12	66/F	O	L	with stalk	1	-	HCVD	STG with B-II anastomosis	-	+
13	61/M	B	L	without stalk	2.8	+	Cirrhosis	CP	-	Lost follow up
14	77/F	B	L	with stalk	3	-	Osteoporosis, uterine myoma	CP	-	-
15	86/F	B	L	with stalk	1.7	-	HCVD, CAD, CHF, Old CVA, Dementia, VHD, COPD, CRF	SR	Postoperative death	Expired
16	69/F	O	L	without stalk	0.8	-	Biliary stone, Status post cholecystectomy, DM	SR	-	-
17	67/M	O	L	with stalk	3.5	-	HCVD, BPH, Hyperuricemia, Obstructive sleep apnea	CP	-	+
18	52/F	O	M	without stalk	1	+	PPU status post STG with B-II anastomosis	CP	-	-
19	75/F	B	L	without stalk	1.3	+	DM, HCVD, CRF, Old CVA, Dementia	CP	-	+
20	55/F	O	U	without stalk	1	+	HCVD	CP	-	-
21	74/M	B	L	with stalk	5	+	Old CVA, Dementia, BPH, HCVD	CP	-	-
22	66/M	B	W	with stalk	4	+	Arrhythmia	TG	Ventilator dependent chronic respiratory failure	TG
23	70/F	B	M	without stalk	2	-	HCVD, CAD, Obesity, Fatty liver	CP	-	-
24	68/F	B	M	without stalk	4	+	Papillary carcinoma of thyroid, HCVD	EMR	Gastric perforation	-

25	74/M	O	L	with stalk	1.3	+	Biliary stone(s), Status post cholecystecomy, HCVD	CP	-	-
26	70/F	O	L	without stalk	5	+	DM, VHD, CHF, HCVD, CAD, CRF, Dyslipidemia	ESD	-	-
27	79/M	O	U	with stalk	1.5	+	DM, HCVD, Status post STG, Biliary stone(s)	EMR	-	-
28	68/M	O	L	without stalk	1.2	+	Adenocarcinoma of prostate	CP	-	-
29	66/M	B	M	with stalk	2	-	HCVD, DM	CP	Delayed bleeding	-
30	63/F	O	M	without stalk	5.2	+	HCVD, DM, CAD, Arrhythmia	ESD	-	-
31	50/F	O	U	with stalk	4	+	HCVD, Dyslipidemia, PSVT, VHD	EMR	-	-
32	70/M	O	W	with stalk	1	+	Uremia; HCVD; Hyperuricemia	EMR	-	-

Abbreviations and explanations:

S/S, symptoms/signs; M, male; F, female; B, bleeding; O, obstruction, L, lower one-third of the stomach; M, middle one-third; U, upper one-third; W, whole stomach; +, presence; -, absence; HCVD, hypertensive cardiovascular disease; DM, diabetes mellitus; BPH, benign prostate hyperplasia; CAD, coronary artery disease; Af, atrial fibrillation; VHD, valvular heart disease; CRF, chronic renal failure; GERD, gastroesophageal reflux disease; HCC, hepatocellular carcinoma; CHF, congestive heart failure; CVA, cerebrovascular accident; COPD, chronic obstructive pulmonary disease; PPU, perforated peptic ulcer; STG, subtotal gastrectomy; SR, surgical resection; EMR, endoscopic mucosal resection; CP, conventional polypectomy; ESD, endoscopic submucosal dissection; TG, total gastrectomy; UTI, urinary tract infection; PSVT, Paroxysmal Supraventricular Tachycardia

or appeared to be malignant. One of the 7 patients treated by surgery received a total gastrectomy while another was treated by subtotal gastrectomy. Laparotomy with surgical resection was performed on the remaining 5 patients. Fifteen patients were treated by CP. Ten patients underwent EMR or ESD.

Endoscopic and surgical findings

The locations of the gastric hamartomatous polyps were as follows: 47% (n = 15) in the antrum, 25% (n = 8) in the body, 6% (n = 2) in the angularis, 6% (n = 2) in both the body and antrum, 3% (n = 1) in both the body and fundus, 3% (n = 1) in the cardia, 3% (n = 1) in the fundus, and 6% (n = 2) in the whole stomach. Ulcerated polyps were found in 19 patients (59%). No significant correlation (P = 0.123) was found between the number of polyps and age. The gastric hamartomatous polyps displayed a pedunculated appearance in 53% (n = 17) of the patients and sessility in the remaining 47%. No significant (P = 0.077) correlation was found between the shape of the polyps and age; 7 (70%) of the 10 patients under 65 years old had no stalk, whereas 14 (64%) of the 22 patients age 65 or older had a stalk. The bleeding tendency of the polyp was associated with the number of polyps (P < 0.001) and a cirrhotic background (P = 0.013), rather than the size of the polyp (P = 0.940). Polyps had a median diameter of 20 mm with a range from 5 to 52 mm (Table 1).

Treatment and post procedure course

The seven patients undergoing surgical resection or gastrectomy were compared with the 25 patients who underwent endoscopic excision, including CP, EMR, and ESD. No significant differences in baseline characteristics were found between cohorts (Table 2). In one patient, adenocarcinoma in situ was diagnosed by pathologic examination after EMR. No malignancy was found in the other patients during this study. The clinical outcomes are shown in Table 3. There were three postsurgical complications. One patient (case 10) had a urinary tract infection, another (case 15) died 6 days after surgery owing to continued bleeding postoperatively and the third (case 22) had postoperative respiratory failure but survived. There were two postendoscopic complications. One patient (case 24) had a gastric perforation during EMR, which was treated successfully with the endoscopic omentum-patch method. Delayed bleeding occurred in Case 29 three days after endoscopic CP and this patient recovered after 5 days of conservative treatment with no oral intake, nasogastric feeding, and proton pump inhibitor therapy. There was a statistically significant difference between groups in the overall complication rates

Table 2 Patient Characteristics of Surgery versus Endoscopic Excision Groups

Characteristics	*Surgery (n = 7)*	*Endoscopic excision (n = 25)*	*P value*
Median age, year (range)	66 (38-86)	68 (50-80)	0.331
Men, n. (%)	3 (42.9%)	12 (48%)	0.817
Polyp size (mean±SD) mm	22.1±13.4	2.42±1.42	0.739
Site, n (%)			0.795
Fundus	0 (0%)	1 (4%)	
Cardia	0 (0%)	1 (4%)	
Body	1 (14.3%)	7 (28%)	
Angularis	1 (14.3%)	1 (4%)	
Antrum	4 (57.1%)	11 (44%)	
Whole stomach	1 (14.3%)	1 (4%)	
Body & antrum	0 (0%)	2 (8%)	
Body & fundus	0 (0%)	1 (4%)	
Underlying conditions, n (%)			
Cirrhosis	2 (28.6%)	4 (16%)	0.468
DM	3 (42.9%)	9 (36%)	0.750
HCVD	4 (57.1%)	18 (72%)	0.470
CAD	1 (14.3%)	7 (28%)	0.475
Chronic renal failure	1 (14.3%)	5 (20%)	0.742
Subtotal gastrectomy	0 (0%)	2 (8%)	0.456
Biliary stone	2 (28.6%)	4 (16%)	0.468
Number of polyps, n (%)			0.593
six polyps or more	3 (42.9%)	8 (32%)	
less than six polyps	4 (57.1%)	17 (68%)	
Tumor features (%)			0.576
With stalk	4 (57.1%)	13 (52%)	
Without stalk	3 (42.9%)	12 (48%)	
Hemoglobin (mean ± SD) g/dl	11.1 ± 3.0	10.8 ± 2.4	0.809

n, number; SD, standard deviation

Table 3 Outcomes of Surgical versus Endoscopic Excision

Clinical outcomes	*Surgery (n = 7)*	*Endoscopic excision (n = 25)*	*P value*
Technical success, n (%)	7 (100%)	23 (100%)	1.000
Treatment success, n (%)	6 (86%)	25 (100%)	1.000
Complications, n (%)	3 (43%)	2 (9%)	0.459
Mean length of stay, day (range)	21.4 (6-35)	6.8 (1-21)	< 0.001
Follow-up			
Median month (range)	85 (23-213)†	50 (8-180)‡	0.044
Recurrence	3 (60%)†	4 (17%)‡	0.046

†One patient was expired during the post-operative period and one patient underwent total gastrectomy.

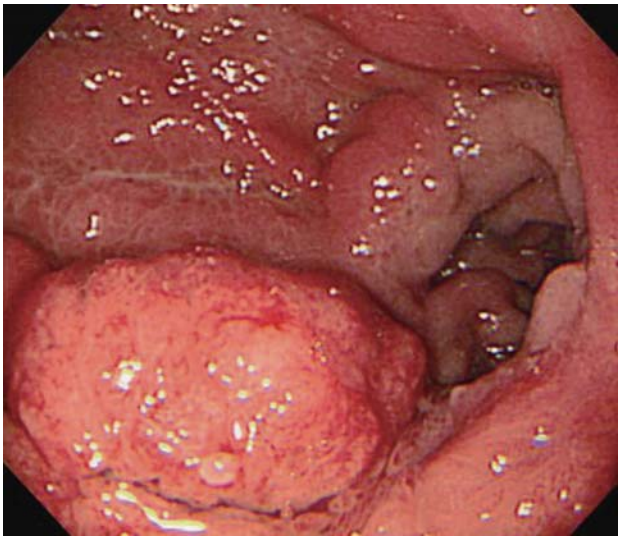

Fig. 1 Upper gastrointestinal endoscopy reveals a recurrent polyp (45 mm) at the anastomotic site.

(surgery group 43% vs. endoscopic excision group 8.7%, P = 0.034). The mean length of hospital stay was longer for patients with than those without gastrointestinal hemorrhage (13.8±10.8 vs. 7.4±5.5 days; P = 0.022; range 1 to 35 vs. 1 to 16 days). The mean length of the post-procedure hospital stay was significantly shorter in the endoscopic excision cohort than the surgical excision group (7.6 vs. 21.4 days; $P < 0.001$; range 1 to 21 vs. 6 to 35 days).

Long-term follow-up data

The patients received endoscopic follow-up for 23 to 213 months (median 58 months). One patient (case 15) died during the postoperative period and one patient (case 22) underwent a total gastrectomy. The long-term follow-up evaluation of the remaining 28 patients showed that 7 of them (25%) had recurrences, but none developed other gastrointestinal neoplasms (Tables 1 and 3). The recur-

rence rate in the endoscopic excision group was significantly lower than the surgical excision group (17% vs. 60%, $P = 0.048$). One patient (case 7) who had a subtotal gastrectomy with Billroth-I anastomosis had a recurrence eight years after the procedure. Because an obstructive polyp (45 mm) was discovered at the anastomotic site by endoscopy (Figure 1), this patient underwent ESD with complete resolution of the tumor and associated symptoms. Another patient (case 1) undergoing surgical excision of polyps had recurrence with polyp bleeding 9 months after the operation. He was then treated by EMR and no residual tumors were found.

DISCUSSION

Since the initial description of gastric hamartomatous polyps in 1977,[18] there have been few reports and few cases of these rare polyps.[6,9,19,20] Previous reports indicate a relationship between the abnormal growth of oxyntic glands and sex hormones, because gastric hamartomatous polyps are mainly found in menopausal and postmenopausal women.[5,9] However, in our series, gastric hamartomatous polyps tended to appear in populations at an advanced age with no predominance related to sex. Therefore, the pathogenesis still needs further investigation.

Iishi *et al*.[5] reported that hamartomatous polyps are usually located in the body or the fundus. In this study, however, these polyps were mainly located in the antrum. Thus, gastric hamartomatous polyp can be one of the differential diagnosis of polypoid lesions of the lower stomach.

There are two types of gastric hamartomatous polyps. Those without a stalk are the "submucosal tumor (SMT) type" because the tumor is inverted into the submucosal layer. Those with a stalk are the "polyp type."[1] Tissue diagnosis is a requirement for therapeutic decision making in gastric hamartomatous polyps. Pathological diagnoses from endoscopic biopsy are often negative, especially in SMT type lesions. Additionally, small gastric lesions are easily overlooked in forceps biopsy material.[21] In this study, 91% of the patients were not diagnosed with hamartomatous polyps during the first superficial biopsy. Therefore, decision-making based on an endoscopic forceps biopsy will be incomplete. Endoscopists should diagnose the lesion promptly during endoscopic studies. EMR or ESD is practical if findings are equivocal because these procedures can be helpful in confirming the diagnosis. Hamartomatous polyps with stalks can be treated with EMR/ESD, because the stalks are often large and these polyps connect with the muscularis propria or even the submucosa. We believe that EMR/ESD is a better choice than polypectomy to resect these lesions completely and achieve a lower recurrence rate.

Iishi H *et al*.[5] found that the polyps in 7 (50.0%) of 14 patients spontaneously decreased in number or disappeared, but the causes were unknown. In contrast, in our series, there was no significant decrease in their number or size, but 27% of the patients had symptomatic recurrence after removal of polyps. Of note, one case in our series was the third case of early gastric adenocarcinoma accompanied by gastric hamartomatous polyps reported in the current English-language literature.[2,14] Therefore, an immediate and careful diagnosis should be made with these points in mind during endoscopic studies.

Polyps with a growth tendency or other symptoms should be removed. However, no consensus has been reached on the therapeutic strategy. Perforations can occur during EMR or ESD, but our findings suggest these can be managed endoscopically. Endoscopic resection was associated with a shorter postprocedure hospital stay in comparison with surgical excision. Finally, in our series, two patients undergoing surgery had recurrences and they were then treated by ESD and EMR. EMR or ESD is still an option in recurrent disease.

Hamartomatous polyps are usually multifocal. During endoscopic resection, the whole hamartomatous polyps resected under direct vision, and other nonsymptomatic polyps are also resected at the same time. The higher recurrence rate after surgical treatment might be the result of more residual polyps in patients treated with surgery. We believe that, compared with CP, EMR/ESD can more completely resect hamartomatous polyps, which are connected with the muscularis mucosae. However, no significant difference in recurrence rates was found between the polypectomy group and the EMR/ESD group (3/15, 20% vs. 2/12, 16.7%), which might be related to the low number of these patients in this study.

There were some limitations to this study. First, the retrospective design of this study had instinctive limitations. Second, the study was undertaken at a tertiary-referral center whose staff had expertise in therapeutic endoscopy. Third, the follow up period in the endoscopy group was shorter than that in the surgery group. This also could affect the recurrence rate. Thus, a prospective, randomized, controlled trial is needed to demonstrate whether endoscopic treatment has a role in the primary management of gastric hamartomatous polyps. However, a randomized trial is actually difficult to conduct in a short period of time because of the relatively low inci-

dence of hamartomatous polyps.

In conclusion, this study provides new observations of gastric hamartomatous polyp(s), including a preponderance to appear in populations at an advanced age with no predominance related to sex, a predominant antrum location for tumors, and a high rate of hemorrhaging in patients with cirrhosis or six or more polyps. Moreover, the gastric hamartomatous polyp is a paracancerous lesion and is associated with gastric cancers. Based on these data, endoscopic resection is an effective procedure to resect gastric hamartomatous polyps and offers a less-invasive alternative to surgery.

DISCLOSURE

The authors have no conflict of interest to declare.

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