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AN EVALUATION OF THE USEFULNESS OF MAGNIFYING COLONOSCOPY FOR THE DIAGNOSIS OF TUMOR INVASION DEPTH IN EARLY COLORECTAL CANCER

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Magnifying colonoscopy can be used to observe colonic mucosal pits. Using this technique, a pit pattern classification system consisting of seven categories has been established. We evaluated the role of magnifying colonoscopy for the diagnosis of colorectal tumors, particularly for the assessment of the invasion depth of early colorectal carcinoma, which is an important indicator for successful and complete endoscopic resection. Thirty-two of early colorectal cancers in twenty-seven cases were examined by magnifying colonoscopy using 0.05% crystal violet solution. The main and accessory pit patterns of all of the lesions were classified by magnifying colonoscopy. The depth of vertical invasion of the tumor was also assessed by endoscopic ultrasonography as well as by histological examination following endoscopic mucosal resection or surgical operation. An accurate determination of tumor depth by magnifying colonoscopy was possible in 84.3% of the cases, compared to 78.1% that were properly diagnosed by endoscopic ultrasonography.

Key words: magnifying colonoscopy, pit pattern, early colorectal cancer

INTRODUCTION

Over the last decade, magnifying colonoscopy (MC) has been developed with the possible clinical use for examining the gastrointestinal mucosal pit pattern during endoscopic diagnosis. It has been possible by MC to distinguish not only neoplasm from non-neoplasm (1-3) but also carcinoma from adenoma (4-6). The microscopic pit pattern on the surface of the gastrointestinal mucosa may reflect the histological characteristics of gastrointestinal tumors and the depth of their invasion (7), whereas the diagnostic role of MC in determining the depth of tumor invasion still remains controversial. Endoscopic diagnosis of tumor invasion is critically important for the selection of treatment, since endoscopic mucosal resection (EMR) of the colorectal neoplasm is possible only when the depth of tumor invasion is limited to portions of the colorectal wall shallower than the superficial submucosal layer (8,9).

In the present study, we tried to elucidate the usefulness of MC in diagnosing the depth of tumor invasion. In addition, we compared the diagnostic accuracy of MC and endoscopic ultrasonography (EUS) for determining the depth of tumor invasion, since EUS is believed to be the most reliable method for this purpose (10,11).

PATIENTS AND METHODS

A total of 32 early colon cancers in 27 patients (mean age 65.5 years old, Male:Female = 16:11) were examined by both MC (CF Q420ZI or PCF Q240ZI, Olympus Optical Co., Ltd., Tokyo, Japan) and EUS by probe method (UM-3R-3 and EU-M20 or EU-M2000, Olympus Optical Co., Ltd.) in the Division of Gastrointesinal Endoscopy, Shimane Medical University Hospital and Department of Gastroenterology, Nogi Clinic from January, 2001 to August, 2002. The study was conducted in accordance with the Declaration of Helsinki.

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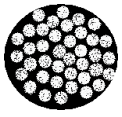
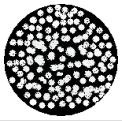
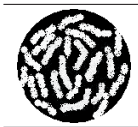
MC was performed after sufficient washing of target tumors by water followed by 0.05% crystal violet vital staining. Observed pit patterns were classified into the following seven categories by three expert endoscopists according to previous publications (4,7,8): normal round pit (type I), star-like pit (type II), small tubular pit (type IIIs), large tubular pit (type III_L), branched or gyrus-like pit (type IV), non-structural pit with amorphism (type V_A), and non-structural without pit (type V_N). In this study, these patterns were re-classified into the following three patterns as shown in Table 1. The pit pattern suggesting tumor invasion within the superficial submucosal layer is classified as "endoscopic resection" (ER), and that indicating deeper invasion is classified as "surgical operation" (SO). The former consists of the IIIs, III_L, IV, and V_A pit patterns, while the latter correlates with the V_N pattern, even if it occupies a minute area of the tumor. The other pit patterns, I and II, are classified as "non-tumor" (NT). On the other hand, EUS diagnosis of the tumor depth was also made with taken photographs or video-recorded findings by the same three expert endoscopists. The pit patterns diagnosis by MC and the depth diagnosis by EUS were retrospectively compared with the histological degree of the tumor invasion.

Statistical analysis was performed using the chi-squared test, and a p-value less than 0.05 was considered significant.

Table 1. Classification of colorectal mucosal pit pattern

	Kudo's classification	Our new classification
 round pits	type I	non-tumor pattern (NT type)
 asteroid or papillary pits	type II	
 small tubular or roundish pits	type IIIs	enodoscopic resection pattern (ER type)
 large tubular or roundish pits	type III_L	
 branch-like or gyrus-like pits	type IV	
 irregular pits with amorphism	type V_A	
 non-structural pits	type V_N	surgical operation pattern (SO type)

RESULTS

The depth of tumor invasion as diagnosed by EUS and MC is shown in Table 2. When the histological diagnosis of tumor invasion was used as a gold standard[8], the rates of correct diagnosis of the degree of tumor invasion by EUS and MC were 78.1% and 84.3%, respectively, although this differ-

Table 2. Tumor-depth diagnosis of early colon cancers

			Tumor-depth diagnosis		
No.	Macroscopic type	Size (mm)	Pit	EUS	Histology
1	LST (PG)	65	ER (III_L >IV)	sm-1	m
2	LST (PG)	50	ER (III_L = IV)	m	m
3	LST (PG)	42	ER (III_L >IV)	m	mi
4	LST (PG)	34	ER (III_L)	m	m
5	LST (PG)*	28	ER (III_L)	m	m
6	IIa + IIc	35	SO (V_A >> V_N)	m	m
7	IIa + IIc	28	ER (III_L)	m	m
8	IIa + IIc	18	SO (V_A = V_N)	sm-3	sm-3
9	IIa + dep**	15	ER (III_L > V_A)	m	m
10	IIa + dep	15	SO (V_A = V_N)	sm-3	sm-3
11	IIa + dep	12	SO (V_A >> V_N)	sm-2	m
12	IIa + dep**	10	ER (III_L > V_A)	m	m
13	IIa + dep**	10	ER (III_L)	m	m
14	IIa + dep	9	ER (III_L)	m	m
15	IIc	12	SO (III_S = V_N)	sm-3	sm-3
16	IIc	5	ER (III_S)	m	m
17	IIc	3	ER (III_S)	m	m
18	Is	25	ER (V_A > III_L)	sm-3	sm-3
19	Is	20	SO (V_A = V_N)	m	m
20	Is	18	ER (III_L)	sm-1	m
21	Is**	15	ER (V_A)	m	m
22	Is**	15	ER (III_L)	sm-2	m
23	Is**	10	ER (V_A > III_L)	m	m
24	Is	10	SO (V_A > V_N)	m	sm-2
25	Isp	22	ER (III_L > V_A)	m	m
26	Isp	22	ER (III_L)	m	m
27	Isp**	20	ER (V_A)	sm-1	sm-3
28	Isp**	18	ER (III_L)	m	m
29	Isp	16	ER (IV)	sm-3	m
30	Isp	16	ER (III_L > V_A)	sm-1	m
31	Isp	12	ER (V_A)	m	m
32	Isp	16	ER (IV)	m	m

LST: lateral-spreading tumor. PG (polypoid growth type), IIa+IIc, IIa+dep, IIc, Is, and Isp are the classified types defined in Ref. (19).
ER: endoscopic resection pattern, SO: surgical operation pattern.
*: presented case in the paper, **: carcinoma in adenoma. sm-1,-2,-3, and m are the depth defined in the same Ref. (19).
Sizes show long diameter of lesions. Underlined marks show wrong diagnosis.

ence was not significant. The cases observed for diagnostic correspondence by EUS and MC showed a high rate of correct diagnosis (92.3%). In the flat type of early colorectal cancers, a more successful diagnosis was possible (88.2% and 88.2%, respectively) than in protruded type (66.7% and 80.0%, respectively).

Presentation of a representative case

Case1: A lateral-spreading tumor was found in the mid-descending colon of a 69-year-old male when he was examined by screening colonoscopy at the Shimane Preventive Center of Cancer and Cardiovascular Diseases because of a positive result from the stool occult blood test. He was admitted to the Division of Gastrointestinal Endoscopy, Shimane Medical University Hospital for treatment by EMR in June, 2002. On admission, he had no clinical symptoms and there were no abnormal findings in his physical examination. His laboratory data, including the results of repeated stool occult blood tests, were all within normal ranges.

A photograph of the tumor taken during the colonoscopy is shown in Fig. 1. The lesion was a granular type of lateral-spreading tumor, and had conversing folds suggestive of invasion into the submucosal layer. It also showed conversing folds (Fig. 2-a) and arch-like deformity in the profile view (Fig.2-b) on barium-enema examination. X-ray findings also indicated tumor invasion into the submucosal layer. Submucosal invasion was further suggested by the results of the EUS examination, which ultrasonographically showed that the third layer of the colonic wall, the submucosal layer, was irregularly thinned and thickened at the tumor base (Fig. 3). The pit pattern of the tumor surface observed by MC with the aid of 0.05% crystal violet solution showed III_L with a small area of V_A in the center of the tumor (Fig. 4). This combination of pit patterns suggests that this tumor invaded only within the superficial part of the colonic mucosal layer after development along the adenoma-cancer sequence. Thus, only MC indicated that this tumor could be completely resected by EMR.

Complying with the patient's wishes, EMR was

Fig. 1. Chromoendoscopic view of the case 1, showing polypoid growth type of lateral-spreading tumor.

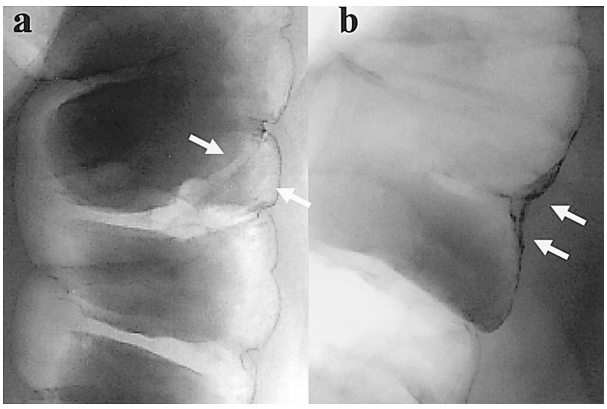


Fig. 2. Pictures of barium-enema examination in the case 1. Conversing fold is observed (arrow) in the *en face* view (a), and arch-like deformity (arrows) is observed in the profile view (b).

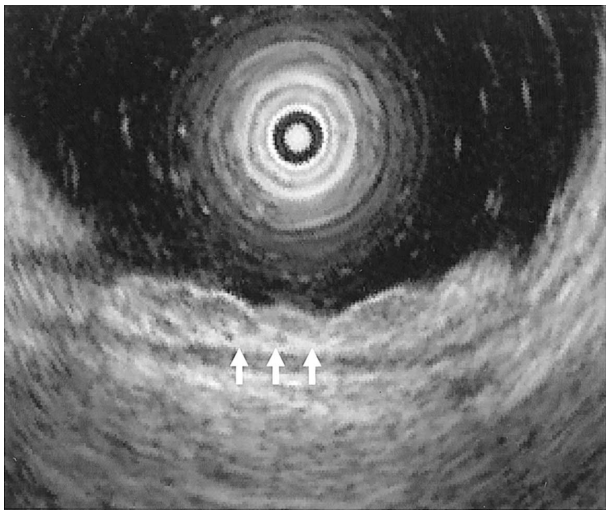


Fig. 3. EUS picture of the case 1. An irregularity is shown in the 3rd layer, submucosal layer (arrows).

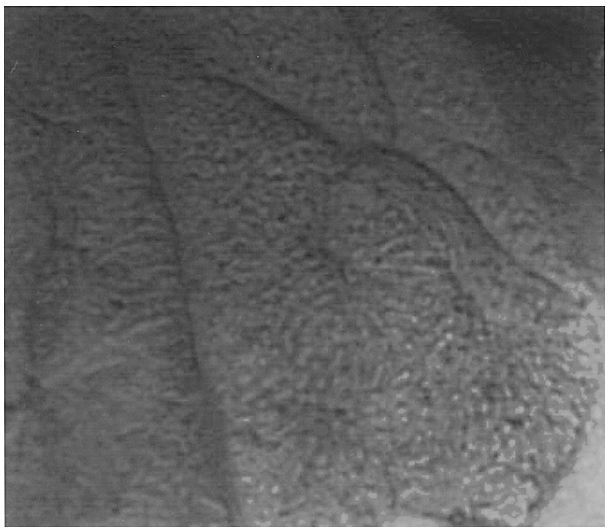


Fig. 4. Pit pattern of the case 1 on magnifying colonoscopy. Most of pits show III_L pattern.

performed and the tumor was determined histologically to be a carcinoma in adenoma invading within the mucosal layer (Fig. 5). Therefore, in this case only MC was able to correctly diagnose the degree of tumor invasion and to guide successful EMR treatment without open surgery.

This was a typical case where the pit pattern by MC was very helpful for diagnosis of the degree of tumor invasion. In all examinations, only the pit pattern indicated the correct depth of tumors.

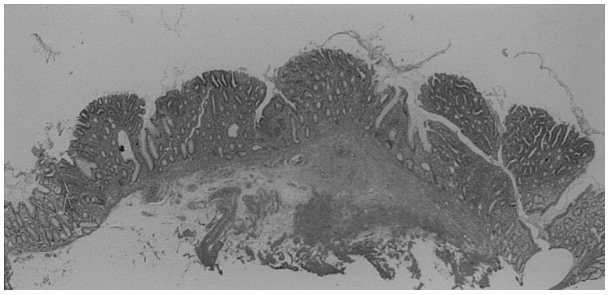


Fig. 5. Histological findings of the case 1, showing carcinoma in adenoma which is limited within the mucosal layer.

DISCUSSION

The difference between pit patterns of normal colorectal mucosa and those of tumors including adenomas and adenocarcinomas was first described in 1980 (12). In the last 10 years, the development of MC has brought a higher resolvability. Subsequently, the classification of pit patterns for clinical purposes was established by Kudo et al. (4, 7, 8). This classification makes it possible to differentiate endoscopically between adenomatous and non-adenomatous lesions as well as between carcinomas and adenomas. Some investigators have recently tried to use pit patterns to diagnose the degree of tumor invasion (8, 13-17). According to these studies, the depth of colorectal cancer invasion can be speculated from the pit pattern on the tumor surface. No tumors with III_L pits are reported to invade beyond the mucosa. Most of the lesions with IIIs, IV, and V_A pits show limited invasion within the mucosal and superficial submucosal layers. In contrast, V_N pits are reported to correlate with invasion into the submucosal layer, even when this pattern is found only in a small area (8, 17, 18).

We divided pit patterns into three groups as proposed by Fujii et al. (13). The NT group consists of I and II pits, which are indicative of non-neoplastic lesions. The ER group includes IIIs, III_L, IV, and V_A pits and is usually suggestive of limited tumor invasion down to the most superficial part of the submucosal layer or to the mucosal layer. However, the SO group, which includes V_N, shows deeper tumor invasion into the deep submucosal layer. Our results confirmed the previous publication suggesting the value of MC and further showed that MC was better than EUS for diagnosing the depth of tumor invasion, although the difference in diagnostic accuracy did not reach a statistically significant level. The rate of accurate diagnosis for the degree of tumor invasion was 92.3% in the cases with a corresponding result of pit pattern and EUS, although it was 78.1% in the cases with EUS alone. This fact clearly suggests that additional pit pattern diagnosis by MC for tumor invasion is very useful.

EUS has been considered the most reliable diagnostic method for determining the degree of tumor invasion, and it is regularly used in pre-procedure diagnosis for EMR treatment. Once EUS shows massive tumor invasion into the submucosal layer, EMR treatment for colorectal cancer is considered to be impossible and to have a higher post-procedure recurrence rate, even if the resection is technically possible. As shown in the case reports described in this study, EUS is not feasible to discriminate easily between submucosal tumor invasion and submucosal

fibrosis caused by inflammation of the colorectal wall. In contrast, the pit pattern on the tumor surface reflects the histological growth pattern of the tumor tissue and is not influenced by inflammation-induced submucosal fibrosis. Therefore, combining the results of MC and EUS may provide an easier and more accurate method for diagnosing the depth of tumor invasion and thereby increasing the success rate of EMR treatment of colorectal tumors.

In conclusion, we report the usefulness of MC for the diagnosis of invasion depth of colorectal cancer and emphasize the role of MC in pre-procedure examination for endoscopic mucosal resection of colorectal tumors.

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