

Mucosal Prolapse Syndrome of the Rectum: Correlation between Macroscopic Type and Location in a Discussion on Its Natural History

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Received January 14, 1993

Summary. One hundred and six lesions of mucosal prolapse syndrome (MPS) of the rectum were examined in regard to macroscopic type, location, histological stage and mucosal thickness in order to analyse the natural history of the disease.

Sixty-six lesions belonged to the polypoid type. In 61 of these, the distance from the dentate line was able to be verified. Fifty-one lesions (83.6%) occurred in the lower rectum within 2cm proximal to the dentate line. Forty-six of the 66 lesions (69.7%) showed a low-grade fibromuscular stage, but no high-grade fibromuscular stage. The thickness of polypoid mucosa excluding the muscularis mucosae which could be measured in 27 of the 66 lesions had a mean of 1.96 mm at the top area, and 0.75 mm in the surrounding area.

Twenty-five lesions belonged to the flat type. Twenty-four of these were located within 2cm from the dentate line. Seventeen (68.0%) belonged to low-grade fibromuscular stage, 7 (28.0%) to the vascular stage and 1 (4.0%) to the high-grade fibromuscular stage. The mucosal thickness of 15 lesions averaged 0.54 mm.

On the other hand, there were 21 ulcerative type lesions, with the distance from the dentate line verified in 20 of them. Thirteen lesions (65.0%) were located within 2-17 cm proximal to the dentate line. They were distinct from the other types in their higher incidence of fibromuscular stage (95.2%), particularly of a high-grade stage (47.6%). The mucosal thickness of 9 lesions was a mean of 0.78 mm in the ulcer-marginal area and 0.58 mm in the surrounding area.

In both the polypoid and ulcerative types, arteries showed a thickening of the media and intima in the submucosa. These findings were most conspicuous in the ulcerative type.

It is concluded that MPS initially occurs in flat types as a result of reversible mucosal prolapse, and then either changes into a polypoid (glandular hyperplasia) type-especially near the dentate line-by a process of

non-transmural rectal prolapse, or changes into an ulcerative type especially within a distance of 2-17 cm proximal to the dentate line by the process of transmural rectal prolapse which causes severe ischemic change.

INTRODUCTION

Mucosal prolapse syndrome (MPS) of the rectum is referred to by a variety of synonyms, including solitary ulcer,¹⁻³⁾ solitary ulcer syndrome,⁴⁾ solitary rectal ulcer syndrome,^{5,6)} localized colitis cystica profunda (CCP),^{7,8)} inflammatory cloacogenic polyp⁹⁾ or lesions secondary to mucosal prolapse.¹⁰⁾ Recently these diseases have been ascribed to the same mechanism, i.e., mucosal prolapse. Watanabe et al¹¹⁻¹³⁾ have already proposed a classification for the macroscopic types and histological stages of MPS. There still remain, however, unresolved problems about its natural history such as macroscopic changes with time, the mechanism of formation for each macroscopic type and the synthesis of fibromusculosis. In this thesis, the correlation between location and macroscopic type of the lesions in the rectum is examined and the natural history of MPS discussed.

MATERIALS AND METHODS

I. Materials

During the period January, 1981-March, 1991, our department obtained 112 lesions in 98 patients with MPS of the rectum. These were obtained as follows: 4 lesions by colectomy, 72 by partial resection of rectum, 9 by endoscopic resection and 27 by forceptic

biopsy.

Among the 112 lesions, there were 56 lesions in which the precise location (distance proximal to the dentate line) could be verified (32 polypoid, 20 flat and 4 ulcerative types) and 50 lesions in which the approximate location could be estimated with the methods described later (29 polypoid, 5 flat and 16 ulcerative type). Consequently, 106 lesions were selected for this study.

II. Methods

1. Definition of gross type and histological stage

The lesions of MPS were classified into three macroscopic types as follows: polypoid, flat and ulcerative type.¹¹⁻¹³⁾ Polypoid types were lesions with localized mucosal elevation (Fig. 1), ulcerative types, lesions with an open ulcer (Fig. 2), and flat types, lesions without localized mucosal elevation or ulceration.

Each polypoid or ulcerative type accompanied with a flat type within the same lesion was classified as either a polypoid type or ulcerative type, respectively (Fig. 1, 2). In cases where plural lesions existed spatially independently from each other, macroscopic classification was done for each lesion.

The MPS were divided into three histological stages by Watanabe et al.¹¹⁻¹³⁾ The initial stage is a vascular stage characterized by mild to moderate dilatation and proliferation of capillaries with swollen endothelial cells in the superficial part of the lamina propria mucosae (Fig. 3). In the deep part of the lamina propria mucosae, a slight proliferation of collagen fibers and smooth muscle fibers, so-called fibromusculosis, might be recognized. The next stage, the low-grade fibromuscular stage, is characterized by fibromusculosis which extends up to the lower two-thirds of the lamina propria mucosae, in addition to the features of the vascular stage (Fig. 4). The late stage, the high-grade fibromuscular stage, is characterized by fibromusculosis which spreads from the lower two-thirds to the whole lamina propria mucosae, with a widening of the lamina propria mucosae and decrease in the number of the crypts (Fig. 5). Even in this stage, dilatation and proliferation of capillaries with swollen endothelial cells is frequently recognized.

2. Location of lesions

Location here indicates two positions: one is the distance proximal to the dentate line, and the other is a clockfaced location in the rectum as will be explained later.

1) *Distance from the dentate line*

Location of each lesion was expressed as the distance (cm) from the dentate line. In the 56 lesions where this could be precisely determined, the distances of both the distal and proximal margin of each lesion from the dentate line could be measured on H-E stained sections using a micrometer. In the other 50 lesions, the distances from the dentate line could be decided by clinical and histological information.

2) *Distance from the dentate line to the summit of elevation*

Distance (cm) from the dentate line to the summit of the elevation was able to be examined in 27 polypoid type lesions.

3) *Distance from the dentate line to the center of open ulcer*

Distance (cm) from the dentate line to the center of the open ulcer was able to be examined in 5 ulcerative type lesions.

4) *"Clockfaced" location in rectal wall*

The 70 lesions (43 polypoid, 13 flat and 14 ulcerative type) could be divided according to the position on a clock face of the rectum, according to clinical information and histological confirmation of the two rectal tenias (corresponding to 6 and 12 o'clock on a clock) according to the mesenteric tenia (6 o'clock) and the antimesenteric tenia (12 o'clock).

3. Thickness of the mucosa

1) *Thickness of the mucosa excluding the muscularis mucosae*

Thickness of the mucosa—excluding the muscularis mucosae—was histologically measured with a micrometer in each macroscopic type of lesions. In the 27 polypoid lesions, measurement was done at three sites; the top, the beginning area of the polyp and the surrounding flat mucosa. In the 9 ulcerative types, the marginal mucosa of the ulcer (except for single-cell layered flat regenerating mucosa), and the surrounding area were chosen for the measurements. In the flat types, the mucosal thickness measured in 15 lesions was expressed as a mean value. As a control, macroscopically and microscopically normal rectal mucosa from 25 patients with rectal cancer resected surgically was selected.

2) *Thickness of the muscularis mucosae*

Thickness of the muscularis mucosae was measured in the same way as described above for the 15 flat and



Fig. 1-a. Gross appearance of polypoid type MPS.

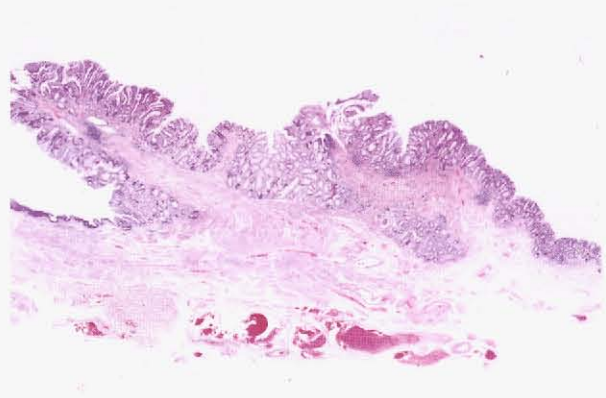


Fig. 1-b. Low-magnified view of polypoid type MPS with increased mucosal thickness.

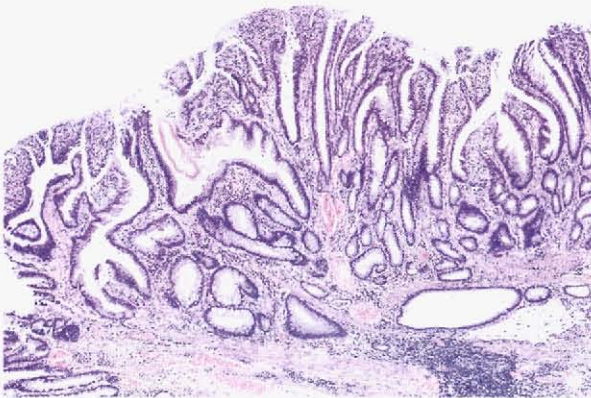


Fig. 1-c. High-magnified view of polypoid type MPS with glandular hyperplasia.



Fig. 2-a. Gross appearance of ulcerative type MPS.

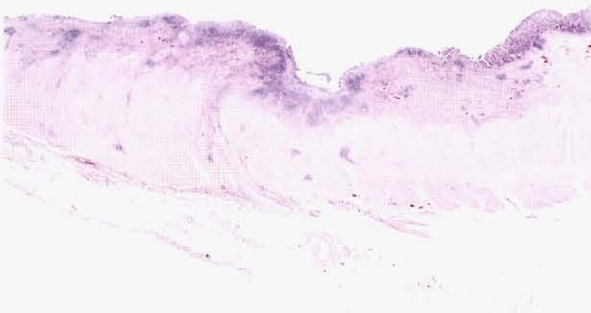


Fig. 2-b. Low-magnified view of ulcerative type MPS with hypertrophy of the proper muscle and elevation of the inner muscle toward the lumen.

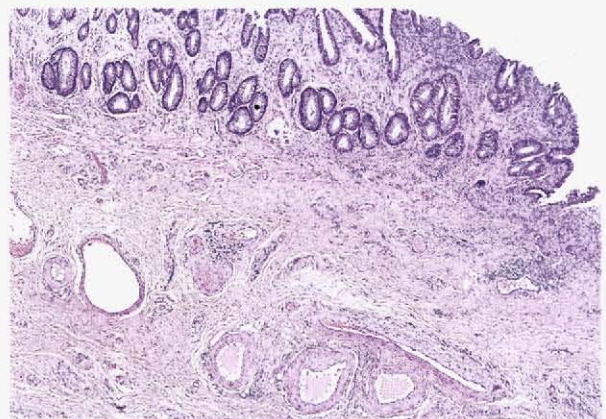


Fig. 2-c. High-magnified view of ulcerative type MPS with dilatation of large arteries and thickening of the wall in the submucosa.

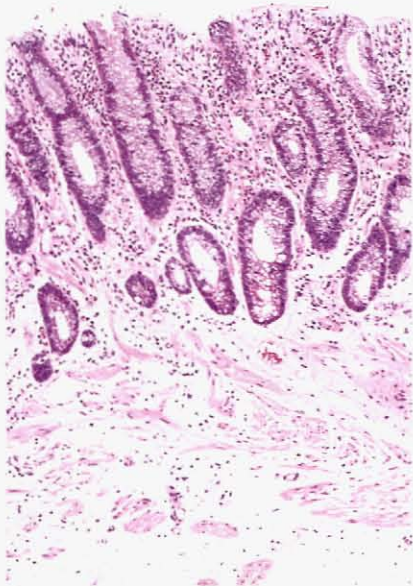


Fig. 3. Vascular stage of MPS.

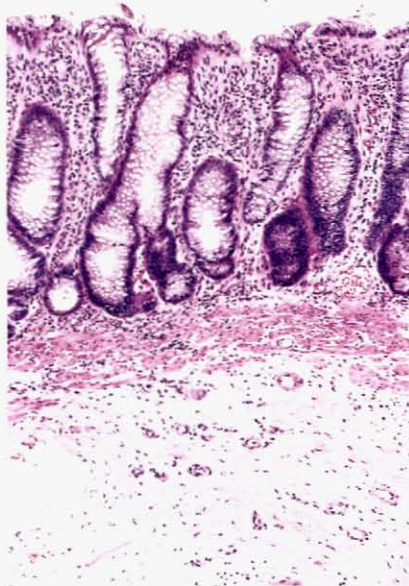


Fig. 4. Low-grade fibromuscular stage of MPS.



Fig. 5. High-grade fibromuscular stage of MPS.

9 ulcerative lesions and 25 control cases. In the 27 polypoid lesions, however, the thickness between the beginning area of the polyp and the surrounding flat mucosa was measured, because of tangential sectioning and a splitting of the muscularis mucosae in the polypoid lesion.

4. Histological examination of the submucosa and muscle

1) *Submucosa*

In the submucosa, the following histological changes were examined: edema, fibrosis and vascular changes (dilatation, winding, thickening of wall, degeneration of wall) and the depth of the vascular changes (superficial or deeper), in the 66 lesions (36 polypoid, 21 flat and 9 ulcerative type). The presence of CCP was examined histologically and macroscopically (Fig. 6).

2) *Proper muscle*

The thickening of the muscle and its elevation toward the luminal side were studied in both the inner and outer muscles in 13 lesions (6 polypoid and 7 ulcerative type).

5. Macroscopic examination

Macroscopic observations were done in detail on 13 lesions (6 polypoid and 7 ulcerative types) which were obtained by colectomy. In addition, flat type lesions connected with the above polypoid or ulcerative

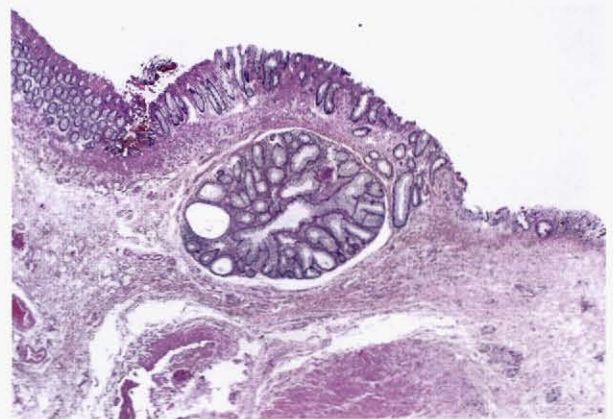


Fig. 6. Microscopic view of colitis cystica profunda in the submucosa.

lesions were utilized as representative flat type lesions because there were no surgically resected cases of a pure flat type in our series.

RESULTS

1. General data on 112 lesions of 98 patients with MPS

1) *Sex and age of 98 patients with MPS*

The 98 patients with MPS comprised 77 male and 21 females (Table 1). There were no significant differences in age between males and females by t-test.

2) Number of lesions and clinical diagnosis

Table 2 shows the number of the lesions by method of obtaining and macroscopic type (Table 2). Two of the three colectomy lesions of the ulcerative type were diagnosed as rectal cancer at the preoperative state. All the flat type lesions were complicated with hemorrhoids.

2. Correlation between macroscopic type and histological stage

The 66 polypoid type lesions consisted of a low-grade fibromuscular stage 69.7% (46/66), vascular stage 30.3% (20/66) and no high-grade fibromuscular stage (Table 3). The 25 flat types consisted of low-grade fibromuscular stage 68.0% (17/25), vascular stage 28.0% (7/25) and high-grade fibromuscular stage 4.0% (1/25) (Table 3). The 21 ulcerative types consisted of

high-grade fibromuscular stage 47.6% (10/21), low-grade fibromuscular stage 47.6% (10/21) and vascular stage 4.8% (1/21) (Table 3). High-grade fibromuscular stage lesions were most frequent among the ulcerative types than in other two macroscopic types.

Among the 32 polypoid-type lesions in which the precise location could be verified, 26 lesions belonged to the low-grade fibromuscular stage. Additionally, 19 of the 26 lesions had accompanying vascular stage lesions at their periphery.

3. Location

1) Distance from the dentate line

The distance by macroscopic type is shown in Fig. 7. Within 2cm from the dentate line, polypoid types occurred at a rate of 83.6%(51/61), flat types at 96.0% (24/25) and ulcerative types at 35.0% (7/20). On the other hand, in the upper rectum more than 2 cm proximal to the dentate line, polypoid types developed at 16.4% (10/61), flat types at 4.0% (1/25) and ulcerative types at 65.0% (13/20).

2) Distance from the dentate line to the summit of elevation

In 26 polypoid lesions, the mean \pm SD (range) of the distance was 0.46 \pm 0.37(0-16)cm.

Table 1. Sex and age of 98 patients with MPS

	Number of patient (%)	Age	
		Mean \pm SD	Range
Male	77(78.6)	50.4 \pm 17.04	11-84
Female	21(21.4)	52.8 \pm 19.29	15-86
Total	98(100.0)	50.9 \pm 17.57	11-86

*No significant difference (t-test)

Table 2. Number of lesions of each macroscopic type by method of obtaining

Method	No. of lesions by macroscopic type			Total No. of lesion
	Polypoid	Flat	Ulcerative	
Colectomy	1	0	3	4
Local resection	42	23	7	72
Endoscopic resection	9	0	0	9
Forceptic biopsy	14	2	11	27
Total	66	25	21	112

Table 3. Correlation between macroscopic type and histological stage for 112 lesions with MPS (%)

Macroscopic type	Histological stage			Total
	Vascular	Low-grade fibromuscular	High-grade fibromuscular	
Polypoid	20(30.3)	46(69.7)	0(0.0)	66(100.0)
Flat	7(28.0)	17(68.0)	1(4.0)	25(100.0)
Ulcerative	1(4.8)	10(47.6)	10(47.6)	21(100.0)

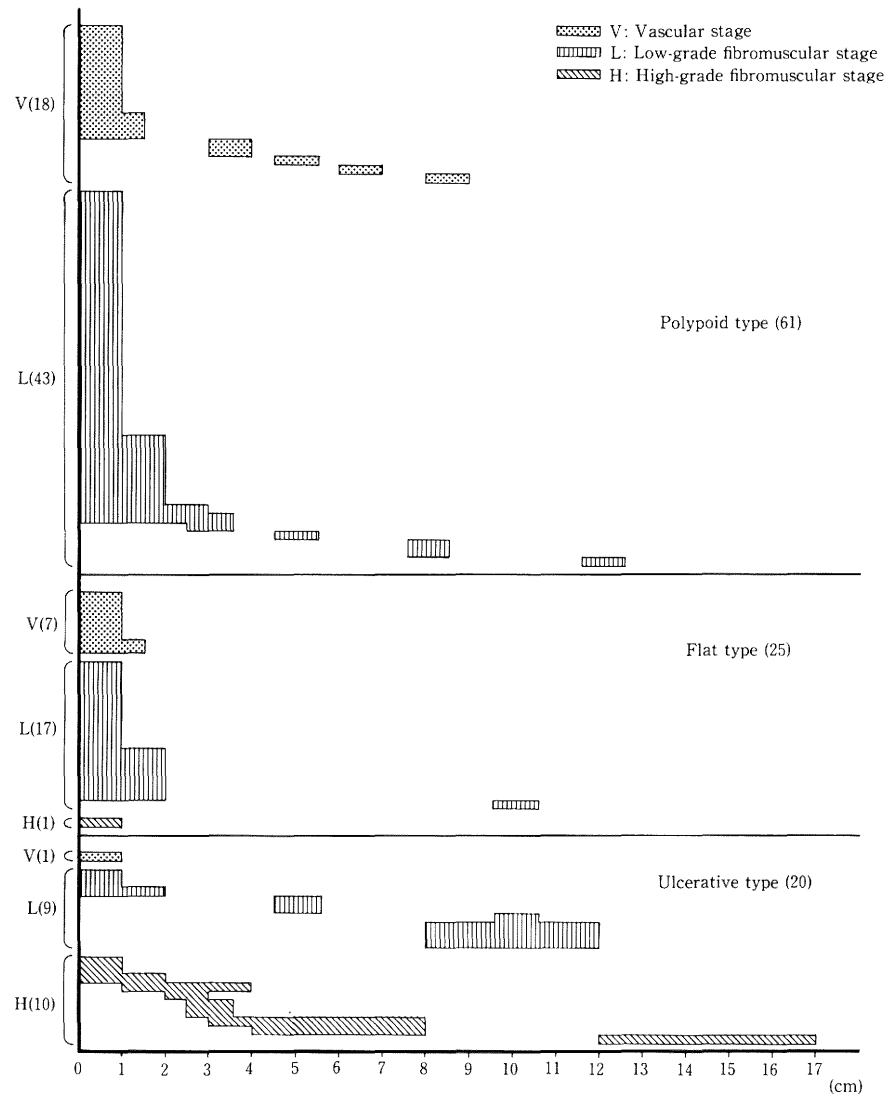


Fig. 7. Distance from the dentate line. P: Polypoid type, F: Flat type, U: Ulcerative type, V: Vascular stage, L: Low-grade fibromuscular stage, H: High-grade fibromuscular stage, (n): Number of lesion.

3) *Distance from the dentate line to the center of open ulcer*

In 5 ulcerative type lesions, the mean \pm SD(range) of the distance was $4.7 \pm 5.5(0.3-15.2)$ cm.

4) *"Clockfaced" location in rectal wall*

Polypoid and ulcerative type lesions occurred at 12 o'clock, with each incidence of 28.0% (12/43) and 50.0% (7/14) (Fig. 8). Flat types occurred at 7 o'clock at an incidence of 47.0% (6/13), a frequent site of hemorrhoids.

4. Thickness of the mucosa

1) *Thickness of the mucosa excluding the muscularis mucosae*

Compared with control cases, the mucosa evidently increased in thickness in all the measured areas in each macroscopic type (Fig. 9). Thickness at the top area of polypoid type lesions was 1.96 ± 1.03 mm. Even in the marginal area of ulcerative type lesions, thickness was 0.78 ± 0.23 mm.

2) *Thickness of the muscularis mucosae*

Compared with control cases, the muscularis mucosae

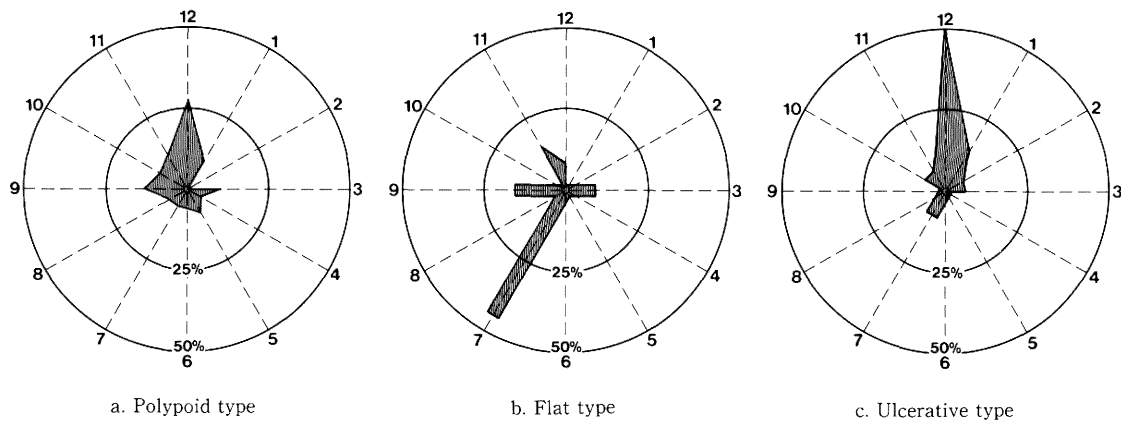


Fig. 8. "Clockfaced" location in rectal wall (%)

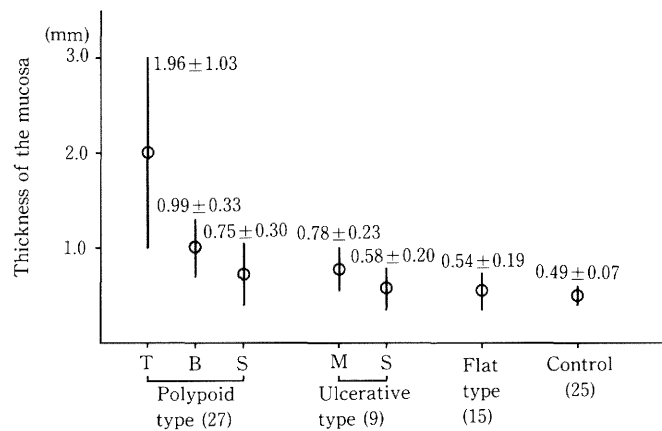


Fig. 9. Thickness of the mucosa (excluding the muscularis mucosae) by macroscopic type (51 lesions). T: Top area, B: Beginning area, M: Marginal area, S: Surrounding area.

increased in thickness in all the measured areas in each macroscopic type (Fig. 10).

5. Histological examination in the submucosa and muscle

In all the examined lesions (36 polypoid, 21 flat and 9 ulcerative type), the submucosa showed edema, dilatation and winding of blood vessels, thickening of arterial media and intima (Fig. 2-c). These findings were especially remarkable in the ulcerative type. Additionally, blood vessels, 100–150 μ m in diameter, which are usually observed in the deeper part of the submucosa, appeared in the upper part of the submucosa close to the open ulcer and in the neighborhood of the ulcer base.

CCP were observed in the deeper part of the mucosa to the upper part of the submucosa, with an incidence of 7.6% (5/66) in polypoid and 14.3% (3/21)

in ulcerative types (Fig. 6). There was no CCP among the 25 flat types. Fibromusculosis was slight in CCP.

The proper muscle showed hypertrophy of both layers, especially the inner layer, and elevation toward the lumen (Fig. 2-b).

6. Macroscopic examination

The polypoid type lesions showed broad-based mucosal elevations, with a brownish gyral and villous appearance (Fig. 1-a). Transition from the elevation to the surrounding mucosa was smooth, which differed from neoplastic lesions. The ulcerative type lesions showed oval-shaped, shallow (U1-II, microscopically (Fig. 2-b)) ulcers with sharply-demarcated margins and a flat ulcer-base. Marginal elevation was edematous, yellow-white and gently sloping to the surrounding mucosa. In the flat type lesions, the mucosa showed a congestive and edematous appear-

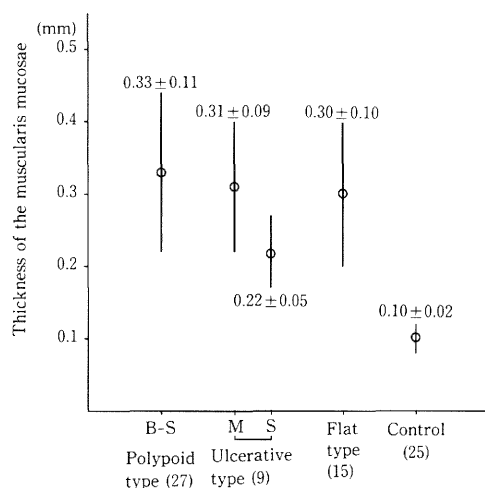


Fig. 10. Thickness of the muscularis mucosae by macroscopic type (51 lesions). B~S: Beginning to surrounding area, M: Marginal area, S: Surrounding area.

ance. The mucosal area-pattern was enlarged.

DISCUSSION

1. Difference of macroscopic type by location

It has already been pointed out that MPS can assume the form of polypoid or flat lesions as well as ulcerative lesions.^{1,3-5,7)} However, its natural history is not

yet fully understood. Watanabe et al.^{11,12)} insists that macroscopic types of MPS vary with the location of the lesions, i.e. MPS-lesions in the terminal rectum usually grow into polypoid type lesions and those in the upper rectum usually grow into ulcerative type lesions. The results obtained from this study confirmed the correlation between location and macroscopic type of lesion.

Polypoid and flat type lesions occurred in the lower rectum within 2cm from the dentate line, with respective incidences of each at 83.6% (51/61) and 96.0% (24/25). On the other hand, ulcerative type lesions occurred at 35.0% (7/20) in the rectum within 2cm from the dentate line, and at 65.0% (13/20) within 2-17 cm from the dentate line.

On the other hand, 82 lesions in the lower rectum within 2cm from the dentate line were 51 polypoid (62.2%), 24 flat (29.3%) and 7 ulcerative (8.5%). Further, 24 lesions in the upper rectum within 2-17 cm distant from the dentate line consisted of 10 polypoid (41.7%), one flat (4.1%) and 13 ulcerative (54.2%) types.

In other words, a boundary may be established at a line 2 cm proximal to the dentate line. It appears quite likely that lesions of the rectum proximal to the boundary become polypoid types, and lesions distal to it become ulcerative types.

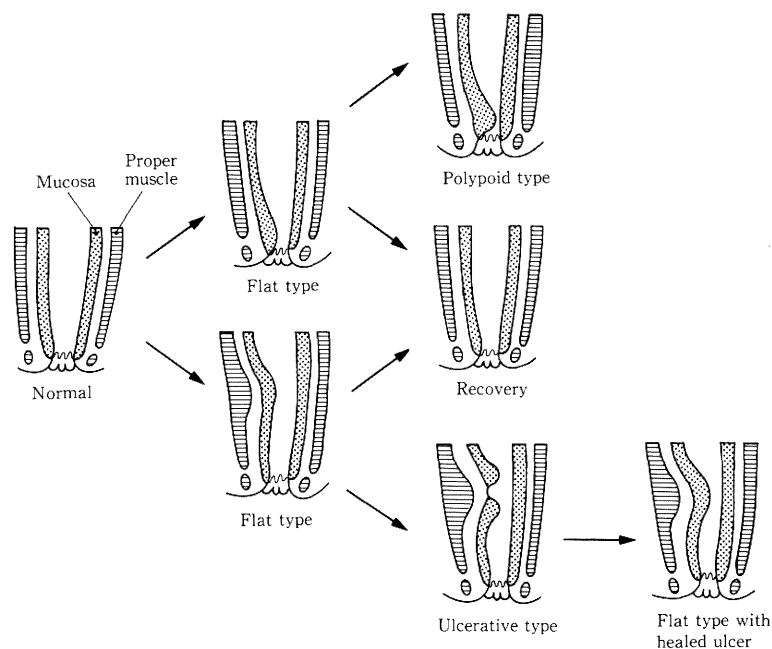


Fig. 11. Morphological natural history of MPS.

2. Two morphological courses in natural history of MPS

Madigan and Morson³⁾ proposed that polypoid lesions of MPS were pre-ulcerative lesions. Their opinion is based solely on fibromusculosis in common histological feature. Watanabe et al.¹¹⁾ speculated on the transformation of morphological types: 1) in lesions of MPS at the terminal rectum, no transformation occurs between polypoid types and ulcerative types, and flat types can grow into polypoid types but rarely into ulcerative types; and 2) in lesions in the upper rectum, flat types should be a precursory lesion of ulcerative types. In order to discuss this transformation of each macroscopic type in MPS, it is necessary to certify their definition and conditions of observation.

Macroscopic morphology in one lesion of MPS varies *in vivo* or out of the living body (resected material). Even in one identical living body, it varies depending on physiologic conditions, for example during straining or not. Every lesion of MPS reveals an elevation at the state of mucosal prolapse under physiologic conditions. There exists a possibility that elevation is not recognized in resected material.

The author would insist that a flat type lesion is just an initial precursory lesion independent from its location (distance from the dentate line), and that there is no transformation between polypoid type lesions with glandular hyperplasia and ulcerative type lesions. Between the polypoid and ulcerative types, there are distinct differences in histological stages and histological features (Table 3). The incidence of low-grade fibromuscular stage was 69.7% (46/66) for the polypoid types and 47.6% (10/21) for the ulcerative types. On the other hand, 47.6% of the ulcerative type lesions were accompanied with high-grade fibromuscular stages in the ulcer-marginal and surrounding mucosa. Although all the polypoid type showed glandular hyperplasia, the ulcerative type did not (Fig. 1-a, b). From these facts, one can hardly suppose that ulceration on a polypoid type forms an ulcerative type or that healing of an ulcer results in a polypoid type.

A flat type is supposed to be a precursory state of a polypoid type with glandular hyperplasia, since any polypoid type should exhibit each precursory state until it becomes a polypoid lesion. All the polypoid types are accompanied by flat types in the parts surrounding them. Further, 73.1% (19/26) of them were in the vascular stage. These facts support the author's hypothesis that a flat type is a precursory lesion of a polypoid type, and suggests a possibility

that especially a vascular stage lesion is a precursory lesion in a flat type.

The ulcerative type showed high-grade fibromusculosis at the ulcer-marginal areas, and the enlarged edematous submucosa which reveals stimulation due to chronic rectal prolapse for a long term. Since one flat type (4.0%) showed similar findings to those of the ulcerative type, a flat type in the high-grade fibromuscular stage is thought to be a precursory lesion of an ulcerative type.

The natural history of MPS is concluded as follows (Fig. 11): 1) Lesions of MPS, which occur in the rectum within 2 cm proximal from the dentate line, initially arise as a flat type of vascular stage. Some of them (68.0% of the flat type) macroscopically remain as flat types and proceed to the low-grade fibromuscular stage. A small number of flat types go through the high-grade fibromuscular stage into ulcerative types. 2) Lesions of MPS, which occur in the rectum at a distance more than 2 cm proximal from the dentate line, initially arise as flat types of a vascular stage, and change into ulcerative types of a high-grade fibromuscular stage through a flat type of high-grade fibromuscular stage. Only a few lesions transform into polypoid types with glandular hyperplasia.

3. Mechanism of formation of polypoid types and ulcerative types

The reason why there are two different natural courses (polypoid and ulcerative type) probably depends on the degree of ischemia induced by rectal prolapse (Table 4). The rectal wall near the dentate line, where polypoid types frequently occur, is sufficiently fixed by the anal sphincter, and transmural rectal prolapse hardly occurs. Therefore, lesions of MPS in this region grow into polypoid types with reactive mucosal thickening.

On the other hand, the rectal wall distant from the dentate line is insufficiently fixed. Therefore, lesions in this region grow into ulcerative types with a state of severe chronic intermittent arterial ischemia, due to the stretching of intramural arteries induced by chronic long-termed transmural prolapse.

In the ulcerative type, there appeared marked edema in the submucosa, dilatation and winding of vessels, thickening of the arterial intima and media, suggesting an ischemic condition. Of course these vascular changes also arise as secondary changes following ulceration, so that similar changes appear in chronic open ulcers of the stomach. In those cases, the changes are almost limited to the areas just under

Table 4. Comparison between polypoid type and ulcerative type in order to discuss the natural history of MPS in the rectum

	Polypoid type	Ulcerative type
Site of lesion	Lower rectum, within 2 cm from the dentate line 83.6% (51/61)	Upper rectum, more than 2 cm distant from the dentate line 65.0%(13/20)
Histological stage	Low-grade fibromuscular stage 69.7% (46/66)	High-grade fibromuscular stage 47.6% (10/21)
	Vascular stage 30.3%(20/66)	Low-grade fibromuscular stage 47.6% (10/21)
Mucosal thickness*	Top area 1.96 mm	Marginal area 0.78 mm
	Surrounding area 0.75 mm	Surrounding area 0.58 mm
Morphological change	Glandular hyperplasia, marked	Ulcer formation with mild glandular hyperplasia
Rectal prolapse	Non-transmural (incomplete prolapse)	Transmural (complete prolapse)
Vascular change	Mild to moderate	Severe

*Excluding thickness of the muscularis mucosae

the ulcer bases. However, on lesions of MPS, the changes are noticed not only just under the polyps or the ulcers but also in the surrounding submucosa. Therefore, the possibility of secondary changes is rejected. In addition, the ulcerative type showed windings of dilated arteries, 100–150 μ m in diameter (which usually exist in the deeper part of the submucosa), in the upper part of submucosa. This fact strongly suggests that ulcerative types are performed by ischemia due to transmural rectal prolapse.

Histologically, normal intestinal arteries¹⁴⁾ penetrate the muscularis externa running from the subserosa, enter the submucosa and form a large plexus in the deep part of the submucosa. After that the plexus gives off branches directly toward the surface. Some of these break up into capillaries supplying the muscularis mucosae, and others form capillary networks throughout the mucosa and surrounding the glands. As the ulcerative types showed shallow ulcers in the depth of U1-II, the site of arterial disturbance is believed to be in the upper part of the submucosa at the periphery of the plexus.

There are several theories concerning the mechanism of formation of ulcerative type lesions, namely: 1) injury of vessels in the submucosa^{15–17)}; 2) trauma induced by self-interference of the patients¹⁸⁾; 3) ulceration of CCP.³⁾ The traumatic theory is hardly conceded because 65.0% (13/20) of the ulcerative type occurred in the rectum distant from the dentate line. Thomson and Hill¹⁸⁾ also admitted that the ulcerative type cases did not always have traumatic histories.

The ulceration theory of CCP is contradictory to the histological features. On the condition that the

ulcerative type is formed by ulceration of CCP, CCP ought to exist along the ulcer base. Supposing that it drops out of CCP, residual CCP ought to be observed under the ulcer base, because ulcers were shallow in the depth of U1-II. In our materials, 14.3% (3/21) of ulcerative types were accompanied by CCP, and CCP were rarely observed from the deep part of the mucosa to the upper part of the submucosa in ulcer-marginal areas. Furthermore there was no residual CCP under the ulcer bases. Fibromusculosis seen in CCP lesions was slight, so it is likely that CCP arises as a misplacement of crypts subsequent to ulceration and not as a cause of ulceration.

Acknowledgments. The author expresses her appreciation to Prof. Hitoshi Asakura, Prof. Hidenobu Watanabe, Ass. Prof. Teiichi Motoyama, Dr. Mituya Iwafuchi and Dr. Yoichi Ajioka for their instructive advice, and to Mr. Eiichi Koyama, Mr. Yukio Iwafuchi, Mr. Makoto Yoshida, Mrs. Yumiko Tamaki, Mrs. Kazuko Kojima and all the other members in the First Department of Pathology, Niigata University School of Medicine for their technical assistance.

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