

Imaging Findings of Mantle Cell Lymphoma Involving Gastrointestinal Tract

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Clinical manifestations and imaging findings of mantle cell lymphoma involving gastrointestinal tract were evaluated. The subjects were 7 cases of mantle cell lymphoma involving the gastrointestinal tract. All cases were pathologically confirmed in our hospital during the period from April 1994 to July 2000. Five patients were male and 2 were female, and their age ranged from 49 to 63 years (average 57.4). The objectives were: 1) characteristics and distribution of multiple polyposis, 2) presence, location and enhancement pattern of bowel wall thickening or mass formation, 3) presence of splenomegaly, 4) presence and location of abdominal lymph node enlargement, 5) involved extra-abdominal organs, 6) combined cancer and location, and 7) other findings. All mantle cell lymphomas occurred in elderly persons, over 40 years, and most showed multiple polyposis (6/7), bowel wall thickening or mass formation (6/7), lymph node enlargements (6/7) and extra-abdominal involvement (5/7). All cases of polyposis involved the small bowel and colon, and the size of the polyps ranged from 0.1-4.0cm. Four of 6 patients showed combined sessile and polypoid polyps, while the other 2 showed only sessile polyps. Most of or some of the polyps in 3 patients showed small central ulcerations. Most of the patients (5/6) showed an uncountable number of polyps. Polyposis was predominant in the rectum, ascending colon, rather than other sections in the colon, and the ileum were almost always involved by polyposis. Bowel wall thickening or mass formation developed exclusively in the ascending colon, rectum or ileum. Extra-abdominal involvement developed either simultaneously or nonconcurrently with gastrointestinal involvement. Some of patients showed splenomegaly (3/7), appendiceal enlargement (2/7), and intussusception (1/7), and some had associated adenocarcinomas (3/7).

Key Words: Abdomen, neoplasms, intestinal neoplasm, diagnosis, lymphoma, diagnosis

INTRODUCTION

Mantle cell lymphoma is a kind of B cell origin lymphoma and has been referred to by various names, including diffuse or nodular intermediate lymphocytic lymphoma, lymphocytic lymphoma of intermediate differentiation, centrocytic lymphoma, mantle zone lymphoma.¹⁻⁵ The unique histologic and biologic features of mantle cell lymphoma have renewed interest in this lymphoma subtype. Thus, in 1994, the European Lymphoma Task Force defined the diagnostic criteria of mantle cell lymphoma, conversely, this subtype of malignant lymphoma has been included as a distinct entity in the Revised European-American Classification of Lymphoid Neoplasm.^{6,7} Histologically it is characterized as proliferation of atypical lymphoid cells with preservation of germinal center. Occasionally diagnosis of mantle cell lymphoma has been difficult with only histologic findings. But accurate diagnosis of mantle cell lymphoma has become possible, because detection of cyclin D1 has recently been suggested to be the highly specific marker of mantle cell lymphoma.⁸

Mantle cell lymphoma has the following unique clinical features: development in elderly males with advanced disease, relatively aggressive clinical evolution, poor response to conventional therapeutic regimens and a short median survival duration.⁸⁻¹³ To our knowledge, imaging findings of mantle cell lymphoma proven by cyclin D1

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have been rarely reported after being determined as a distinct entity on the Revised European-American Classification of Lymphoid Neoplasm. So in this study, we evaluated the pattern and the imaging characteristics of gastrointestinal involvement of mantle cell lymphoma.

MATERIALS AND METHODS

Seven patients confirmed with mantle cell lymphoma from April 1994 to July 2000 were included in this study and all showed positive on cyclin D1. Age ranged from 49-63 years (mean 57.4) and 5 patients were male and 2 were female. All were pathologically confirmed by endoscopic biopsy or operation. Four of the 7 underwent surgery, because of combined adenocarcinomas in 3 patients and intussusception in the other. The operations were subtotal gastrectomy with small bowel resection, total gastrectomy, total colectomy with small bowel resection, and right hemicolectomy with small bowel resection, respectively.

We performed CT scan on 6 of the 7 patients, barium enema on 5, small bowel series on 2 and upper G-I study on 4 (Table 1). Spiral CT scan was performed on 5 patients, and conventional CT scan on 1. Spiral CT used was Somatom Plus S (Siemens, Erlangen, Germany), while Somatom 2 (Siemens, Erlangen, Germany) was used for conventional CT scan. Two phase scan (45 sec, 5 min delay) was done on spiral CT after bolus

injection of 130 ml of Ultravist 300 (Iopromide, Schering, Korea), while conventional CT scan was performed with continuous intravenous dripping of the contrast media.

The objectives were: 1) characteristics and distribution of multiple polyposis, 2) presence, location and enhancement pattern of bowel wall thickening or mass formation, 3) presence of splenomegaly, 4) presence and location of abdominal lymph node enlargement, 5) involved extra-abdominal organs, 6) combined cancer and location, and 7) other findings. Radiologic findings were evaluated by 2 radiologists in consensus. Lymph node enlargement was determined to be positive, when its short diameter was over 1 cm, and splenomegaly was determined when its length was longer than 11 cm. Bowel wall thickening or mass formation was considered when one side of the bowel wall was thickened by more than 1cm or when there was conglomerated soft tissue density more than 2cm in diameter on CT scan. For bowel evaluation, endoscopic findings and resected specimens were included in this study. In terms of the stomach, 6 of the 7 patients underwent either upper G-I study or endoscopy, and also for colon examination, all but one patient underwent either barium enema or colonoscopy. For the small bowel, the whole small bowel was evaluated with small bowel series in 2 patients, only the ileum was evaluated by retrograde filling of contrast during barium enema in 2 patients, and by resected

Table 1. Sex/Age, Performed Studies and Operations of the Patients

	Sex/age	G-fiber	UGI	SBS	Colonoscopy	BE	CT	OP
Case 1	M/49	+	+	+	+	+	+	-
Case 2	M/55	+	-	+	+	+	+	-
Case 3	M/63	+	+	-	+	+	+	+*
Case 4	M/58	+	+	-	+	-	+	+ [†]
Case 5	M/55	-	-	-	-	+	-	+ [‡]
Case 6	F/61	+	-	-	-	-	+	+ [¶]
Case 7	F/61	+	+	-	+	+	+	-

*Subtotal gastrectomy and small bowel resection.

[†]Total gastrectomy.

[‡]Total colectomy and small bowel resection.

[¶]Right hemicolectomy and small bowel resection.

specimens in the other 2.

RESULTS

Multiple polyposis

Multiple polyposis was seen in 6 of the 7 patients, in the small bowel and colon in 5, and in the stomach, small bowel and colon in 1 (Fig. 1), (Table 2).

The size of the polyps ranged from 0.1 - 4.0 cm. Four of the 6 patients showed combined sessile and polypoid polyps and the other 2 showed only sessile polyps. Most of or some of the polyps in 3 patients showed small central ulcerations. The number of polyps was uncountable in 5 patients and countable in the other.

Polyposis in the colon was seen in 6 patients; 5 of whom showed it in the whole colon but the other showed it only in the ascending colon, sigmoid colon and rectum. The distribution of

polyps was even in 1 patient, uneven in 4, and unable to be determined in the other because only right colectomy was done without evaluation of other portions of the colon. Among the 4 patients having uneven distribution, the rectum was the most involved portion in 2 and the ascending colon including cecum was the most involved in the other 2.

All of the 6 patients having polyposis in the small bowel showed them in the ileum. Two patients who underwent small bowel series showed polyposis in both the jejunum and ileum (Fig. 2). In the other 4 patients, we found polyposis in the ileum visualized by reflux of barium during barium enema or resected surgical specimens.

Bowel wall thickening or mass formation

Bowel wall thickening or mass formation was seen in all 6 patients who underwent CT scans; in the small bowel and colon in 3 patients, in the stomach in 1, in the small bowel in 1, and in the

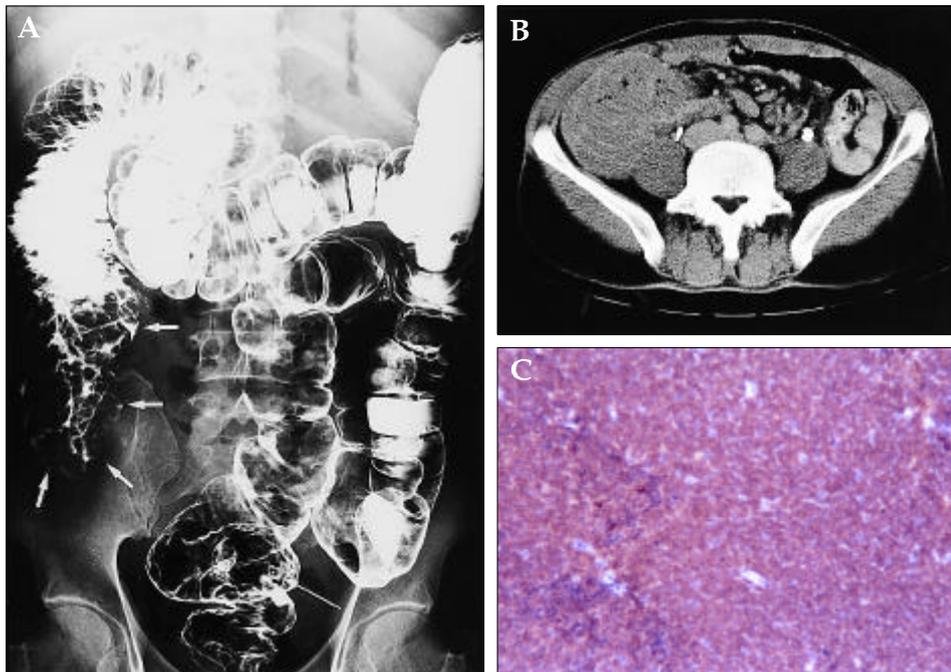


Fig. 1. Forty-nine year old male patient (case 1). (A) Barium enema shows marked fold thickening of the ascending colon (short arrows) with nearly complete obliteration of the lumen. Multiple round filling defects suggesting polyposis, measuring from 1.0 to 1.5 cm, are seen in whole colonic loop and most prominently in the rectum. All of the polyps are sessile and some of them have a central barium collected portion, suggesting small ulceration. One of the polyps containing central ulceration is indicated with a long arrow. (B) Contrast enhanced abdominal CT scan shows marked wall thickening in the ascending colon. Wall thickening shows poor enhancement, while proximal small bowel dilatation is not seen. Scattered air densities in the remained lumen are surrounded by ascending colon wall thickening. (C) The tumor cells show positive deep brown nuclear immunoreactivity for cyclin D1 immunostaining ($\times 200$).

Table 2. Characteristics of the Polyposis of Mantle Cell Lymphoma

	Involved organs	Number	Size	Shape	Central ulceration	The most involved portion in the colon
Case 1	St, Sm, Co	UC	0.3 - 1.5 cm	S	+	RE
Case 2	Sm, Co	UC	0.3 - 4.0 cm	S, P	-	RE
Case 3	Sm, Co	C	0.5 - 3.5 cm	S, P	-	AC
Case 4	-	-	-	-	-	-
Case 5	Sm, Co	UC	0.1 - 0.5 cm	S, P	+	E
Case 6	Sm, Co	UC	0.2 - 3.5 cm	S, P	-	?
Case 7	Sm, Co	UC	0.3 - 1.5 cm	S	+	AC

St, Stomach; Sm, Small bowel; Co, Colon; UC, Uncountable; C, Countable; S, Sessile; P, Polypoid; RE, Rectum; AC, Ascending colon; DC, Descending colon; E, Even distribution; ?, Not determinable because only right colectomy was done.

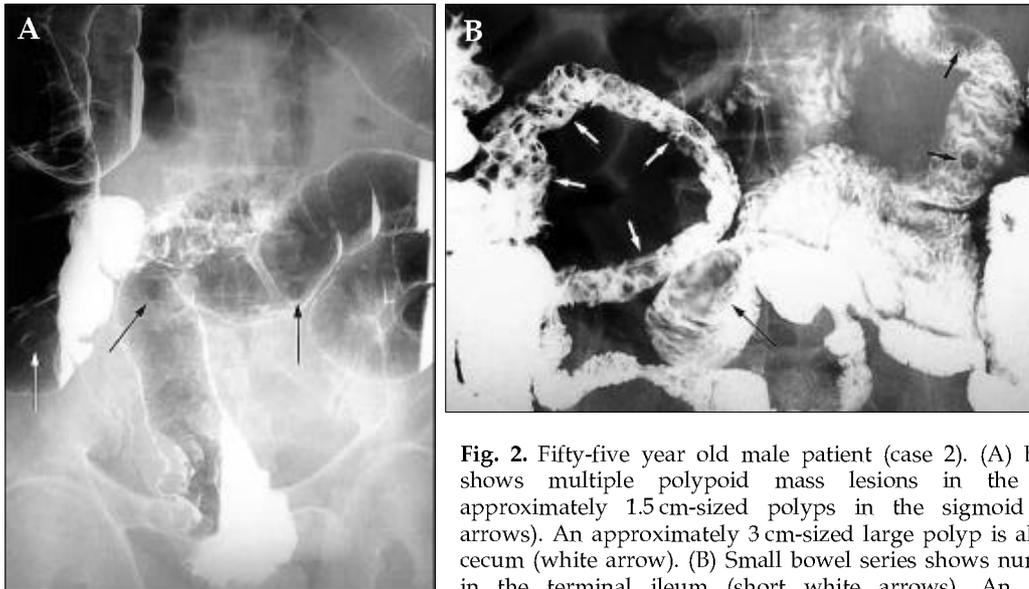


Fig. 2. Fifty-five year old male patient (case 2). (A) Barium enema shows multiple polypoid mass lesions in the rectum and approximately 1.5 cm-sized polyps in the sigmoid colon (black arrows). An approximately 3 cm-sized large polyp is also seen in the cecum (white arrow). (B) Small bowel series shows numerous polyps in the terminal ileum (short white arrows). An approximately 4 cm-sized large polyp in the ileum (long black arrow) and two polyps in the jejunum (short black arrows) can also be seen.

colon in the other (Table 3). With regard to the different sections of the bowel, the stomach was involved in 1 patient, and the small bowel and colon were involved in 4. All of the bowel wall thickening or mass formations in the small bowel loop were in the ileum. All 4 cases of colon wall thickening occurred in the ascending colon, and in 2 patients the thickening occurred simultaneously in the rectum. On enhanced CT, all of the bowel wall thickening or mass formation was homogeneous without definite enhancement, and there

was no definite obstructive bowel dilatation or adjacent mesenteric changes. Wall thickening of the lesions ranged from 1.5 to 4 cm, and the diameter of the mass formations ranged from 3 to 8.5 cm.

Splenomegaly, lymph node enlargement

Splenomegaly was seen in 3 of the 6 patients who underwent CT scan. Lymph node enlargements were seen in all 6 patients (Table 3). Lymph

Table 3. Other Abdominal and Extra-abdominal Manifestations of Mantle Cell Lymphoma

	Wall thickening or mass formation	Lymph node enlargement	Involvement of appendix	Spleno -megaly	Combined Adenocarcinoma	Extra-abdominal involvement
Case 1	Sm, Co	IP, RP	-	+	-	NN, NP, BM
Case 2	Co	RP	-	+	-	-
Case 3	Sm, Co	IP, RP	-	-	St	NN, WL
Case 4	St	IP	-	-	St	NN, IN, WL, BM, PB, MN
Case 5	?	?	+	?	Co	-
Case 6	Sm, Co	IP, RP	-	+	-	NN, WL, BM
Case 7	Sm	IP	+	-	-	NN, BM

St, Stomach; Sm, Small bowel; Co, Colon; IP, Intraperitoneal; RP, Retroperitoneal; NN, Lymph node of neck; NP, Nasopharynx; BM, Bone marrow; WL, Waldeyer's ring; IN, Inguinal lymph node; PB, Peripheral blood; MN, Mediastinal node; ?, Impossible to evaluate because CT was not taken.

nodes were homogeneous without central necrotic portion. The nodes were evident in both the intra-peritoneum and retroperitoneum in 3 patients, in only the intraperitoneum in 2, and in only the retroperitoneum in the other.

Extra-abdominal involvements

Five patients showed extra-abdominal involvement. One showed it before, two showed after and one at the same time as bowel involvement. The other patient showed it both before and simultaneously with bowel involvement of mantle cell lymphoma.

Nasopharynx, cervical lymph node and bone marrow were involved 8 years before involvement of the bowels in one patient. Tonsils and cervical lymph nodes were involved 2 years after in 1 patient, and tonsils, cervical lymph nodes and bone marrow were involved 6 months after bowel involvement in 1. One patient showed cervical lymphadenopathies and bone marrow involvement simultaneously with involvement of the bowel. In one patient, cervical lymph nodes had been involved 2 years before, and Waldeyer's ring, bone marrow, peripheral blood, lymph nodes of the neck, inguinal lymph node, and mediastinum were involved simultaneously with involvement of the bowel.

With regard to involved organs, cervical lymph node enlargements were seen in all 5 extra-abdominal involved patients, and bone marrow and

Waldeyer's ring were involved in 4 and 3 patients, respectively. Involvement of Nasopharynx, peripheral blood, mediastinal lymph node and inguinal lymph node was seen in 1 patient each (Table 3).

Combined cancer

Adenocarcinomas were combined in 3 patients, 2 with stomach cancer and the other with colon cancer (Table 3). One patient with stomach cancer showed lymphoma involvement of the small bowel and colon without stomach involvement. The cancer was located at the angle of the stomach showing Borrmann type II pattern; the size was about 4cm. One patient showed simultaneous stomach involvement of adenocarcinoma and lymphoma. The cancer was located in the antrum of the stomach showing ulceroinfiltrating mass, Borrmann type III pattern; the size was about 7cm. The other patient showed simultaneous involvement of adenocarcinoma and lymphoma in the colon as well as multiple polyposis in the colon composed of both adenomatoid and lymphomatous polyps (Fig. 3). An approximately 3cm-sized adenocarcinoma was present in the transverse colon showing an apple core appearance with near total obstruction.

Other findings

One patient manifested as intussusception (Fig. 4). Two patients had involved appendices, which

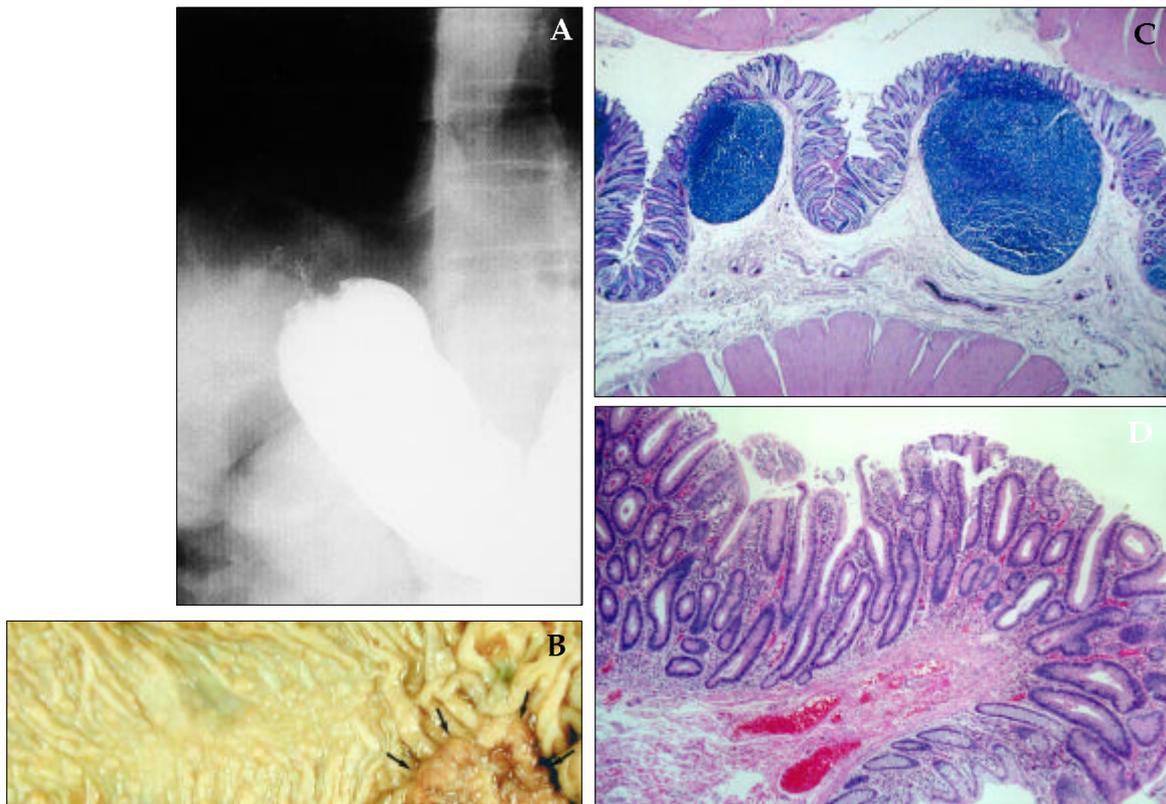


Fig. 3. Fifty-five year old male patient (case 5). (A) Barium enema shows a typical apple core appearance, suggesting adenocarcinomas in the transverse colon. (B) Resected colon specimen shows numerous scattered polypoid lesions and an ulceroinfiltrating adenocarcinoma, measuring 3.5 × 3 cm (arrows). (C) Microscopic finding of the polypoid lesions shows nodular aggregates of the centrocytes, suggesting a lymphomatous polyp (× 10, H & E). (D) Another polypoid lesion shows a well defined stalk, polypoid glandular architecture, and low grade epithelial dysplasia, suggesting an adenomatous polyp (× 40, H & E).

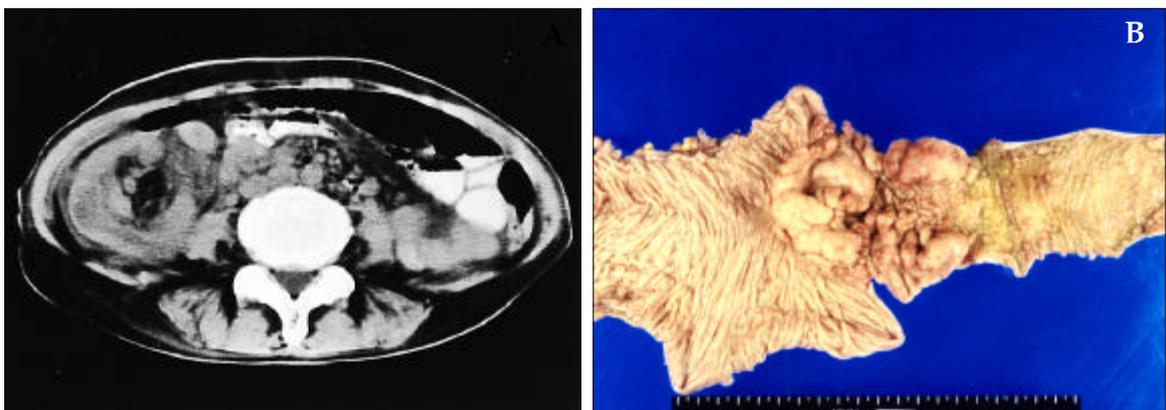


Fig. 4. Sixty-one year old female patient (case 6). (A) Abdominal CT scan shows target sign in the right lower quadrant, suggesting intussusception. The patient underwent right hemicolectomy, including distal ileum resection, and it was revealed to be ileocolic type intussusception induced by polypoid mass lesion in the ileocecal valve. (B) The mucosa of the ileocecal area shows polypoid grayish mass, measuring 3.5 cm in diameter. Multiple small polyps are also seen in the

was confirmed in one patient by surgery and in the other by radiologic findings and clinical manifestation, enlargement of the appendix on CT scan, extrinsic compression of the cecum, non filling of the appendix on barium enema and the absence of clinical symptoms related to appendicitis. One patient showed a huge mass, approximately 10cm in diameter, encircling the left internal iliac artery, severely compressing the bladder.

DISCUSSION

Mantle cell lymphoma develops as an advanced disease, with relatively aggressive clinical evolution, poor response to conventional therapeutic regimens and a short median survival duration.⁸⁻¹³ Therefore it should be differentiated from other types of lymphoma. Furthermore, it should not be misdiagnosed as adenomatous or hamartomatous polyposis because of lymphomatous polyposis, one of characteristic finding of it. Mantle cell lymphoma was classified as one of 11 types of B cell lymphoma in the Revised European-American Classification of Lymphoid Neoplasms on the basis of morphologic, immunophenotypic and genetic findings in 1994.⁷

It is a disease of middle-aged people, and rarely occurs in those under 50.³ The male to female ratio is 2.4 - 5:1, showing a male predominance, in contrast to the ratio of chronic lymphoid leukemia and small sized Lymphoma which is 1.47 - 2.5:1.^{3,14,15} In this study, 6 of the 7 patient were over 50 and the male to female ratio was 5:2.

Gastrointestinal involvement of mantle cell lymphoma is 10 - 20%, and the most frequent finding is multiple lymphomatous polyposis. Common associated findings are mass formation and lymph node enlargement.^{8,16,17} Multiple lymphomatous polyposis can develop not only in mantle cell lymphoma, but also in follicular lymphoma and MALT (marginal zone B cell lymphoma of mucosal associated type).^{17,18} Furthermore, it has been reported that mantle cell lymphoma was developed without multiple lymphomatous polyposis.¹⁹ In this study, multiple lymphomatous polyposis was found in 6 of 7 patients; the other showed only stomach wall

thickening. All the patients who underwent CT scan showed bowel wall thickening or mass formation, and furthermore, all the patients showed lymph node enlargements.

Mantle cell lymphoma shows extra-nodal organ involvement, and these organs are gastrointestinal tract, bone marrow, spleen, Waldeyer's ring, liver, CNS, peripheral blood, lung, pleura, ovary, parotid gland, skin and breast.^{8,10,20} In this study, the involvement of bone marrow in 4 patients, Waldeyer's ring in 3, nasopharynx in 1, and peripheral blood in 1 were pathologically confirmed. Splenomegaly was observed on CT scan in 3 patients.

Three adenocarcinomas were combined with mantle cell lymphoma in this study; 2 developed in the same portion of the bowel where the lymphoma was involved and the other developed in a different portion of the bowel. It is very rare that adenocarcinoma and non-epithelial tumor developed simultaneously, but there are a few reports of lymphoma or leukemia developing with adenocarcinomas.^{21,22} To our knowledge, there are only two reports about the simultaneous development of adenocarcinoma with multiple lymphomatous polyps or mantle cell lymphoma. Hopster reported a case of multiple lymphomatous polyposis and adenocarcinoma simultaneously in the colon²³ and Jeong reported a case of adenocarcinoma of the stomach synchronously developed with gastro-intestinal polyposis involving the stomach, ileum and colon.²⁴ We cannot predict the relationship between adenocarcinoma and mantle cell lymphoma from only these 2 previous case reports and the 3 in this study. Nevertheless, the possibility of a certain relationship between these two diseases is suggested by the simultaneous involvement of two different diseases in the same organ in 4 of the 5 cases. This hypothesis is strengthened by the one case in this study, involving the colon, which showed multiple polyps mixed with lymphomatous polyps and adenomatous polyps as well as the simultaneous development of adenocarcinoma and mantle cell lymphoma. Further study to confirm this relationship is necessary.

Mantle cell lymphoma is originated from the cells located in the mantle zone of the lymph node. In morphology, it has slightly irregular,

inconspicuous nucleoli, and the absence of both large transformed (noncleaved) cells and proliferation centers. Immunophenotypically, it coexpresses pan B-cell antigens (CD19, CD20, CD22) and CD5, a pan T-cell antigen. The above mentioned morphologic and immunophenotypical findings cannot be the characteristic findings for a diagnosis of mantle cell lymphoma, because of subjective determination by observers and overlapping findings with other types of lymphoma. But recently, cyclin D1 has been used as a useful marker for diagnosis of mantle cell lymphoma. Cyclin D1 was known to be closely related to the genetic characteristics of mantle cell lymphoma. Most cases of mantle cell lymphoma are associated with the chromosome translocation characterized as t (11;14)(q13;q32), resulting in rearrangement of the bcl-1 gene locus and overexpression of the cyclin D1 gene.^{8,10} Although there are a few reported cases of detection of cyclin D1 in aggressive variants of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and a small percentages of cases of multiple myeloma, cyclin D1 may be a highly specific marker of mantle cell lymphoma because it is expressed in virtually all of these tumors.⁸ All cases included in this study, were positive in cyclin D1.

Multiple lymphomatous polyposis is difficult to differentiate from adenomatous polyposis, either by radiologic or endoscopic findings. If polyposis is found in radiologic or endoscopic evaluation, adenomatous polyposis should be considered first, rather than lymphomatous polyposis, because of its high incidence. But the possibility of multiple lymphomatous polyposis, one manifestation of mantle cell lymphoma, has to be considered when it is found in elderly persons, especially when the patient shows predominant polyposis in the ascending colon, rectum, compared with other sections of the colon, polyposis in the ileum, bowel wall thickening or mass formation in the ascending colon or ileum, wide spread lymph node enlargements, splenomegaly, or preexistent or simultaneously developed extra-abdominal involvement. Combined bowel wall thickening or mass formation would be helpful to differentiate lymphomatous polyposis from adenomatous polyposis, but diagnosis has to be

made carefully, because adenocarcinoma can be associated with adenomatous polyposis.

In conclusion, most mantle cell lymphomas occurred in elderly persons and showed multiple polyposis, bowel wall thickening or mass formation, lymph node enlargements and extraabdominal involvement. Polyposis in the colon was predominantly in the ascending colon or rectum, and the ileum was almost always involved by polyposis. Bowel wall thickening or mass formation developed exclusively in the ascending colon, rectum or ileum. Extra-abdominal involvement developed simultaneously or nonconcurrently with gastrointestinal involvement. Some patients showed splenomegaly and appendiceal enlargement, and may have associated adenocarcinomas.

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