

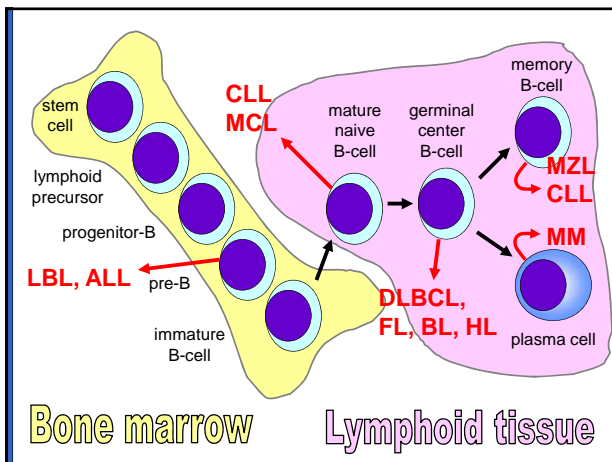
Endoscopic Diagnosis of the GI Lymphoma

Jun Haeng Lee, M.D.

Department of Medicine, Samsung Medical Center,
Sungkyunkwan University School of Medicine, Seoul, Korea

Diagnosis of lymphomas

Biologically rational classification	Clinically useful classification
Diseases that have distinct <ul style="list-style-type: none"> • morphology • immunophenotype • genetic features • clinical features 	Diseases that have distinct <ul style="list-style-type: none"> • clinical features • natural history • prognosis • treatment



WHO classification (2001)


- B cell neoplasm ← *mature field*
 - Precursor B-cell lymphoblastic leukemia/lymphoma
 - Mature B-cell neoplasm
- T and NK cell neoplasm ← *young field*
 - Precursor T-cell lymphoblastic leukemia/lymphoma
 - Mature T-cell and NK cell neoplasm

B-cell neoplasms of GI tract

- MALT lymphoma
- Diffuse large B-cell lymphoma (DLBCL)
- Follicular lymphoma
- Mantle cell lymphoma
- Burkitt lymphoma

T-cell neoplasms of GI tract

- Adult T-cell leukemia/lymphoma (HTLV-1+)
- Enteropathy-type intestinal T-cell lymphoma
- Anaplastic large cell lymphoma, T- or null cell type
- NK/T-cell (angiocentric) lymphoma
- *Peripheral T-cell lymphoma, unspecified*



GI lymphoma의 임상상과 분포

Clinical manifestations of GI lymphoma

- Presenting symptoms are various.
- Some lymphomas are very difficult to diagnose.
- High index of suspicion is required.

Non-Hodgkin's lymphoma of the GI tract

- Danish Lymphoma Study Group

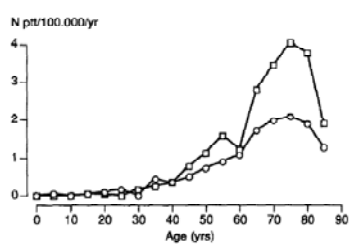



Fig 1. Mean annual age-specific IRs of gastric (□) and intestinal (○) NHL in western Denmark.

d'Amore. JCO 1994;1994;12:1673-1684

Frequency of organ involvement

GI lymphoma	Stomach	Small intestine	Colon
DLBCL	55%	55%	60%
MALToma	40%	20%	15%
Burkitt's lymphoma	3%	5%	15%
PTCL	<1%	15%	10%
Mantle cell lymphoma	< 1%	<1%	1%
Follicular lymphoma	< 1%	<1%	1%

Modified from J Am Coll Surg 2003;197(1):127-141



GI lymphoma의 내시경 진단

Endoscopic diagnosis of GI lymphoma

- Relatively low incidence
- Variable endoscopic findings in the particular type of lymphoma. → **BUT, think about the gastric adenocarcinoma!**
- Some entities has highly specific findings.
- Close consultation to the pathologist is the key.
 - “There is lymphoid hyperplasia with mild to moderate cellular atypism, but these findings are not sufficient for the pathologic diagnosis of GI lymphoma.”

Morphology and histology


Table 2 장관 림프관 악성 림프종에 있어서의 조직 분류와 육안형의 관련

조직형	육안형					합계
	윤기	궤양	MLP	미만	기타	
Low-grade B-cell lymphoma						
MALT lymphoma	15	10	1	2*	5	33(29)
Follicular lymphoma	4	1	4	0	0	9(8)
Mantle cell lymphoma	0	0	2	0	0	2(2)
High-grade B-cell lymphoma						
Diffuse large B-cell lymphoma**	13	29	0	1	3	46(41)
Burkitt lymphoma	4	2	0	0	1	7(6)
Lymphoblastic lymphoma	1	0	0	1	1	3(3)
T-cell lymphoma	1	6	0	4	2	13(12)
합계	38	48	7	8	12	113

*: Immunoproliferative small intestinal disease. **: MALT 림프종 병변 예를 포함한다.

▲ 병력과 육안조건이 감별진단에 어느 정도 도움이 되지만 결정적이지는 않다

위와 정, 2006



GI lymphoma의 진단은 지연될 수 있다

Primary Colon Lymphoma in Korea: A KASID (Korean Association for the Study of Intestinal Diseases) Study

Y.-H. KIM, MD,* J. H. LEE, MD,* S. K. YANG, MD,† T. I. KIM, MD,‡ J. S. KIM, MD,§ H. J. KIM, MD,* J. I. KIM, MD,§ S. W. KIM, MD,|| O. KIM, MD,** I. K. JUNG, MD,** S. A. JUNG, MD,†† M. K. JUNG, MD,‡‡ H. S. KIM, MD,§§ J. MOYUNG, MD,† W. H. KIM, MD,|| C. RHEE, MD,* K. Y. CHOI, MD,|| S. S. SONG, MD,|| J. H. HYUN, MD,||§§ and Y. I. MIN, MD||

TABLE 2. FIRST IMPRESSION OF THE ENDOSCOPICIST DURING COLONOSCOPY

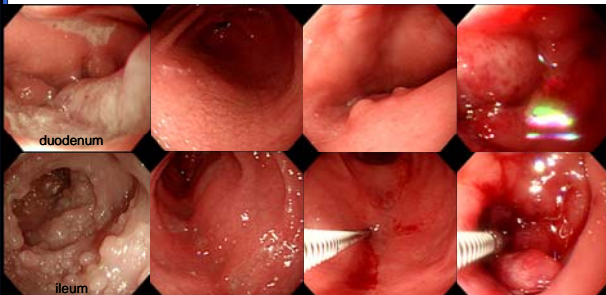
Impression	B-cell lymphomas (n = 63)	T-cell lymphomas (n = 15)	All (n = 78)
Colon cancer	46	2	48 (61.5%)
Colon lymphoma	8	4	12 (15.4%)
Tuberculosis	3	3	6 (7.8%)
Infectious colitis	2	1	3 (3.8%)
Ulcerative colitis	0	3	3 (3.8%)
Crohn's disease	0	1	1 (1.3%)
Others	4	1	5 (6.4%)

Kim. Dig Dis Sci 2005;50:2243-2247

Delayed diagnosis of colon lymphoma was seen in T cell lymphomas (n=6, 35.3%)

Age /Sex	Symptoms	Initial impression	Initial management	Time to final diagnosis
24/M	Abdominal pain	UC with perforation	Persistent Sx after operation	3 months
66/F	Frequent loose stool	UC	Persistent Sx after steroid	13 months
45/M	Hematochezia	Intestinal tuberculosis	Weight gain after anti-tbc	12 months
67/M	Frequent loose stool	Intestinal tuberculosis	Weight gain after anti-tbc	6 months
33/M	Abdominal pain	Crohn's Disease	Medication	15 months
30/M	Diarrhea	r/o amebiasis	Medication	6 months

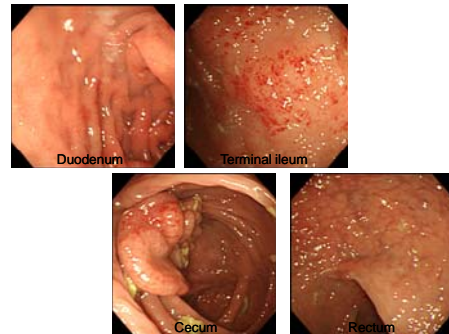
43 YO female with chronic diarrhea, loss of weight (15 kg) & night sweat for 6 months




Initial diagnosis: chronic and acute duodenitis with ulceration (duodenum)
chronic and acute ileitis (ileum)

Final diagnosis: peripheral T cell lymphoma (stomach, duodenum, ileum)

치질 수술 전 대장내시경 이상 소견으로 의뢰된 환자의 상부위장관 내시경 소견은 매우 경미하였다



All biopsies: mantle cell lymphoma, CD20 (+), CD3 (-), Cyclin D1 (+), IgH gene rearrangement (monoclonal)



DLBCL of the Stomach

- ### DLBCL of the stomach
- The commonest of the NHL.
 - The median age: mid 60s.
 - Rapidly progressive adenopathy.
 - Extranodal involvement: approximately 40%
 - Bone marrow involvement: 10% to 20%
 - Involving the bone marrow, testes, and paranasal sinuses and elevated LDH at presentation → the risk of disease involving the CNS

- ### Endoscopic findings described in the textbook (Yamada eds.)
- Grossly indistinguishable from adenocarcinoma
 - Actually a diffusely infiltrating submucosal lesion
 - May present as a polypoid lesion with ulcerations
 - Like other submucosal lesions, the overlying mucosa may traverse the mass as a characteristic bridging fold.
 - More likely than other cancers to present with diffuse infiltration and enlarged rugal folds.

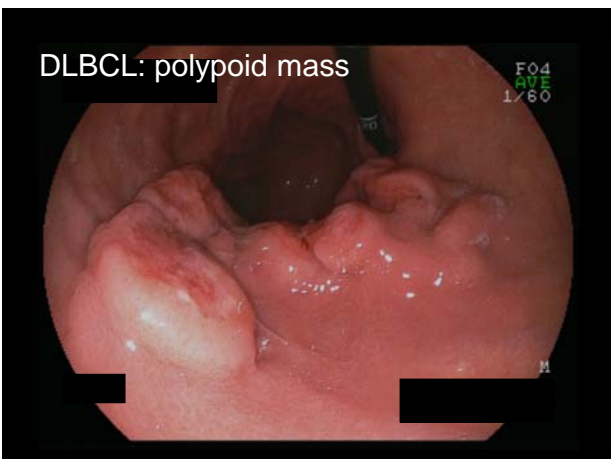
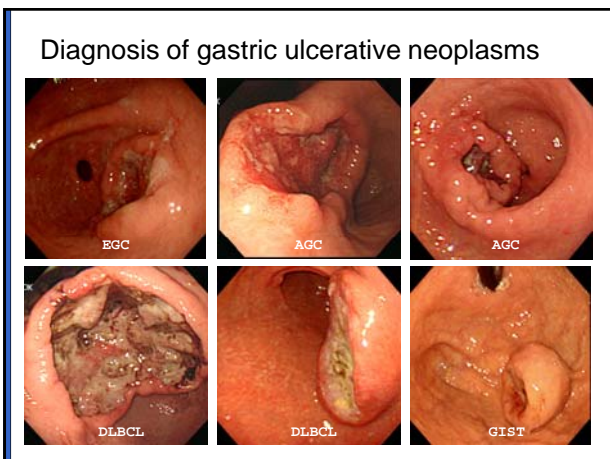
TABLE II Endoscopic findings in primary non-Hodgkin's lymphoma of the stomach according to the grade of malignancy related to the MALT concept

	Low grade malignancy (n=51)	High grade malignancy (n=63)	p Value	Total (n=114)
Main patterns:				
Ulceration:				
large	17 (31)	22 (35)	0.69*	38
multiple, small	10 (20)	7 (11)		17
Diffuse infiltration	9 (18)	9 (14)		18
Polypoid mass	13 (25)	21 (33)		34
Not classified	2 (4)	4 (6)		7
Endoscopic diagnosis:				
Malignancy:	24 (47)	45 (71)	0.008*	69
NHL	9 (18)	8 (13)		17
Carcinoma	13 (25)	25 (40)		38
NHL or carcinoma	2 (4)	12 (19)		14
Benign condition:	27 (52)	28 (28)		45
Benign ulcer	17 (33)	10 (16)		27
Gastritis, erosions	4 (8)	0 (0)		4
Other	6 (12)	8 (13)		14
Histological diagnosis:				
NHL on first biopsies	38 (75)	50 (79)		88
NHL on repeated biopsies	11 (22)	5 (8)	0.040†	16
Carcinoma, later NHL	0 (0)	5 (8)		5
NHL on resection material	2 (4)	3 (5)		5

* χ^2 test, †Fisher's exact test. Figures in parentheses are percentages.

Ulceration(s) → Mass lesion(s) → Diffuse infiltration

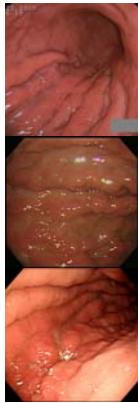
Taal. Gut 1996;39:556-561



Primary NHL of the stomach - diffuse type



Figure 5: The diffuse type of NHL, with thickened, nodular, sometimes giant folds, sometimes difficult to differentiate from linitis plastica.



Taal. Gut 1996;39:566-561

Role of EUS in GI lymphoma

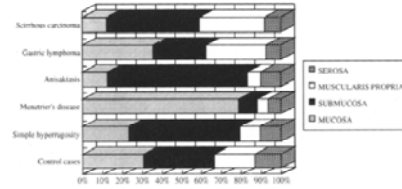
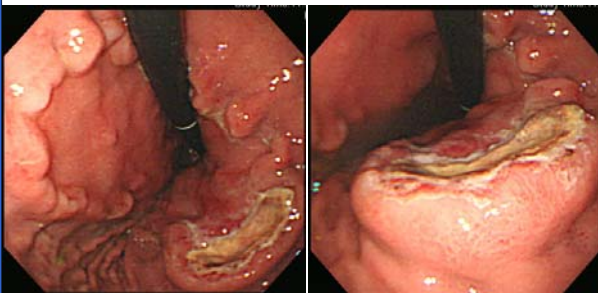


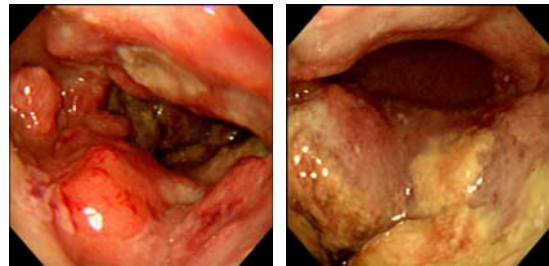
Figure 9. Percentage of total thickness of individual layers in the patient and control groups. Note that the muscularis propria is thickened only in the malignant diseases. There is notable thickening of the mucosa in Ménétrier's disease, and of the submucosa in anisakiasis.

Songur. GIE 1995;41:468-474

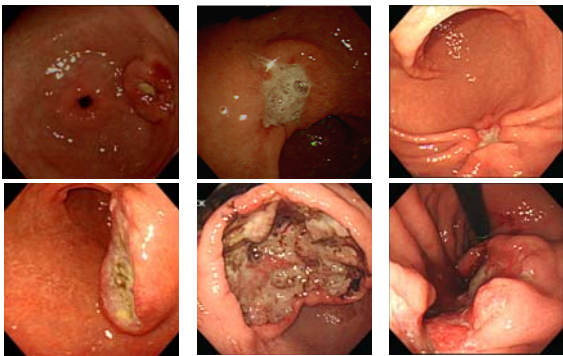
This extensive DLBCL expands well.



This stomach with DLBCL did not expand well by air infusion.



In most DLBL cases, we don't need to evaluate the finding of air expansion.



Does chemotherapy increase the risk of perforation in patients with GI lymphomas?

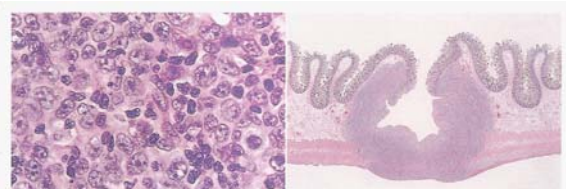


Fig. 6 Histological appearance of diffuse large B-cell lymphoma.
a 수포상(水泡狀) 크로마틴과 뚜렷한 핵소체를 지닌 대형 이형 림프구가 미만성으로 증식하고 있다.
b 종양 세포는 골수모양으로 조밀하게 공장 장막까지 침윤하여 깊은 궤양을 형성하고 있다.

위와 장. 2006

Leukemia & Lymphoma, September 2005;

Management of gastric lymphoma

D. Y. OH, I. S. CHOI, J. H. KIM, M. N. K. KIM
 Department of Internal Medicine, Seoul National College of Medicine, Seoul, Korea

Abstract
 Purpose: The optimal therapy for gastric lymphoma is unclear. We undertook to investigate whether gastric lymphoma patients and methods. A total of 58 patients (M/41) at Seoul National University Hospital at MALToma was excluded from the pathologic results. All patients received initially anti-neoplastic B symptoms were present in 41 (70%). Diffuse large B-cell lymphoma (DLBCL) was 46.7%. The interim 22.4%, high-intermediate in 15.5% and high in and the partial response rate was 12.2%. (ovine response, a further complete response was 100%, the maximum complete response to (III, IV). Median overall survival was 47.4 months. The 5-year survival rate was 46%. Bleeding as a complication was not necessary. Organ preservation performed due to a partial clinical response so it revealed that only 10% had a significant difference. **Conclusion:** Gastric lymphoma except MALT.

Keywords: Gastric lymphoma, chemotherapy.

Toxicities of chemotherapy
 Toxicities of chemotherapy are shown in Table IV. Grades 1 and 2 neutropenia were observed in 19 out of a total of 224 cycles. Neurotoxicity was found in 8.8% and pulmonary toxicity in 3.2%. Microbiologically-documented infection occurred in 5.6% of patients. Bleeding complication developed in 3 out of the 58 patients (5.6%). Of these 3 patients, 1 was controlled by percutaneous transarterial embolization and in the other 2 patients, conservative management was enough to stop the bleeding. One of the most concerning complications associated with chemotherapy in gastric lymphoma is perforation occurring during or after chemotherapy but, in the study, **perforation did not occur.**

Stomach preservation was possible in 57 of the 58 patients. In the single exception, the mass remained after 6 cycles of COPBLAM-V and he underwent surgery, but the operative specimen revealed pathologic CR.

Oh (SNUH). *Leuk Lymphoma* 2005;46:1329-1335

DLBCL of the stomach (M/41)

- detected during screening endoscopy

DLBCL of the stomach (M/41)

- detected during screening endoscopy

Perforation after chemotherapy

Colon Lymphomas

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Primary Colon Lymphoma in Korea: A KASID (Korean Association for the Study of Intestinal Diseases) Study

Y-H KIM, MD*†, H. LEE, MD** S. K. YANG, MD†, J. I. KIM, MD,‡, J. S. KIM, MD,§, H. J. KIM, MD,¶, J. I. KIM, MD,||, S. W. KIM, MD,||, J. O. KIM, MD,**, I. K. JUNG, MD,** S. A. JUNG, MD,†† M. K. JUNG, MD,‡‡ H. S. KIM, MD,§§ S. J. MYUNG, MD,§§ W. H. KIM, MD,||, J. C. BHRLE, MD,§§ K. Y. CHOI, MD,§§ S. SOUNG, MD,§§ J. H. HWUN, MD,§§ and Y. I. MIN, MD†

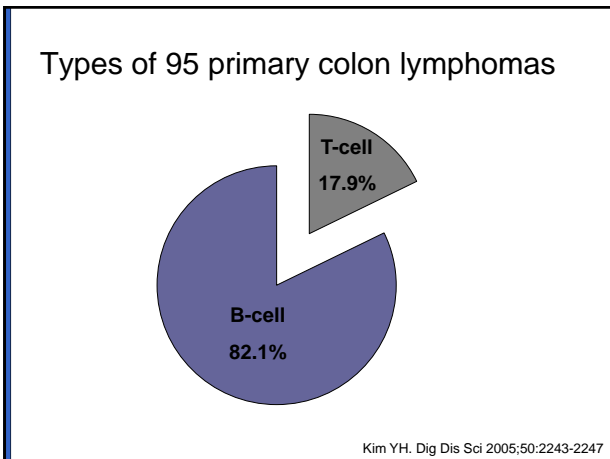


TABLE 1. CLINICAL FEATURES OF COLORECTAL LYMPHOMAS OF T-CELL OR B-CELL ORIGIN

Variable	B-cell lymphomas (n = 78)	T-cell lymphomas (n = 17)	P value
Age (years)	52.9 ± 15.9	42.8 ± 13.0	0.016
Gender (male:female)	52:26	12:5	NS
Fever	0 (0.0%)	6 (35.3%)	<0.001
Weight loss	25 (32.1%)	6 (35.3%)	NS
Night sweat	2 (2.6%)	1 (5.9%)	NS
Anorexia	15 (19.2%)	6 (35.3%)	NS
Nausea	9 (11.5%)	5 (29.4%)	NS
Vomiting	4 (5.1%)	3 (17.6%)	NS
Diarrhea	14 (17.9%)	8 (47.1%)	0.010
Constipation	12 (15.4%)	0 (0.0%)	NS
Abdominal pain	68 (87.1%)	8 (47.1%)	<0.001
Hematochezia/melena	10 (12.8%)	9 (52.9%)	<0.001
Palpable mass	27 (34.6%)	3 (17.6%)	NS
Tenderness	31 (39.7%)	5 (29.4%)	NS
Anemia (hemoglobin <12 g/dl)	46 (59.0%)	9 (52.9%)	NS
Leukocytosis (WBC <10,000)	11 (14.1%)	2 (11.8%)	NS
Diffuse involvement	0 (0.0%)	10 (58.8%)	<0.001
Intussusception	24 (30.8%)	1 (5.9%)	0.035
Perforation	3 (3.8%)	4 (23.5%)	0.005
Fistula	3 (3.8%)	0 (0.0%)	NS

Kim YH. *Dig Dis Sci* 2005;50:2243-2247

First impression of the endoscopists

Impression	B cell (n=63)	T cell (n=15)	All (n=78)
Colon cancer	46	2	48 (61.5%)
Colon lymphoma	8	4	12 (15.4%)
Tuberculosis	3	3	6 (7.8%)
Infectious colitis	2	1	3 (3.8%)
Ulcerative colitis	0	3	3 (3.8%)
Crohn's disease	0	1	1 (1.3%)
Others	4	1	5 (6.4%)

✓ Impression of malignant disease:

B cell: 87.3%, T cell: 40.0% (p<0.001)

Kim YH. Dig Dis Sci 2005;50:2243-2247

Endoscopic classification of ileocecal lymphoma



Figure 1. Colonoscopic view of fungating type ileocecal lymphoma with smooth, lobulated surface.



Figure 2. Colonoscopic view of ulcerative type ileocecal lymphoma showing large ulcer without definite mucosal elevation.

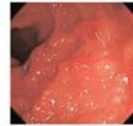


Figure 3. Colonoscopic view of infiltrative type ileocecal lymphoma with a diffuse nodular surface but no definite ulcer or mass.



Figure 4. Colonoscopic view of ulcerofungating type ileocecal lymphoma showing fungating mass with ulceration.



Figure 5. Colonoscopic view of ulceroinfiltrative type ileocecal lymphoma showing diffuse ulcerating lesion with shallow ulceration.

Myung. Gastrointest Endosc 2003;57:343-347

Classification by gross findings

Classification	B cell (n=63)	T cell (n=15)	All (n=78)
Fungating	34 (54.0%)	2 (13.3%)	36 (46.2%)
Ulcerative	3 (4.8%)	7 (46.7%)	10 (12.8%)
Infiltrative	5 (7.9%)	0	5 (6.4%)
Ulcerofungating	17 (27.0%)	1 (6.7%)	18 (23.1%)
Ulceroinfiltrative	4 (6.3%)	5 (33.3%)	9 (11.5%)

Kim YH. Dig Dis Sci 2005;50:2243-2247

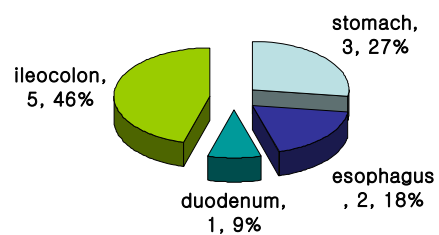
Comparison between B- and T-cell lymphomas

Classification	B cell (n=78)	T cell (n=17)	P-value
Diffuse involvement	0	10 (58.8%)	< 0.001
Intussusception	24 (30.8%)	1 (5.9%)	0.035
Perforation	3 (3.8%)	4 (23.5%)	0.005
Fistula	3 (3.8%)	0	0.411

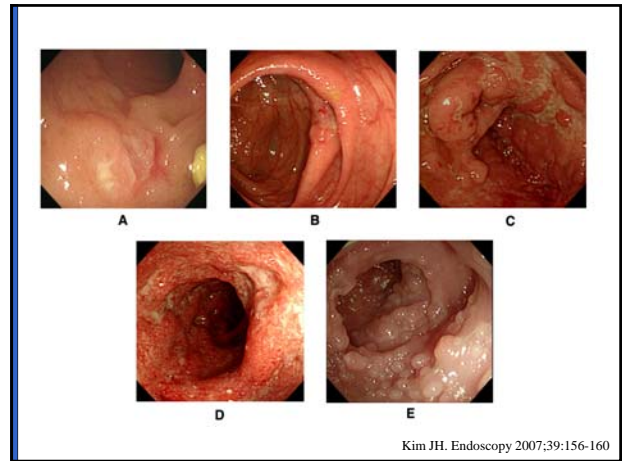
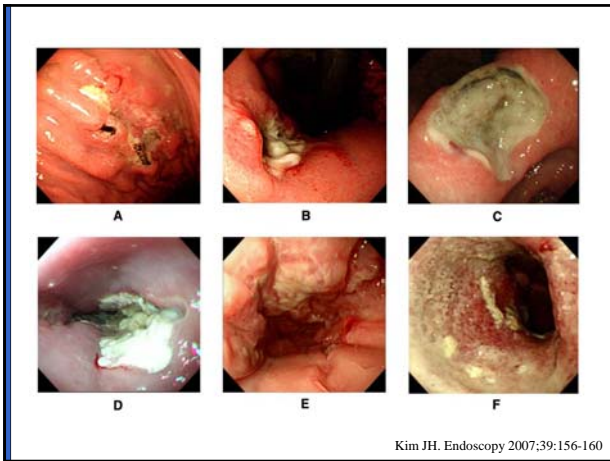
Kim YH. Dig Dis Sci 2005;50:2243-2247

Primary GI NK/T cell Lymphomas

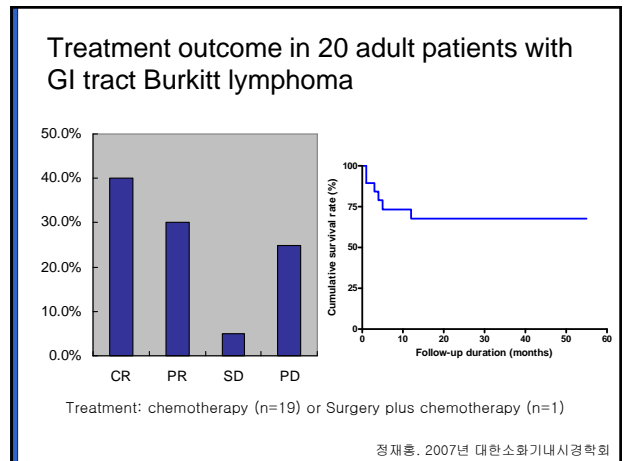
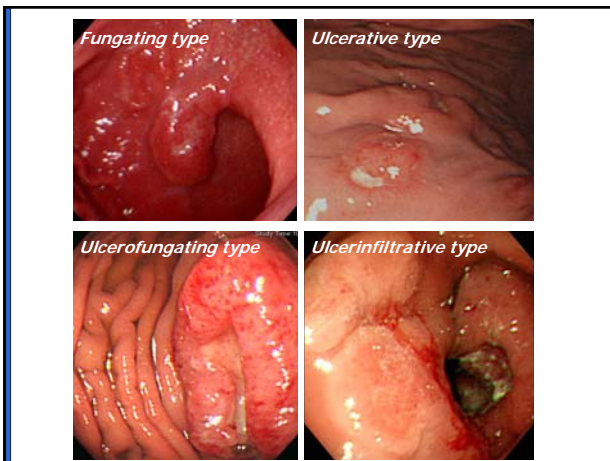
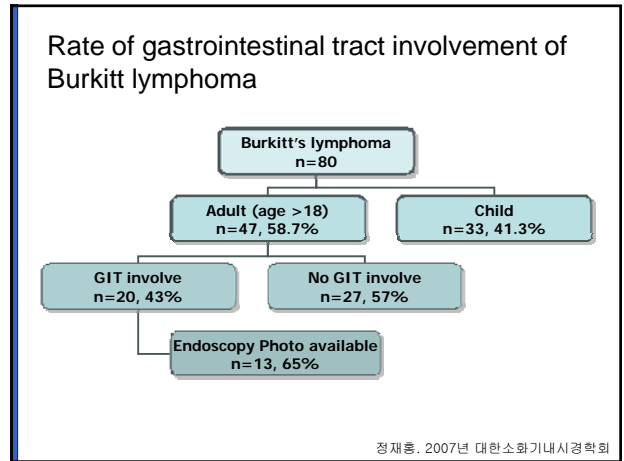
The anatomic locations of primary lesions in GI NK/T cell lymphoma (n=14)




Kim JH. Endoscopy 2007;39:156-160



GI Burkitt Lymphoma
- A single center experience -





Capsule Endoscopy for Small Bowel Lymphoma

Capsule endoscopy for GI lymphoma




Figure 2 Capsule endoscopy images showing small bowel lymphoma features: villous atrophy, ulcerations, and flattened villi.




Figure 3 Capsule endoscopy images showing small bowel lymphoma features: ulcerations and flattened villi.

Table 2 Features of primary intestinal lymphoma in seven patients (multiple features were possible in each patient)

Morphology	Patients (n)
Villous atrophy	7
Ulcerations	4
Flattened villi	1
Necrosis	4

Table 3 Features of small-bowel involvement in 20 patients with gastric lymphoma (multiple features were possible in each patient)

Morphology	Patients (n)
Villous atrophy	2
Ulcerations	0
Flattened villi	3
Necrosis	2

Flieger. Endoscopy 2005;37:1174-1180

CE images in a single patient




Figure 4 Capsule endoscopy images in a single patient. a White villi. b White villi in red. c Erosions in close proximity to white villi. d Focal erythema. e Erosions with fibrin. f Serrated, proliferated ulcerations.

Flieger. Endoscopy 2005;37:1174-1180

Summary: Diagnosis of GI lymphomas

- Understanding of the characteristics of each diseases
- High index of suspicion
- Emphasis on the clinical history and endoscopic findings
- Strategy for cases with negative biopsy result

경청해 주셔서 감사합니다