

Gastro intestinal lymphomas

R3.정세진

GI lymphoma introduction

- 정의

위장관 및 이와 관련된 배액부위 림프절에 국한, 간이나 비장 및 기타 림프절 침범이 없고, 단순흉부촬영상이 정상, 말초혈액검사의 백혈구가 정상인 경우.

- Table 4.** Relative frequency of site of involvement in NHL and comparison with the data in 1998

Site	1998 ⁸		2010		Age (yr)/Sex ratio (M/F)
	No. of cases	%	No. of cases	%	
Lymph node	538	36.7	1,157	30.4	54/1.4
Extranodal	926	63.3	2,650	69.6	53/1.2
Waldeyer's ring	210	10.2	340	9.0	56/1.7
Nasal and PNS	81	5.5	221	5.8	52/1.7
Oral cavity	43	2.9	72	1.9	59/1.5
Gastrointestinal	303	20.7	1,112	29.2	55/1.2
Stomach	196	13.4	761	20.0	56/1.0
Small intestine	60	4.1	209	5.5	54/1.6
Large intestine	47	3.2	145	3.8	56/1.4

Lymphoma classification

• 2001년 WHO

- 형태학적 소견, 세포의 기원(면역표현형으로 결정), 임상소견과 유전자형(핵형, 바이러스 유전자 존재)까지 고려한 새로운 분류를 제안

Table 1. WHO Classification of Lymphoid Neoplasms, 4th Edition⁹

B cell neoplasms

Precursor B-cell neoplasm

- B-lymphoblastic leukemia/lymphoma

Mature (peripheral) B-cell neoplasms

- Chronic lymphocytic leukemia/small lymphocytic lymphoma
- B-cell prolymphocytic leukemia
- Lymphoplasmacytic lymphoma
- Splenic marginal zone B-cell lymphoma
- Hairy cell leukemia
- Splenic lymphoma/leukemia, unclassifiable
- Plasma cell myeloma/plasmacytoma
- Heavy chain diseases
- Extranodal marginal zone B-cell lymphoma of MALT type^{a)}
- Nodal marginal zone B-cell lymphoma
- Follicular lymphoma^{a)}
- Primary cutaneous follicle center lymphoma
- Mantle cell lymphoma^{a)}
- Diffuse large B-cell lymphoma (DLBCL)^{a)}
- Burkitt lymphoma^{a)}
- B-cell lymphoma, unclassifiable

T-cell and NK-cell neoplasms

Precursor T-cell neoplasm

- T-lymphoblastic leukemia/lymphoma

Mature (peripheral) T/NK-cell neoplasms

- T-cell prolymphocytic leukemia
- T-cell large granular lymphocytic leukemia
- Aggressive NK-cell leukemia
- Systemic EBV positive T-cell lymphoproliferative disease of childhood
- Hydra vacciniforme-like lymphoma
- Adult T-cell lymphoma/leukemia (HTLV 1+)
- Extranodal NK/T-cell lymphoma, nasal type^{a)}
- Enteropathy-type T-cell lymphoma^{a)}
- Hepatosplenic T-cell lymphoma
- Subcutaneous panniculitis-like T-cell lymphoma
- Mycosis fungoides/Sézary syndrome
- Primary cutaneous anaplastic large cell lymphoma
- Primary cutaneous aggressive epidermotropic CD8 positive cytotoxic T-cell lymphoma
- Primary cutaneous gamma-delta T-cell lymphoma
- Primary cutaneous small/medium CD4 positive T-cell lymphoma
- Peripheral T-cell lymphoma, not otherwise characterized^{a)}
- Angioimmunoblastic T-cell lymphoma
- Anaplastic large cell lymphoma, ALK-positive
- Anaplastic large cell lymphoma, ALK-negative

* 호지킨 림프종 : 매우 드물음

GI Lymphoma classification

B-cell neoplasms

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

T-cell neoplasms

- 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**

Relative frequency of the histologic subtypes in NHL

	Stomach	Small intestine	Colorectum
No. of cases (%)	761 (100)	209 (100)	145 (100)
CLL/SLL	1 (0.1)	1 (0.5)	0 (0)
MCL	7 (0.9)	11 (5.3)	8 (5.5)
FL	0 (0)	0 (0)	3 (2.1)
DLBCL	267 (35.1)	118 (56.5)	88 (60.7)
MZBCL	427 (56.1)	29 (13.9)	25 (17.2)
PTCL	16 (2.1)	8 (3.8)	7 (4.8)
NK/T	2 (0.3)	4 (1.9)	4 (2.8)
AITCL	0 (0)	0 (0)	0 (0)
ALCL	4 (0.5)	4 (1.9)	1 (0.7)
MF	0 (0)	0 (0)	0 (0)
SQPTCL	0 (0)	0 (0)	0 (0)
ETCL	1 (0.1)	9 (4.3)	3 (2.1)
LBL-B	1 (0.1)	0 (0)	0 (0)
LBL-T	1 (0.1)	0 (0)	1 (0.7)
Others	34 (4.5)	25 (12.0)	5 (3.4)

GI lymphoma distribution

- Stomach – 68 to 75 percent
- Small bowel (including duodenum) – 9 percent
- Ileo-cecal region – 7 percent
- Rectum – 2 percent
- Diffuse colonic involvement – 1 percent

- More than one GI site – 6 to 13 percent

Clinical presentation and diagnosis

- 40-60대에 호발, 남=녀
- 초기: 비특이적 소화불량
 검진 목적 내시경에서 발견되는 경우가 많음
- 진행: 복통, 위장관 출혈, 체중 감소, 복부 종괴
- 주로 전정부에 호발하지만 체부 및 분문에서도 발생
- 내시경에서는 모든 위치에서 다양한 형태

Endoscopic diagnosis

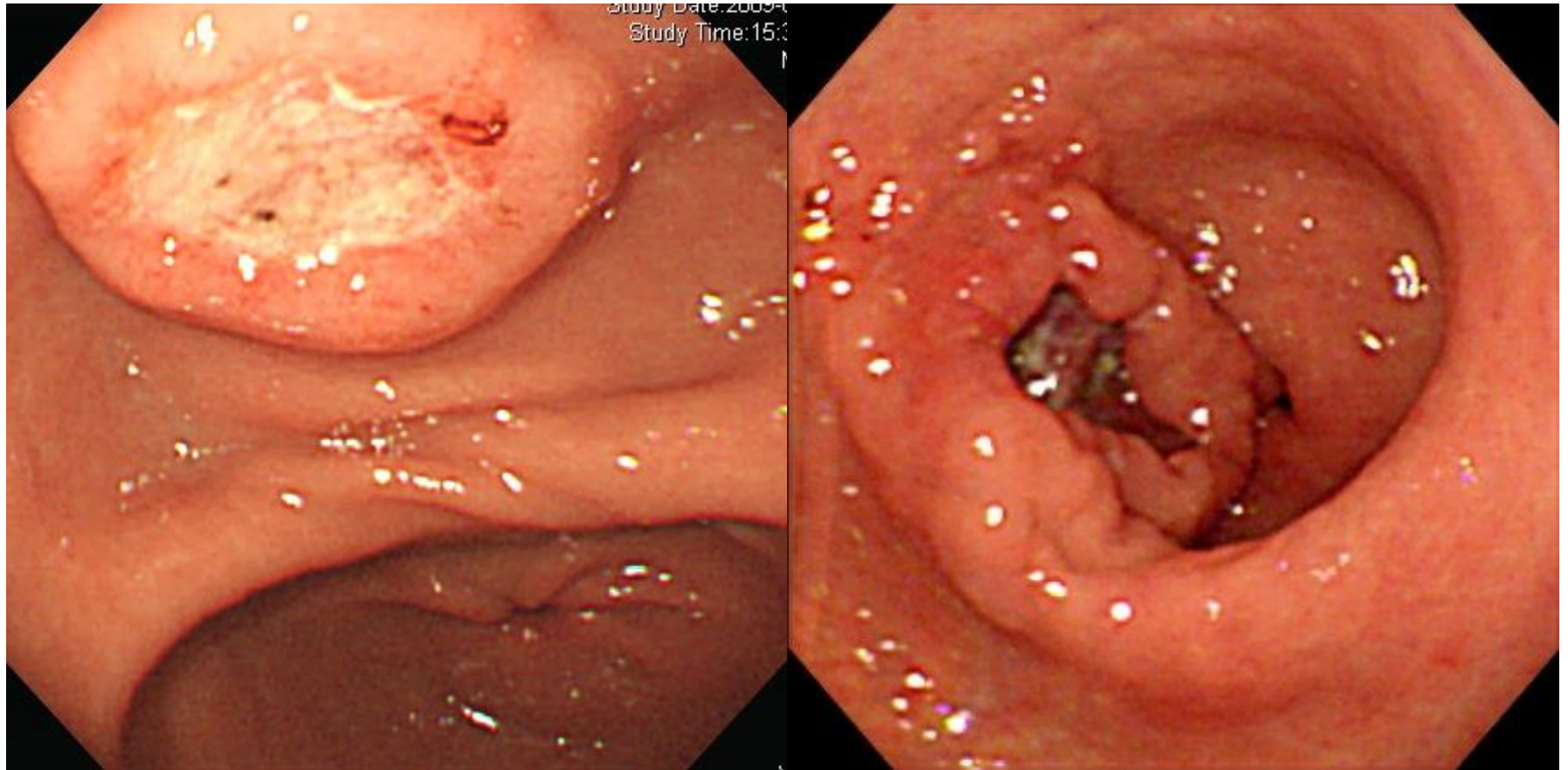
- Variable endoscopic findings in the particular type of lymphoma.
→ **BUT, think about the gastric adenocarcinoma!**
- Close consultation to the pathologist is the key.
- Endoscopic findings described in the textbook (Yamada eds.)
- Gastric lymphoma can be grossly indistinguishable from adenocarcinoma, but is actually a diffusely infiltrating submucosal lesion.
- The tumor may present as a polypoid lesion with ulcerations, but like other submucosal lesions, the overlying mucosa may traverse the mass as a characteristic bridging fold.
- Lymphomas do not have a predilection for any particular region of the stomach, but are more likely than other cancers to present with diffuse infiltration and enlarged rugal folds.

Endoscopic diagnosis

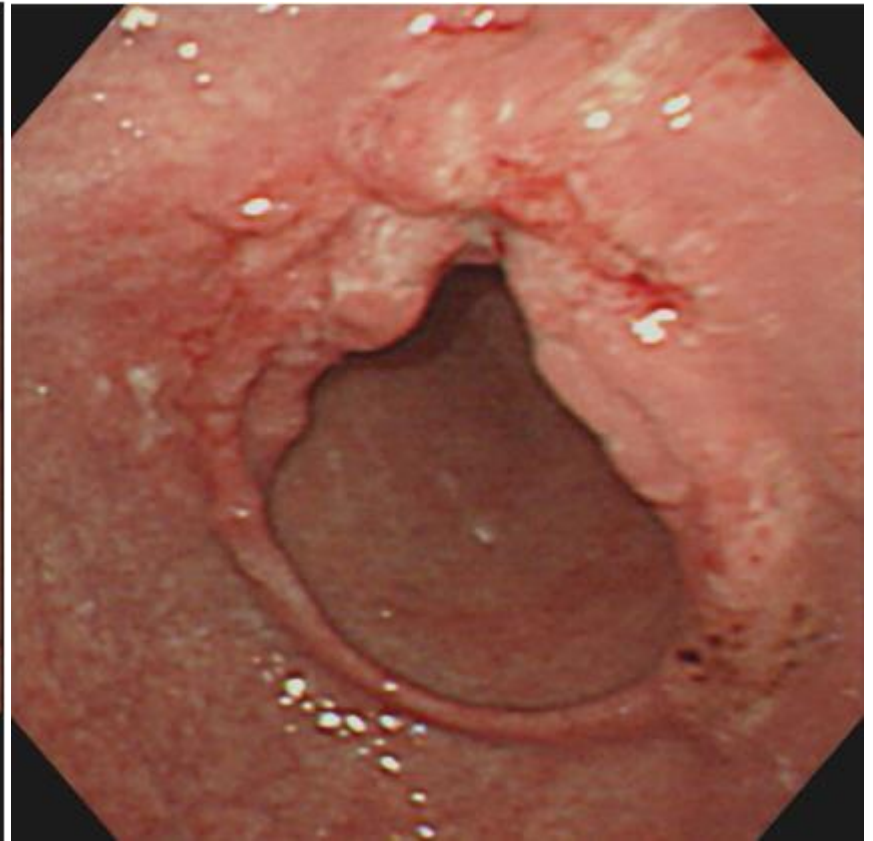
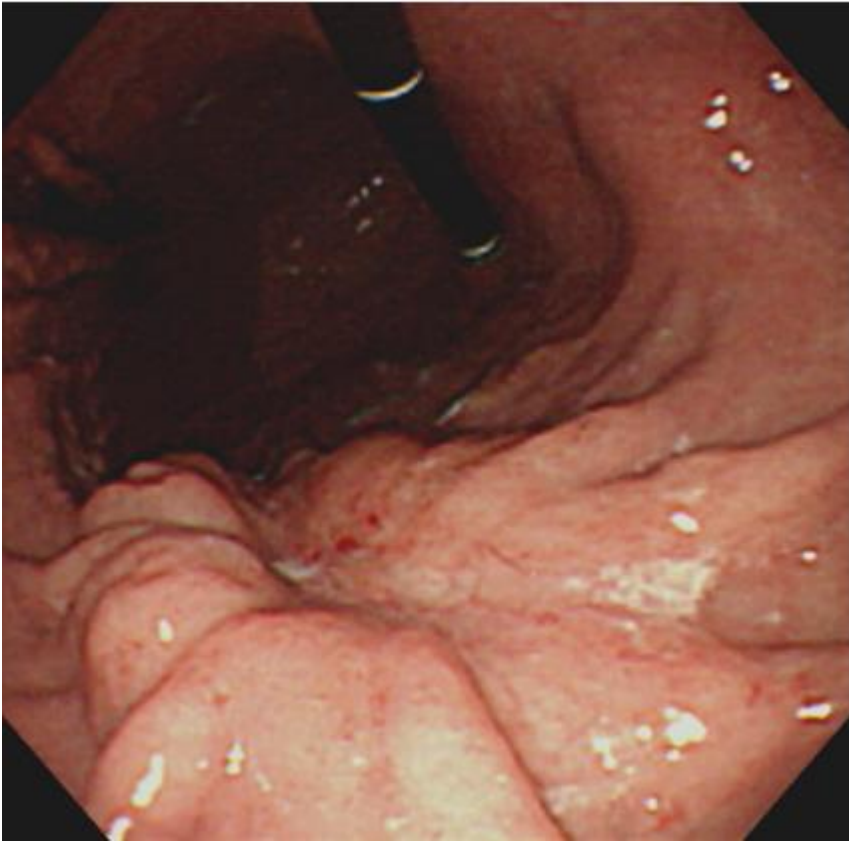
- 림프종에 특징적인 내시경 소견은 없음
- 진단이 지연될 수 있음
- 악성질환은 틀림없는데 선암의 전형적인 모양이 아닐 때, 종양 크기에 비해 obstruction이 가벼울 때, 다발성 병소일 때에는 의심
- 림프종을 의심할 수 있는 소견에서도 선암이 나오는 경우가 있으므로 반드시 조직검사 확인이 필요함

Polypoid lesion with ulcerations

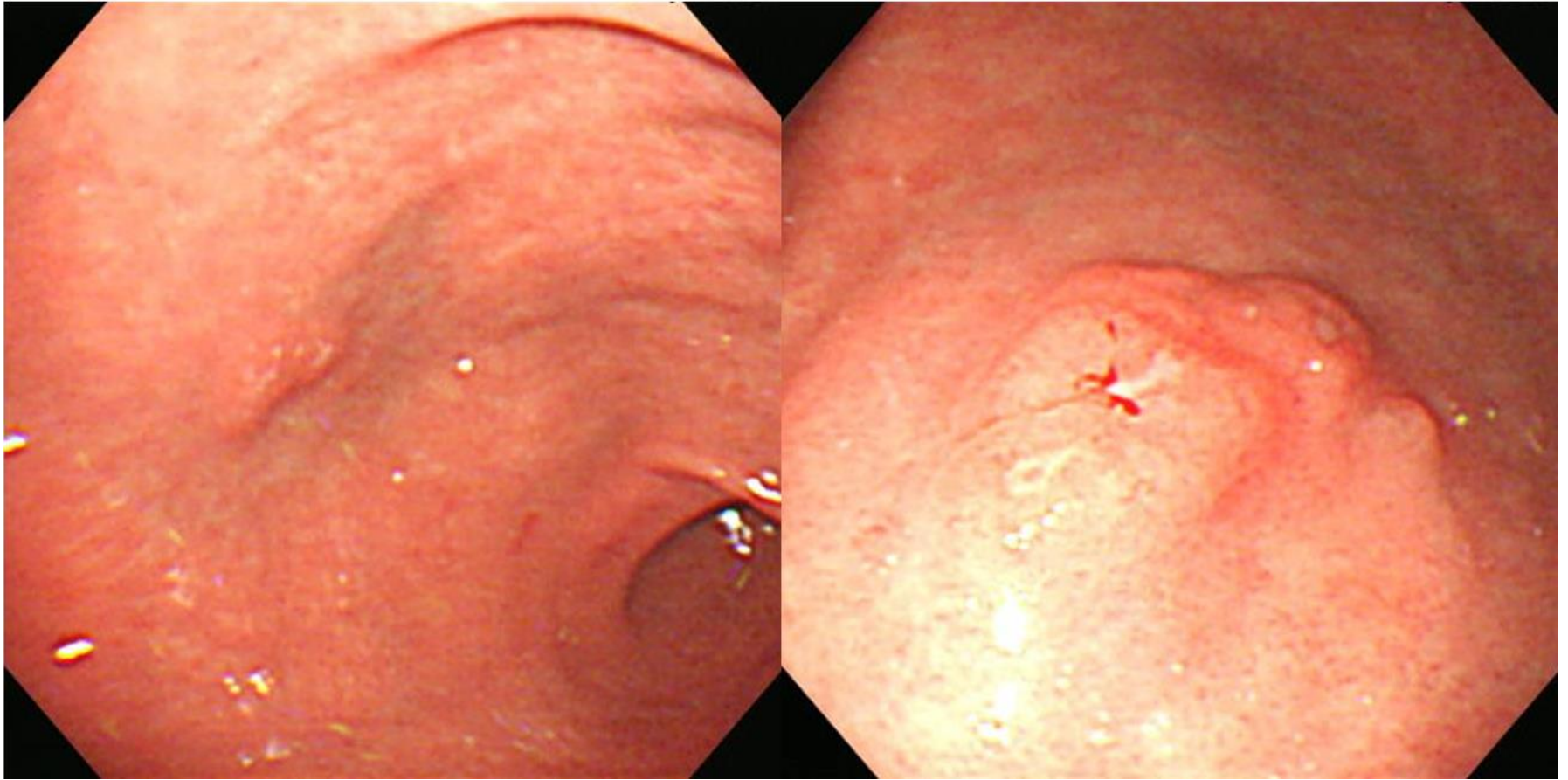
Lymphoma vs. AGC



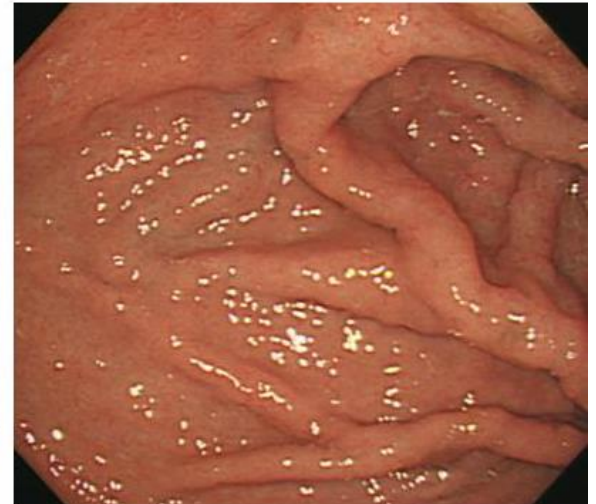
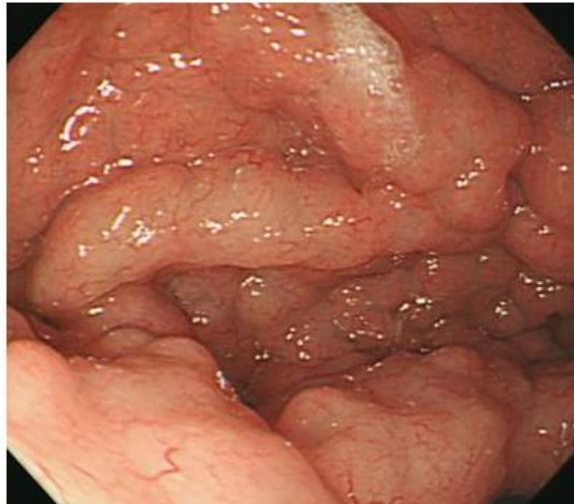
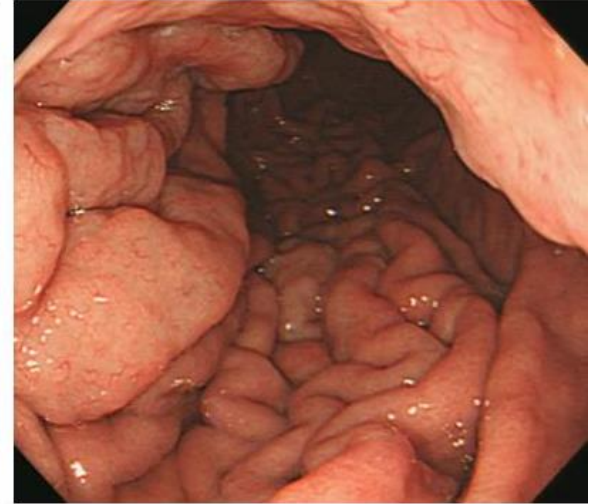
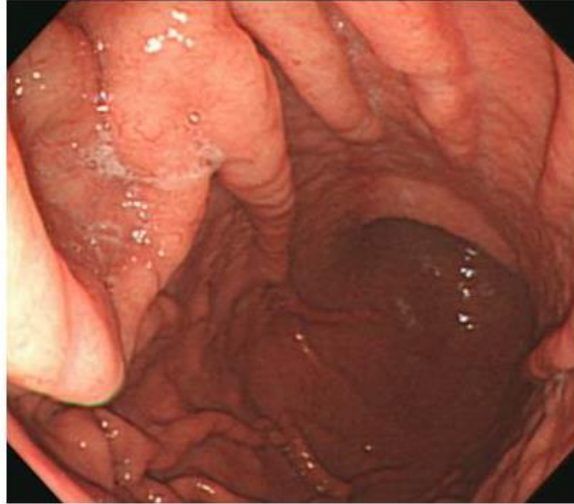
Diffuse infiltration and enlarged rugal folds, Lymphoma vs.EGC



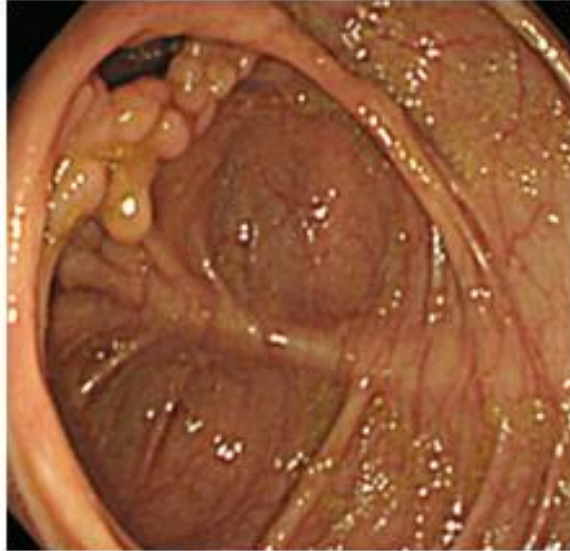
EGC-like lesions



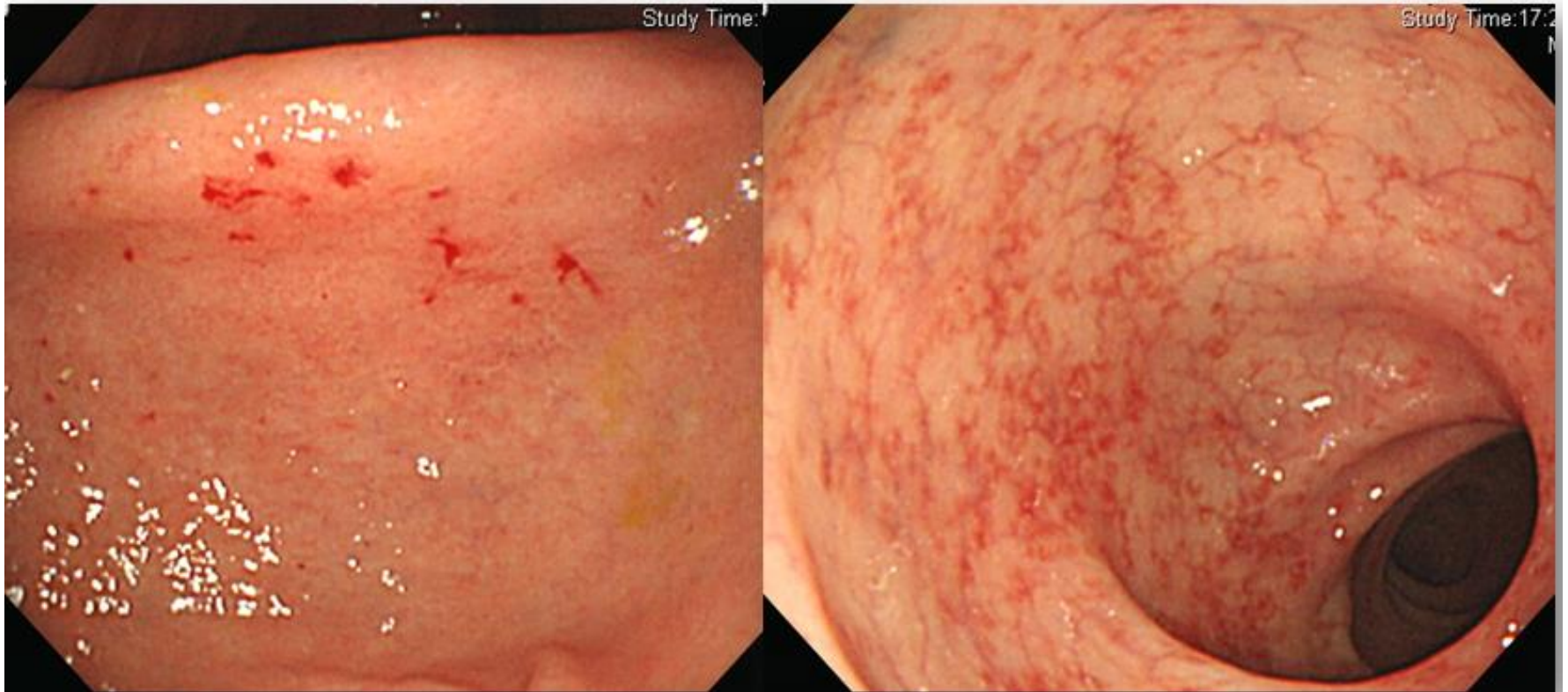
Diffuse type: similar to AGC B-IV



Lymphomatous polyposis

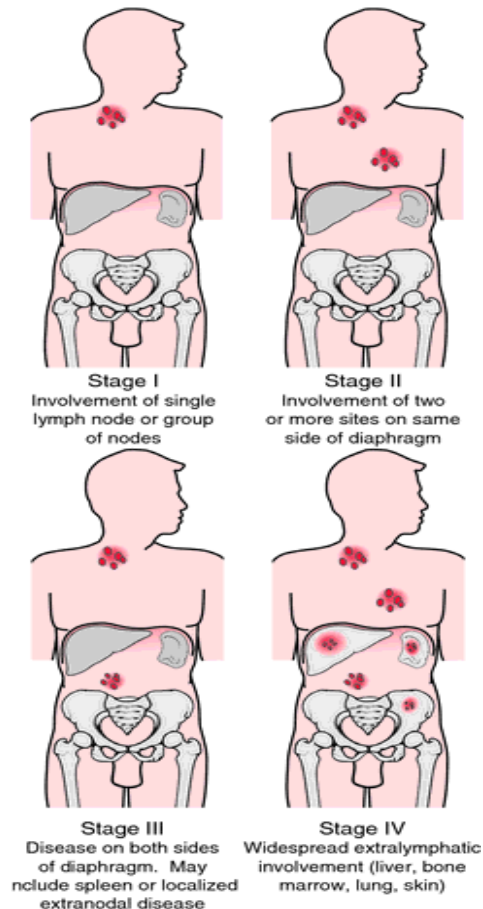


Multiple hemorrhagic & erosions



GI lymphoma staging

Ann Arbor system



Modified Ann Arbor system

Lugano system

Stage	Lugano system
I	Confined to gastrointestinal tract (single primary or multiple, noncontiguous)
II	Extending into abdomen II ₁ =local nodal involvement II ₂ =distant nodal involvement
II _E	Penetration of serosa to involve adjacent organs or tissues
IV	Disseminated extranodal involvement or concomitant supradiaphragmatic nodal involvement

Paris staging system

- 원발장기의 심달도 & 림프절 침범 & 원격장기의 침윤
- TNM staging을 근간

Table 4. Paris Staging System for Primary Gastrointestinal Lymphoma²⁸

Stage	Gastrointestinal lymphomas
TX	Lymphoma extent not specified
T0	No evidence of lymphoma
T1	Lymphoma confined to the mucosa/submucosa
T1m	Lymphoma confined to mucosa
T1sm	Lymphoma confined to submucosa
T2	Lymphoma infiltrates muscularis propria or subserosa
T3	Lymphoma penetrates serosa (visceral peritoneum) without invasion of adjacent structures
T4	Lymphoma invades adjacent structures or organs
NX	Involvement of lymph nodes not assessed
N0	No evidence of lymph node involvement
N1	Involvement of regional lymph nodes
N2	Involvement of intra-abdominal lymph nodes beyond the regional area
N3	Spread to extra-abdominal lymph nodes
MX	Dissemination of lymphoma not assessed
M0	No evidence of extranodal dissemination
M1	Non-continuous involvement of separate site in gastrointestinal tract (eg, stomach and rectum)
M2	Non-continuous involvement of other tissues (eg, peritoneum, pleura) or organs (eg, tonsils, parotid gland, ocular adnexa, lung, liver, spleen, kidney, breast etc.)
BX	Involvement of bone marrow not assessed
B0	No evidence of bone marrow involvement
B1	Lymphomatous infiltration of bone marrow
TNM	Clinical staging: status of tumour, node, metastasis, bone marrow
pTNMB	Histopathological staging: status of tumor, node, metastasis, bone marrow
pN	The histological examination will ordinarily include 6 or more lymph nodes

결론: 위장관 림프종

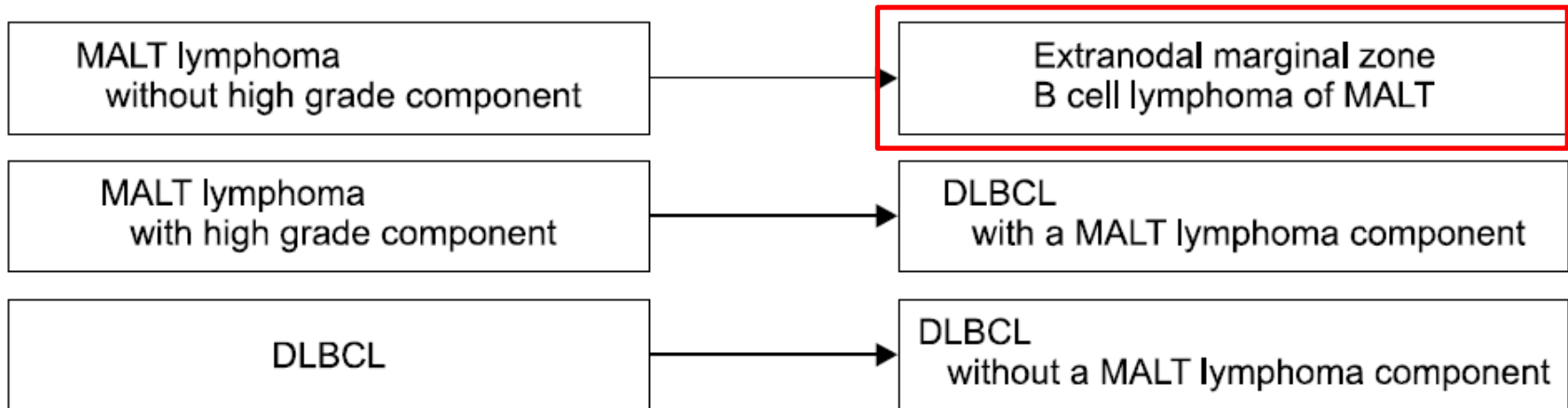
- 내시경 진단이 항상 쉬운 것은 아니다.
- 병리 검사 결과 해석에 주의하자.
- 우리나라에는 장 T-세포 림프종이 많다.
- 진단이 지연될 수 있다.
- 위장관 림프종은 매우 다양하다.

Gastro intestinal lymphomas

-Maltoma

MALToma introduction

2008 WHO
classification



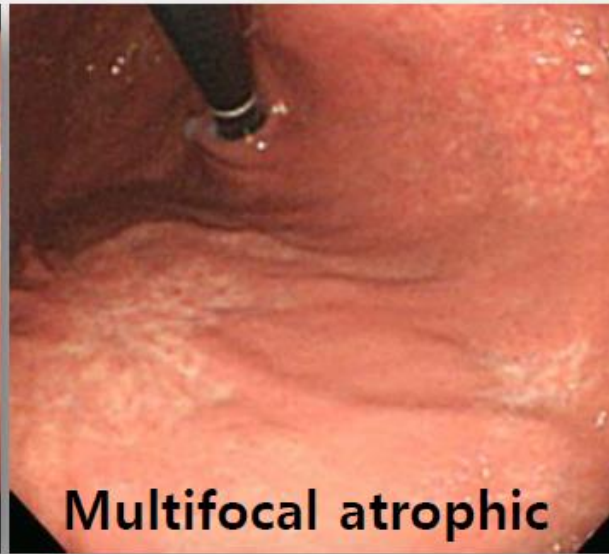
Endoscopic diagnosis of MALToma

- Gastritis-like MALTomas,
 - Multifocal atrophy pattern MALTomas
 - Multinodular MALTomas
 - Ulcerative MALTomas
 - Polypoid MALTomas
 - Early gastric cancer-like MALTomas.
-
- 실제로는 약간 지저분하면서 심하고 불규칙하게 분포하는 미란성 위염과 비슷한 형태를 보이는 경우가 가장 많다.

Endoscopic diagnosis of MALToma



Gastritis-like



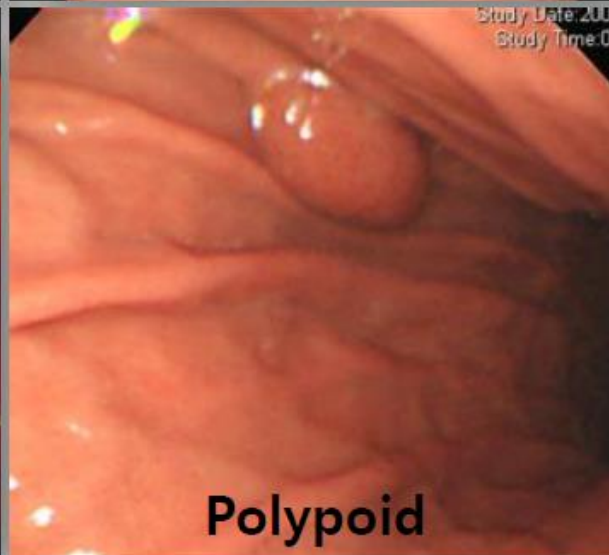
Multifocal atrophic



Multinodular



Ulcerative



Polypoid



EGC-like

Histologic Scoring

- 정상적인 Peyer's patch의 림프조직을 닮은 반응성 림프여포
- Marginal zone/monocytoid B-세포
- Lymphoepithelial lesion
- 소림프구와 형질세포 침윤(plasma cell infiltration)과 함께 여포아세포(centroblast)와 면역아세포(immunoblast)가 출현

Score	Diagnosis	Histological features
0	Normal	Scattered plasma cells in lamina propria. No lymphoid follicles
1	Chronic active gastritis	Small clusters of lymphocytes in lamina propria. No lymphoid follicles. No lymphoepithelial lesions
2	Chronic active gastritis with florid lymphoid follicle formation	Prominent lymphoid follicles with a surrounding mantle zone and plasma cells. No lymphoepithelial lesions
3	Suspicious lymphoid infiltrate, probably reactive	Lymphoid follicles surrounded by small lymphocytes that infiltrate diffusely in lamina propria and occasionally into the epithelium
4	Suspicious lymphoid infiltrate, probably lymphoma	Lymphoid follicles surrounded by marginal-zone cells that infiltrate diffusely in lamina propria and into the epithelium in small groups
5	MALT lymphoma	Presence of dense diffuse infiltrate of marginal-zone cells in lamina propria with prominent lymphoepithelial lesions

MALT, mucosa-associated lymphoid tissue.

Treatment

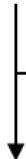
Low-grade MALT lymphoma in the first endoscopic biopsy



Staging work-up including EUS, CT, BM

Stage E-I₂, II, III, IV
or *H. pylori* (-) or high-grade

ChemoRx



H. pylori eradication (PCA 2 weeks) + 2nd eradication, if necessary



UBT 4-6 wks after completing antibiotic treatment



Endoscopy, 3 months after completing eradication

Post-Treatment Evaluation

- GELA staging system이라는 것이 소개되어 큰 혼란
 - pMRD (probable minimal residual disease)가 관해로 해석

Table 3. Groupe d'Etude des Lymphomes de l'Adulte (GELA) Histological Grading System for Post-Treatment Evaluation of Gastric MALT Lymphoma²⁴

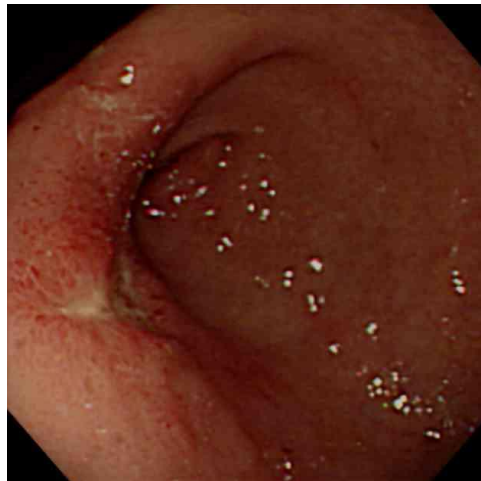
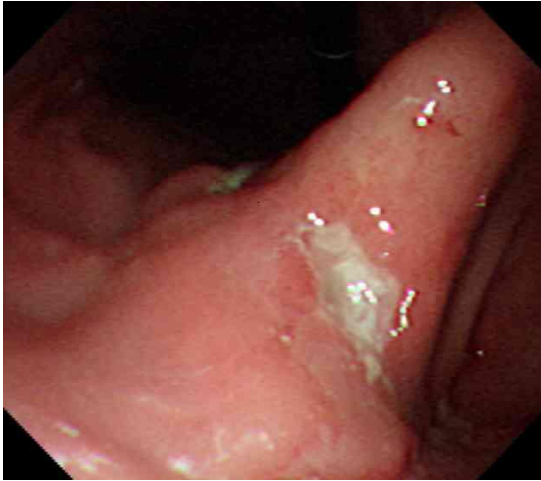
Score	Lymphoid infiltrate	LEL	Stomach changes
CR	Absent or scattered plasma cells and small lymphoid cells in the LP	–	Normal or empty LP and/or fibrosis
pMRD	Aggregates of lymphoid cells or lymphoid nodules in the LP/MM and/or SM	–	Empty LP and/or fibrosis
rRD	Dense, diffuse or nodular extension around glands in the LP	–/+	Focal empty LP and/or fibrosis
NC	Dense, diffuse or nodular	+	No changes

CR, complete histological remission; LEL, lymphoepithelial lesions; LP, lamina propria; MM, muscularis mucosa; NC, no change; pMRD, probable minimal residual disease; rRD, responding residual disease; SM, submucosa.

Treatment failure

- 점막하층을 넘어 침범
 - 고도 요소
 - 내시경초음파에서 위 주위의 림프절이 침범
 - t(11;18)(q21;q21)와 같은 염색체이상이 존재하는 경우
- 방사선치료(30GY)
CTx

Treatment



Initial EGC

2 months later

6 months later

GI lymphomas 에 대한 이준행 교수님의 요약

- 1) 위장관 림프종은 점막하병소처럼 보이는 경우도 있으나 점막병소인 경우가 더 많습니다.
- 2) 아래와 같은 경우에는 림프종을 의심하는 것이 좋습니다.
 - 암은 암 같은데 adenocarcinoma의 일반적인 모양이 아닌 경우.
 - 종양 크기에 비해 obstruction이 가벼울 때 혹은 잘 퍼질 때
 - 조직검사에서 "dense lymphoid infiltration 이나 림프종으로 진단하기 어렵다 (not sufficient for the diagnosis of lymphoma)" 와 같은 결과일 때
 - 짧은 기간에 병소가 많이 커졌을 때
 - 다양하고 bizarre한 모양의 병소가 여러개 있을 때
 - IBD나 기타 염증성 질환 환자가 일반적인 치료에도 호전이 없을 때

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