neral data

- Age: 66y/o
- Sex: male
- Date of admission: 94-04-12

Chief complaint

- High fever and body weight loss, cold sweating for 4 weeks

Present Illness

- DM(+) for 20 yrs under OHA control, HTN(-), CVD(-), smoking(+), drinking(+)
- 1 month ago, cold sweating and tarry stool, poor appetite noted
- GI upset, fatigue noted then he was sent to 忠孝 H.

Present Illness

- Anemia noted, blood transfusion was done in 忠孝 H.
- Tarry stool with body weight loss 2 kg with in 2 weeks (58 kgs to 56 kgs)
- Adbomen echo

  --fatty liver, thicken wall of stomach

Present Illness

- PES

  -- one giant ulcerative tumor over supraangularis to high body, LCS to posterior wall

  -- r/o gastric ca with bleeding

  -- Biopsy: Large B cell Lymphoma

  (CD3-)(L26+)

- Ask our hospital for second opinion for further treatment

Family history

- No cancer family history

Personal history

- Smoking: social
- Alcohol:social
- Food allergy:nil
- Drug allergy:nil
- Betel nut eating:nil
- Social activity:life style:active(+), sedentary()
- living arrangement:normal(+), abnormal()

Medical history

- DM for 20+ years under OHA treatment.
  Metformin
  Amaryl
  Avandia
  Diovan
- Gastric B cell lymphoma: s/p CHOP ; Mabthera
- UGI bleeding
- Surgical history：nil

Physical examination

- General appearance: chronic(+) ill-looking
- conjunctiva: pale(-), sclera: icteric(-)
- T/P/R__37.2___oC/__72____bpm/___20____per minute, BP__140_/_80__mmHg
- Chest : normal pattern
- Abdomen: no specific finding

Lab data

- WBC [4.0-11.0 x10.e3/uL] 0.23
- HGB [12-18 g/dL] 10.4
- PLT [130-400 x10.e3/uL] 50
- %NEUT [40-74 %] 17.4
- %LYM [19-48 %] 60.9
- %MONO [2.0-10.0 %] 13.0
- %EOS [0-7 %] 8.7
- %BASO [0-1.5 %] 0.0

Lab data

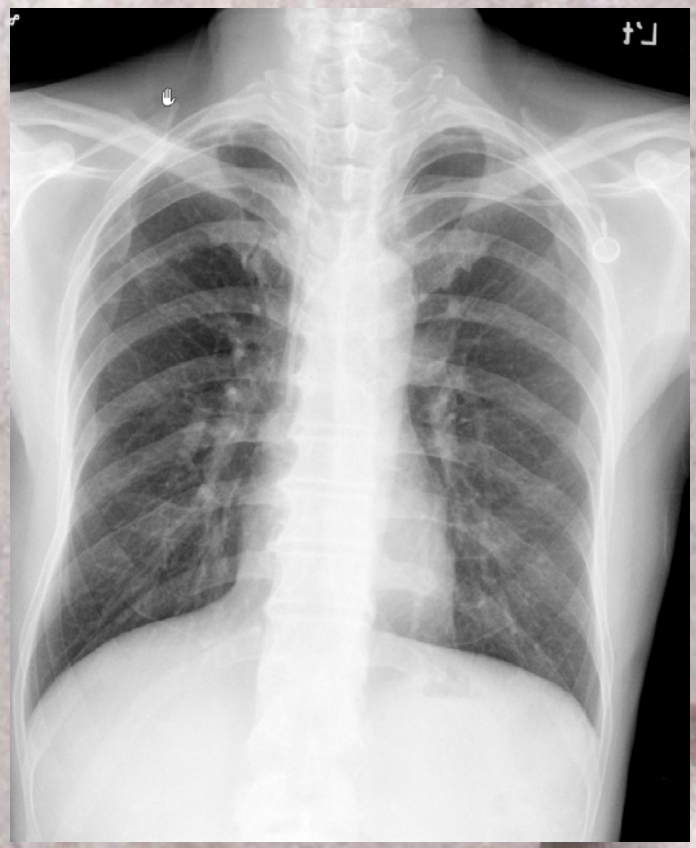
- BUN (血液) [7-18 mg/dl] 21
- Creatinine(血)[0.5-1.3 mg/dl] 1.1
- GOT(血液) [0-40 IU/L] 13
- CRP (血液)[0.0-0.8 mg/dl] 2.50
- Na (血液)[135-158 meq/L] 133.0
- K (血液)[3.5-5.3 meq/L] 3.90
- Stool OB: ++++

Lab data

HBsAg results(0.0-2.0 S/N)	0.84	
HBsAg (血液)	Negative	
Anti-HCV results[0-1.0 S/CO]	0.30	
Anti-HCV (血液)	Negative	
***B2-microglobulin(血液)(委外)[<2700ug/L]**		2505.3

CXR:

- Port-A catheter in place(4/15).
- Linear densities over right upper lung field, may due to previous inflammatory process.
- Normal heart size .
- Normal appearance of bil. costo-phrenic angles.



Impression

- Stomach, large B cell lymphoma s/p CHOP and Mebthera therapy
- UGI bleeding
- DM with medical control of Metformin , Amaryl , Avandia , Diovan

Evaluation

- 4-1 PES:

  esophagus : negative

  stomach: much coffee ground material and blood clot. One giant ulcerative tumor over supra-angularis to high body, LCS to posterior wall. Mild oozing .

  -- r/o gastric ca with bleeding

  duodenum: negative to 2nd portion

Evaluation

- 4-2 abdomen echo: mild fatty liver

  thicken wall of the stomach

- 4-8 biopsy: CD3(-); L26(+)

  Stomach, supra-angularis to the body, lesser curvature site, posterior wall, endoscopic biopsy, showing B cell lymphoma

Evaluation

- 4-12 Gallium scan:

  diffuse inflammation or neoplastic process of the stomach

- 4-13 Abd MRI s/c Gd-DTPA

  gastric B-cell lymphoma

Evaluation

- 4-14 Hb 6.0 ; MCV 93.0; PLT 227 ; BUN 22
- 4-16 LDH 284
- 4-19 Cardiac echo:

  EF: 76 %

  normal LV function, trivial TR and MR
- 4-23 BM biopsy:

  normocellular marrow with myeloid hyperplasia. No tumor involved

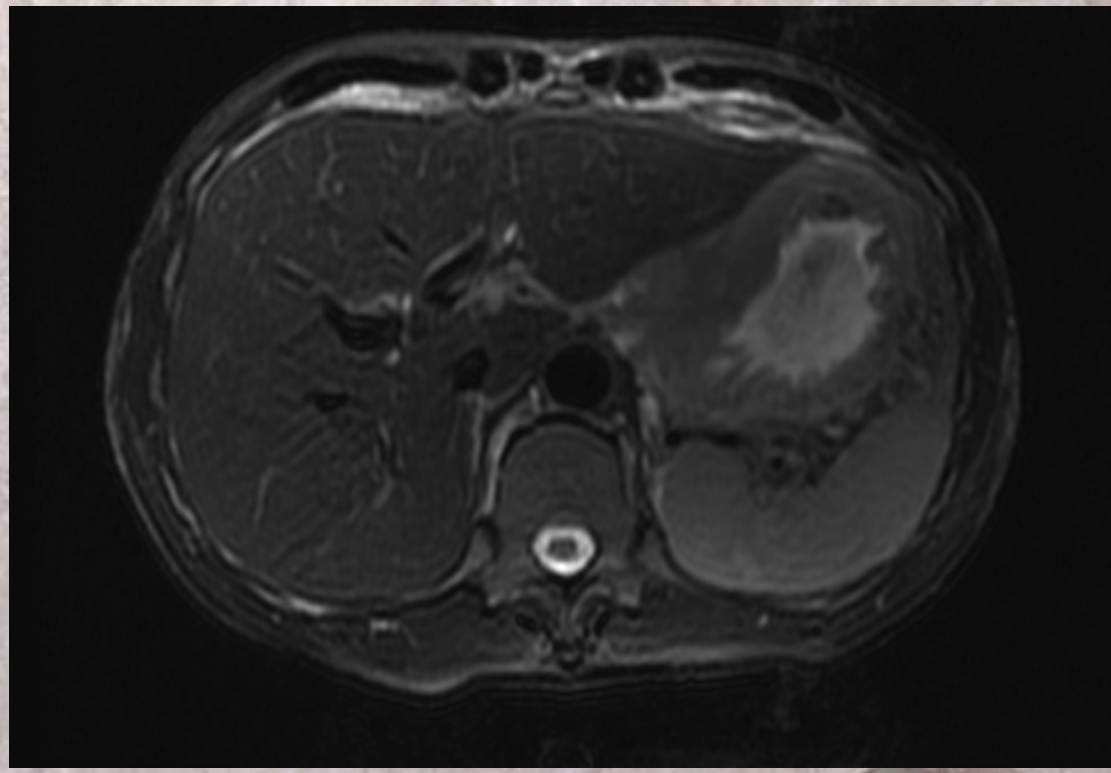
Evaluation

- 4-28 Hb 10.4 ; WBC 230 ; Neu 17.4
- Medication:

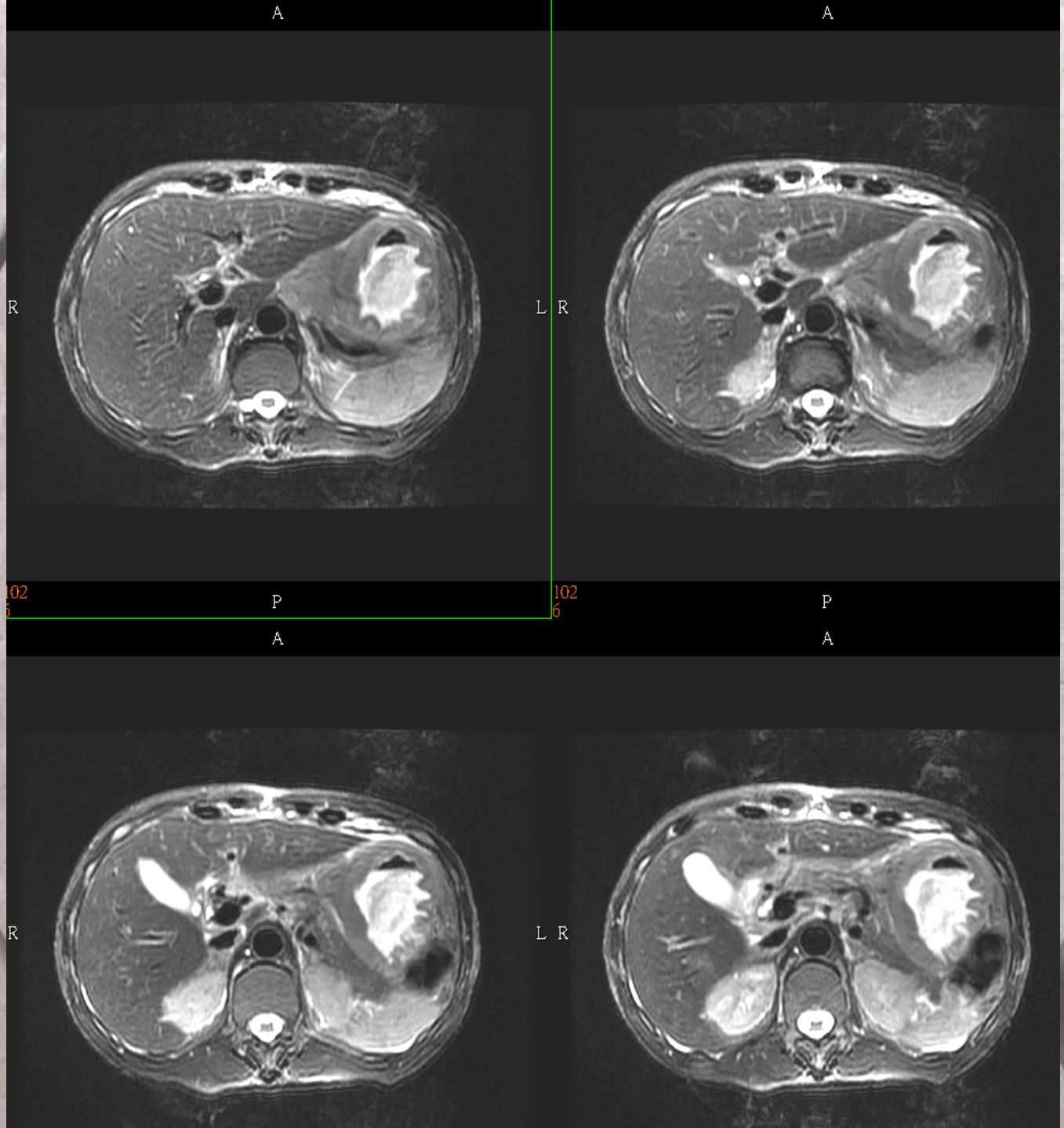
1. CHOP and Mabthera were for B-cell lymphoma
2. Alkalization of urine was for tumor lysis syndrome.
3. GCSF was for leukopenia

MRI

T2 FRFSE Resp Trig Fat



1. Diffuse and evident thickening of gastric folds and its wall
2. Abnormal enhancement involved to gastric fundus and body, especially at greater curvature site


A
A
R
L R
102
6
P
102
6
P
A
A
R
L R

Radiology thinking process

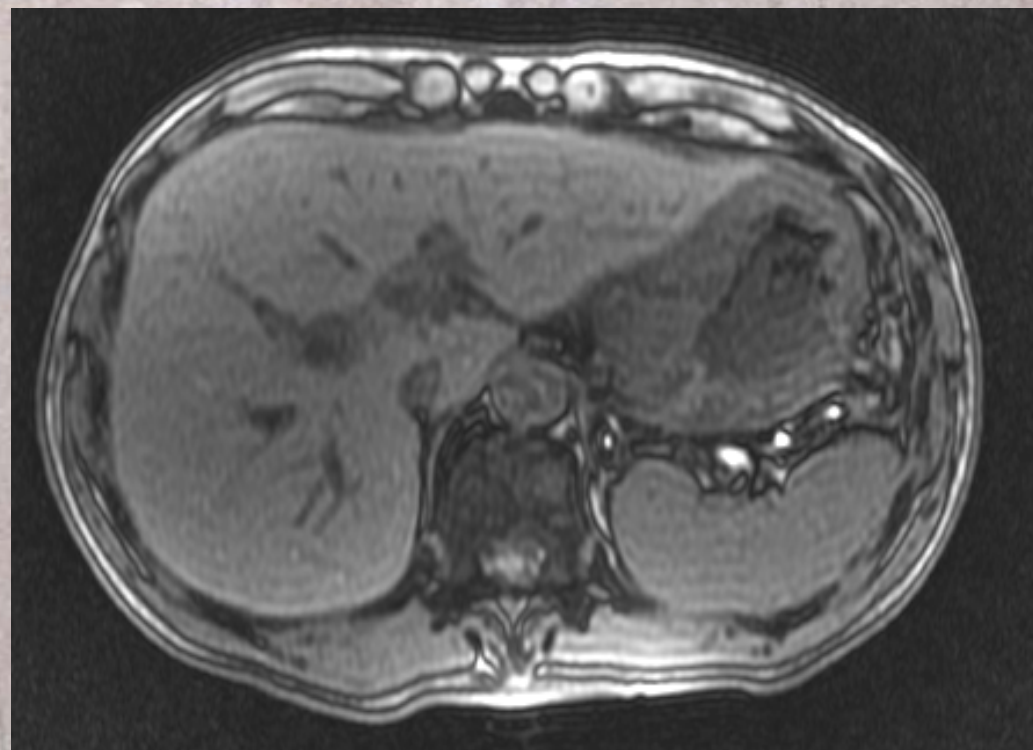
- thickened gastric folds

Hyperacidic disease	Peptic ulcer disease
	Zollinger-Ellison disease
hypoproteinemia	
lymphoma	
pseudolymphoma	
Eosinophilic gastroenteritis	
varices	
Menetrier disease	
IBD, TB, syphilis	

MRI

D/D :

- Gastric inflammation
- Menetrier disease
- gastric lymphoma
- advanced gastric cancer



Differential diagnosis

- Gastric inflammation
- Menetrier disease
- Advanced gastric cancer , carcinoma
- Gastric lymphoma

Gastric inflammation

- H. pylori infection leads to gastric inflammation
- surface epithelial degeneration and infiltration of the gastric mucosa
- H. pylori chemotaxins, chemokines such as IL-8 and GRO-alpha, and pro-inflammatory cytokines liberated by mononuclear phagocytes (TNF alpha, IL-1 and IL-6) as part of non- specific immunity.

Gastric inflammation

- This patient denied gastric ulcer history
- During endoscopy, gastric biopsies should always be obtained to establish the presence of mucosal inflammation.

Differential diagnosis

- Gastric inflammation
- Menetrier disease
- Advanced gastric cancer , carcinoma
- Gastric lymphoma

Menetrier's disease

- hypertrophic gastritis
- thickened gastric rugae with sparing of antrum
- epithelial-cell hypertrophy
- protein wasting
- mucus production increased
- acidity: normal or decreased

Menetrier’s disease

- causes giant folds of tissue to grow in the wall of the stomach.
- The tissue may contain ulcers.
- Menetrier's disease increases a person's risk of stomach cancer.
- The cause of the disease is unknown.

Menetrier's disease

- also called giant hypertrophic gastritis, protein losing gasteropathy, or hypertrophic gastropathy.
- Symptoms include discomfort and tenderness in the top middle part of the abdomen, loss of appetite, nausea, diarrhea, vomiting blood, and ulcer-like pain after eating

Menetrier's disease

- It is diagnosed through x rays, endoscopy, and biopsy of stomach tissue.

Differential diagnosis

- Gastric inflammation
- Menetrier disease
- Advanced gastric cancer , carcinoma
- Gastric lymphoma

Gastric malignancies

- 3rd most common GI malignancy (after colorectal + rectal).
- The stomach is the site of variety of malignant neoplasms. They are primary carcinoma, gastric lymphoma, mesenchymal tumours and metastatic carcinomas.
- The most common of these are carcinoma and lymphoma.

Gastric malignancies

- predisposing factors:
  - pernicious anemia (2X risk)
  - chronic atrophic gastritis
  - adenomatous + villous polyp
  - gastrojejunostomy

Gastric malignancies

(1)Gastric adenocarcinoma:85%

(2)Gastric lymphoma: 5%

(3)Metastatic Disease:

1.malignant melanoma

2.breast carcinoma

3.esophagus,pancreas,transverse colon

(4)Leiomyosarcoma:large exophytic cavitated mass

(5)Kaposi’ sarcoma

Gastric carcinoma *morphology*

- Primary carcinoma of the stomach may be present as:

1. Superficial spreading carcinoma
   (Early gastric cancer)

Type I lesions are elevated and protrude more than 5 mm into the lumen.
Type II tumors are superficial lesions that are elevated (IIa), flat (IIb), or depressed (IIc).
Type III early gastric cancers are shallow, irregular ulcers surrounded by nodular, clubbed mucosal folds.

Gastric carcinoma *morphology*

2. Polypoid or fungating carcinoma

3. Ulcerating or penetrating carcinoma(70%)

4. Advanced bulky carcinoma

5. Infiltrating or cirrhous carcinoma(5~15%)
   (linitis plastica)

Gastric carcinoma *location*

- 60% lesser curvature
- 30% GE junction
- 10% greater curvature

- probability of malignancy of an ulcer
  --fundus 90%
  --greater curvature 70%
  --lesser curvature 10-15%

Gastric carcinoma *UGI*

- A.benign,projecting,lesser curvature ulcer with collar.
- B.malignant,intraluminal ulcer with irregular nodular tumor rim.
- C.nonprojecting benign great curvature ulcer

Gastric carcinoma *UGI*

- Scirrhous carcinoma of the stomach(linitis plastica)

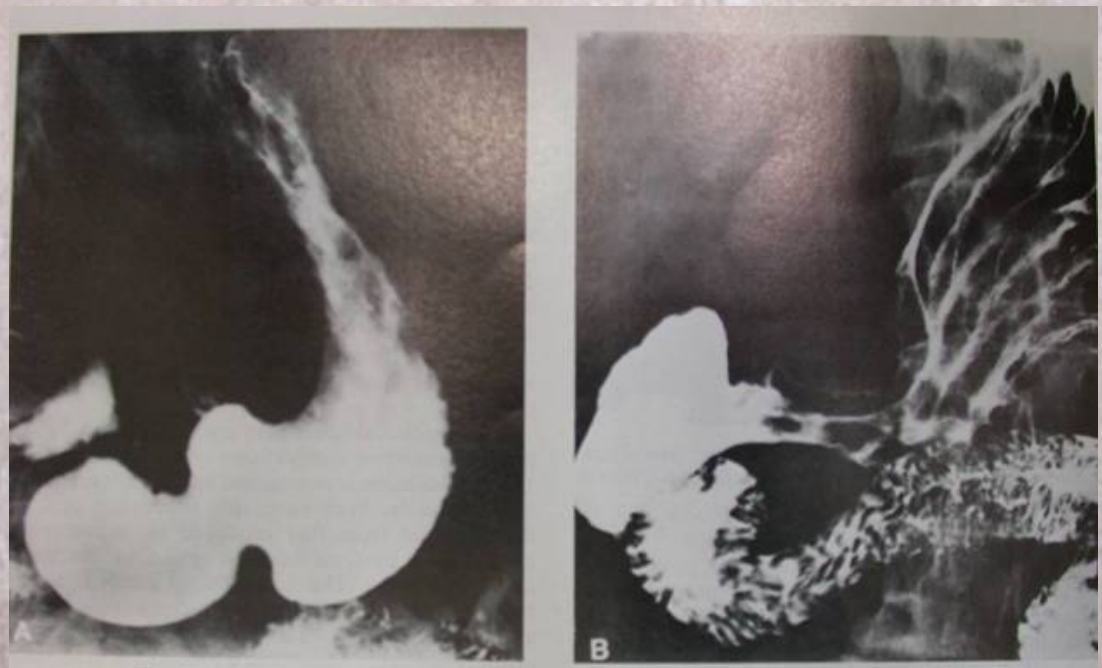


Fig. 8. **A.** Scirrhous carcinoma of the stomach (linitis plastica). The proximal two thirds of the stomach is involved with scirrhous carcinoma. The stomach is narrowed, shrunken, and rigid. The normal mucosal fold pattern has been replaced by thickened, irregular rugae infiltrated with cancer. A discrete ulcerating lesion is not identified. During fluoroscopy, peristalsis was absent, and barium flowed through the stomach by gravity as through a rigid tube. **B.** Air-contrast study reveals the distal half of the stomach to be irregularly narrowed and tubular. The mucosa is thickly infiltrated with scirrhous carcinoma.

Gastric carcinoma *UGI*

thickened wall of antrum and distal body

(mucus producing gastric adenocarcinoma)

Gastric carcinoma *CT*

- thickening of the gastric wall, asymmetric thickening of folds, irregular nodular luminal surface, mass of uniform density

Differential diagnosis

- Gastric inflammation
- Menetrier disease
- Advanced gastric cancer , carcinoma
- Gastric lymphoma

Gastric lymphoma

- Radiographic type:
  1. Polypoid or nodular (47%)
     enlarged nodular folds
  2. Ulcerative (42%)
     ulcerative lesions, may be complicated by perforation; aneurysmal configuration
  3. Diffusely infiltrating(11%)

     diffuse hoselike thickening of bowel; decreased or absent peristalsis

Gastric lymphoma *UGI*

1. Infiltrative, ulcerative, or nodular mass that often mimics the appearance of adenocarcinoma. Flexibility of gastric wall preserved.
2. The antrum and body are most commonly involved. Duodenum often affected when antrum involved.
3. Circumscribed mass with endogastric or exogastric growth
4. Large irregular ulcers

Gastric lymphoma *CT*

1. diffuse involvement of entire stomach, typically more than half of gastric circumference
2. segmental involvement
3. thickened gastric wall
4. luminal irregularity, hyperrugosity
5. spread of the tumor:

   direct extension into pancreas, spleen, transverse colon and liver

Discussion

Gastric lymphoma

Lymphoma grade

- **Low grade:**
  ML, small lymphocytic
  ML, follicular small cleaved cell
  ML, follicular, mixed small and large cell
- **Intermediate grade:**
  ML, follicular, large cell
  ML, diffuse, small cleaved cell
  ML, diffuse, mixed small and large cell
  ML, diffuse large cell
- **High grade:**
  ML, large cell, lymphoblastic
  ML, lymphoblastic
  ML, small non-cleaved cell

Lymphoma

	Hodgkin	non-Hodgkin
Presentation	Usually nodal	Usually extranodal
Spread	Contiguous	Hematogenous, Non-contiguous
Mediastinum	Common	Uncommon(except lymphoblastic type)
Spleen	Common	Uncommon
Bone Marrow	Uncommon	Common
Liver,GI,CNS	Uncommon	Common

Hodgkin's Lymphoma

- Hodgkin's lymphoma

  Young adult

  Malignant Reed-Sternberg cell

  CD30(+), CD20(+/-)

	CD30	CD20
Lymphocyte-predominant	+	+
Classic Hogkin's	+	-

Hodgkin's Lymphoma

- L-P (nodular growth pattern), popcorn cell
- Classic Hogkin's

1. Lymphocyte rich (LR): rare RS
2. Mixed cellularity (MC): EBV-associated
3. Lymphocyte depletion (LD): RS
4. Nodular sclerosis (NS): Lacuna RS +
   fibrous background, women,mediastinum

Non-Hodgkin's Lymphoma

- Small lymphocytic lymphoma

  CD5(+), older adult, Richter's transformation, paraneoplastic syndrome

- Waldenstrom's macroglobulinemia

  IgM, hyperviscosity

- Mantle cell lymphoma

  t(11,14) , BCL1 , GI lymphomatoid polyposis

- MALT lymphoma

  t(11,18) , lymphoepithelial lesion

Non-Hodgkin's Lymphoma

- Follicular lymphoma

  t(14,18) , bcl2 , Nodular growth pattern

- Diffuse large B-cell lymphoma

  Diffuse growth pattern, autoimmune disorder, EBV , plasma cell, aggressive behavier

- Burkitt's lymphoma

  t(8,14) , oncogene myc, EBV , starry-sky pattern

Non-Hodgkin's Lymphoma

- Anaplatic large cell lymphoma (ALCL)

  young adult , good prognosis
- T-lymphoblastic lymphoma

  anterior mediastinum
- Mycosis fungoides / Sezary syndrome

  skin T-cell lymphoma, cerebriform, Pautrier microabscess
- Adult T-cell leukemia-lymphoma

  HTLV-1 retrovirus, hypercalcemia

Gastric lymphoma

- Primary gastric lymphomas: less than 2% of all primary stomach malignancies
- Non Hodgkin's type and of B-cell lineage
- almost 75% of primary gastrointestinal lymphomas were of gastric origin.
- Gastric lymphomas are more prevalent in patients over the age of 50, and men are affected two to three times more frequently than women

Gastric lymphoma

- Usually arise from MALT (mucosa associated lymphoid tissue)- also known as Marginal Zone B-cell lymphoma (Low and High grade).
- Diffuse large B-cell lymphoma include high grade lymphoma of MALT origin and non-MALT type and they are indistinguishable

Gastric lymphoma : clinic sign

- Most common: pain , weight loss, nausea and vomiting, anorexia, and bleeding.
- Early symptoms are vague .
- More advanced lesions may present with hemorrhage, pyloric stenosis, or signs of perforation.

- PE:Abdominal tenderness, a palpable abdominal mass,hepatomegaly
- No physical finding : 62 %

Gastric lymphoma : Stage

- Musshoff's criteria staging system
  Stage IE: limited to the GI stomach
  Stage IIE_1: regional lymph node
  Stage IIE_2: noncontigious subdiaphragmatic lymph node
  Stage III: spread to other organs within the abdomen
  Stage IV: hematogenous spread

Gastric Lymphoma: Prognosis

- IPSS (International prognostic scoring system)

Diffuse large B cell lymphoma

1. *Age>60y/o*
2. *Musshoff's criteria stage Ⅲor Ⅳ*
3. *Extranodal involvement >1 site*
4. *Poor performance status (ECOG 2~4)*
5. *High LDH*

Risk: low(<1),
low-intermediate(2),
intermediate-high(3),
high(4~5)

Gastric Lymphoma: Treatment

- Surgery:

1. No decrease in survival for patients if adjuvant RT or C/T were given than total resection of all gross disease and involved lymph nodes.
2. In surgically treated patients, most recurrences are extraabdominal and local disease is well controlled.
3. Currently, splenectomy is only indicated in cases of direct tumor extension.

Gastric Lymphoma: Treatment

- Radiotherapy:

  Gastric lymphoma seems to be a more systemic disease

  In the absence of obvious persistent local disease, the need for additional local therapy with RT is put in question.

Gastric Lymphoma: Treatment

- Chemotherapy:

1. As stated earlier, the diffuse large cell type is the most. They are quite responsive to current chemotherapy.

2. Stages IE & IIE treated with chemotherapy after surgery: excellent 5-year disease free survival

Gastric Lymphoma: Treatment

- C/T regimens:

CHOP (cyclophosphamide, Adriamycin, vincristine, prednisone)
CHOP-bleo (+ bleomycin)
COPP-bleo (cyclophosphamide, vincristine, procarbazine, prednisone,bleomycin) CVP (cyclophosphamide, vincristine, and prednisone)

Gastric Lymphoma: Treatment

- C/T

Aggressive course without tratment
80% complete remission rate by C/T
40% cure by C/T

Gastric Lymphoma: conclusion

Early stage:

Surgery: for local control and preoperative staging

Adjuvant C/T: for extraabdominal lesion

Invasion stage:

C/T: treatment with either surgery or radiation providing local control.

In those patients with non-diagnostic biopsies, surgical exploration and resection are needed.