

MANAGEMENT OF GASTROINTESTINAL LYMPHOMAS

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Case Presentation

- xx yo female
- HTN
- Lymphoma (mantle cell, dx after left axillary node bx 7 years PTA, not treated)
- Right breast lumpectomy – negative
- No prior endoscopy

Case Presentation

- Hematochezia on/off for 3 weeks PTA
- SOB
- Cough / sputum
- T=103, BP 113/68, HR 136, RR 36
- Pale, no abdominal tenderness, rectal exam – no masses, guaiac +

Case Presentation

- Laboratory: WBC 14 (88% N), Hct 19.8, plt 286, chemistry wnl, LFT wnl
- CXR – questionable retrocardiac infiltrate
- EKG – sinus tachy
- Lavage negative

Case Presentation

- Admitted to Medical Service
- IVF, transfused a total of 4 units PRBC over 5 days
- Zythromax
- GI consult
- Bowel prep, colonoscopy HD#2

Case Presentation

Colonoscopy

- Large amount blood and clots
- Multiple polyps throughout the colon, friable and oozing blood
- Terminated at ascending colon – 5 cm polyp encompassing the colon
- Biopsies taken

Case Presentation

- CT abdomen and pelvis HD#4
- Medical clearance obtained

C: 60.0, W: 450.0

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Contrast: CONTRAST

Gantry: 0°

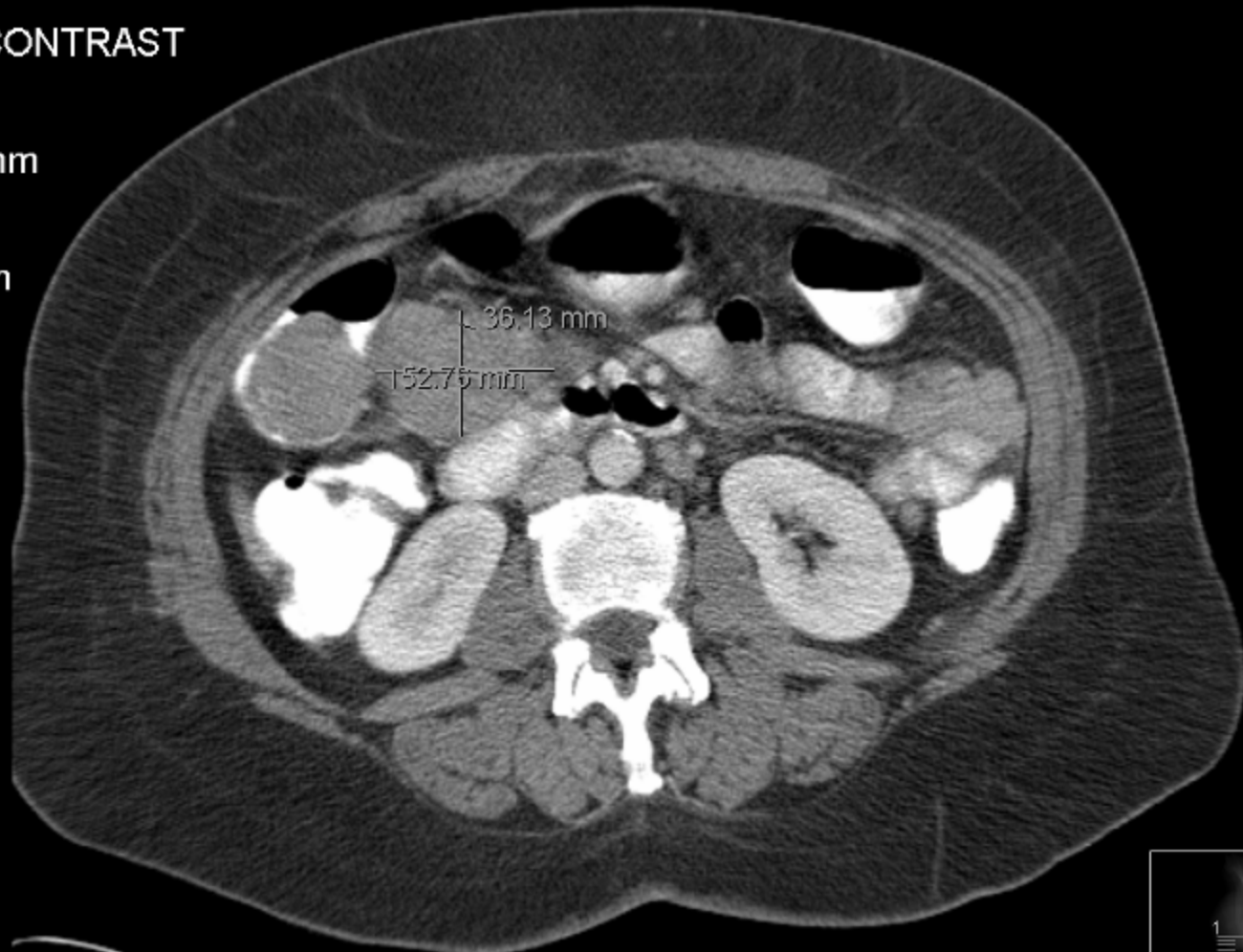
FoV: 370 mm

Time: ms

Slice: 5 mm

Pos: 370

FFS



F: C

403 mA

120 kV

Image no: 38

Image 38 of 94

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Case Presentation

- HD#6 – subtotal colectomy – large cecal mass involving appendix, near-obstructing mass mid-ascending colon with large lymphadenopathy involving the right colic artery origin, large mid-transverse colon mass at insertion of middle colic artery; no blood proximal to ICV
- POD#1 Oncology consult – plan for chemotherapy

Case Presentation

- POD#2 NGT D/C
- POD#3 tolerating diet
- POD#4 D/C home
- Seen in clinic: w/o complaints, no changes in bowel habits
- Received chemotherapy

Management of Gastrointestinal Lymphomas

Overview

- Localized disease - heterogeneous group of unique B- and T-cell lymphoid malignancies
- Presentation with gastrointestinal symptoms or predominant lesions in the GI tract
- In a study of 371 patients registered in the German Multicenter Study GIT NHL 01/92, the following sites were involved:

Stomach — 75 %

Small bowel (including duodenum) — 9 %

Ileo-cecal region — 7 %

More than one GI site — 6 %

Rectum — 2 %

Diffuse colonic involvement — 1 %

Gastrointestinal Lymphomas

- indolent lymphomas of lymph node origin
 - almost always disseminated at diagnosis
 - frequent bone marrow involvement
 - respond to therapy, but continuously recur
 - median survival can exceed 10 years
 - cure is unusual
- extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT)
 - indolent form of lymphoma
 - occurs in older patients
 - localized at diagnosis
 - long-term disease-free survival
 - cure is common

Ann Arbor Staging Classification for Hodgkin's and Non-Hodgkin's Lymphomas[†]

- **Stage I** – Involvement of a single lymph node region (I) or of a single extralymphatic organ or site (IE)*
- **Stage II** – Involvement of two or more lymph node regions or lymphatic structures on the same side of the diaphragm alone (II) or with involvement of limited, contiguous extralymphatic organ or tissue (IIE)
- **Stage III** – Involvement of lymph node regions on both sides of the diaphragm (III) which may include the spleen (IIIS) or limited, contiguous extralymphatic organ or site (IIIE) or both (IIIES)
- **Stage IV** – Diffuse or disseminated foci of involvement of one or more extralymphatic organs or tissues, with or without associated lymphatic involvement

* The designation "E" generally refers to **extranodal contiguous extension** (ie, proximal or contiguous extranodal disease) that can be encompassed within an irradiation field appropriate for nodal disease of the same anatomic extent. A single extralymphatic site as the **only site of disease** should be classified as IE, rather than stage IV.

All cases are subclassified to indicate the absence (A) or presence (B) of the systemic symptoms of significant unexplained fever, night sweats, or unexplained weight loss exceeding 10 percent of body weight during the six months prior to diagnosis.

Clinical stage refers to the extent of disease determined by diagnostic tests following a single diagnostic biopsy. If a second biopsy of any kind is obtained, even if negative, the term pathologic stage is used.

[†]Adapted from Carbone, PP, et al, Cancer Res 1971; 31:1860 and Lister, TA, et al, J Clin Oncol 1989; 7:1630.

Symptoms in Gastrointestinal Lymphoma According to Involved Site[†]

Symptom	Stomach n = 277	Small bowel n = 32	Ileocecal n = 26	Multiple sites n = 24
Pain	78	75	77	58
Loss of appetite	47	41	23	58
Weight loss	24	34	15	25
Bleeding	19	6	12	8
Vomiting	18	31	8	21
Night sweats	11	12	19	46
Diarrhea	4	12	19	29
Constipation	3	25	23	12
Fever	2	6	8	4
Perforation	2	9	-	-
Ileus	-	38	19	4
No symptoms	4	-	-	-

This table shows the percent of patients with the listed symptom at each of the four major sites of disease.

[†] Data from Koch, P, et al. J Clin Oncol 2001 ; 19:3861.

Gastric Lymphoma

- 3 percent of gastric neoplasms
- 10 percent of lymphomas
- the most common extranodal site of lymphoma
- the most common site of gastrointestinal lymphoma
- can arise from two different sources:
 1. Primary involvement of gastric mucosal areas - MALT lymphoma, now called extranodal marginal zone B-cell lymphoma of MALT type in the REAL classification. Diffuse large B-cell lymphoma may also arise within the stomach as a primary lesion
 2. Secondary involvement via spread from adjacent lymph nodes

Gastric Lymphoma

- The vast majority of low-grade B-cell lymphomas of the stomach are MALT type
- Approximately 40 to 50 % present with indolent or low-grade histology, of which 70 to 80 percent are confined to the stomach (stage IE)
- the development of MALT lymphomas is linked to the clonal expansion of B-cells that accompanies chronic gastritis in the presence of *Helicobacter pylori*

Histologic Scoring for Diagnosis of MALT Lymphoma[†]

Grade	Description	Histologic 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 LELs.
2	Chronic active gastritis with florid lymphoid follicle formation	Prominent lymphoid follicles with surrounding mantle zone and plasma cells; no LELs.
3	Suspicious lymphoid infiltrate in lamina propria, probably reactive	Lymphoid follicles surrounded by small lymphocytes that infiltrate diffusely in lamina propria and occasionally into epithelium.
4	Suspicious lymphoid infiltrate in lamina propria, probably lymphoma	Lymphoid follicles surrounded by CCL cells that infiltrate diffusely in lamina propria and into epithelium in small groups.
5	Low-grade B-cell lymphoma of MALT	Presence of dense diffuse infiltrate of CCL cells in lamina propria with prominent LELs.

CCL = centrocyte-like lesion; LEL = lymphoepithelial lesion.

[†]Adapted from Wotherspoon, AC, Dogliogi, C, Diss, TC, et al, Lancet 1993; 342:575.

Gastric Lymphoma

- conditions that predispose to gastric lymphoma:

Helicobacter pylori-associated chronic gastritis

Autoimmune diseases

Immunodeficiency syndromes (eg, AIDS)

Long-standing immunosuppressive therapy
(eg, posttransplantation)

Gastric Lymphoma

- symptoms include
 - Epigastric pain or discomfort – 93%
 - Anorexia
 - Weight loss
 - Nausea and/or vomiting
 - Occult gastrointestinal bleeding, but hematemesis and melena are uncommon
 - Early satiety
- The duration of symptoms preceding the diagnosis is quite variable, ranging from a few days to six years.

Gastric Lymphoma

Physical examination

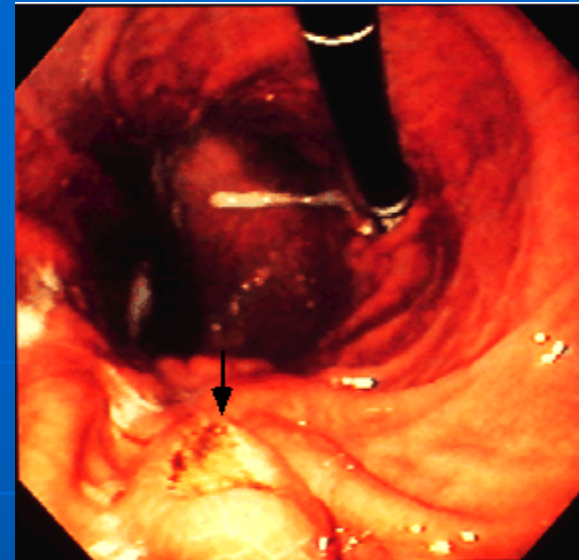
- often normal
- may reveal a palpable mass and/or
- peripheral lymphadenopathy when the disease is advanced

Laboratory studies

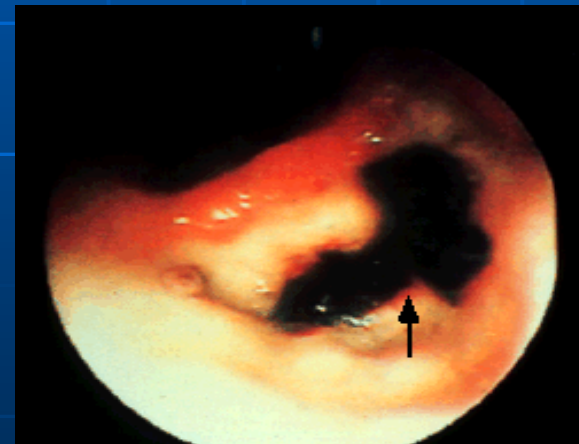
- tend to be normal at presentation
- anemia or an elevated ESR may be present in selected cases

Diagnosis

- EGD and biopsy - can provide a definitive diagnosis
 - mass or polypoid lesion with or without ulceration
 - benign-appearing gastric ulcer
 - nodularity
 - thickened, cerebriform gastric folds



Gastric MALT lymphoma A retroflexed endoscopic view of an ulcerated mass lesion (arrow) on the greater curvature in the body of the stomach; histology was consistent with a MALT lymphoma.



Gastric MALT lymphoma Endoscopic view of a deep benign appearing ulcer crater in the gastric antrum (arrow) with a large blood clot indicating recent hemorrhage. Histology was consistent with a MALT lymphoma.

Endoscopy

- Any suspicious appearing lesion should be biopsied
- Conventional pinch biopsies may miss the diagnosis (gastric lymphoma can infiltrate the submucosa without affecting the mucosa, most likely to occur when no obvious mass is present)
- Jumbo biopsies, snare biopsies, biopsies within biopsies ("well technique"), and needle aspiration can all serve to increase the yield
- EUS-guided FNAB or endoscopic submucosal resection may provide even greater diagnostic capability

Diagnosis

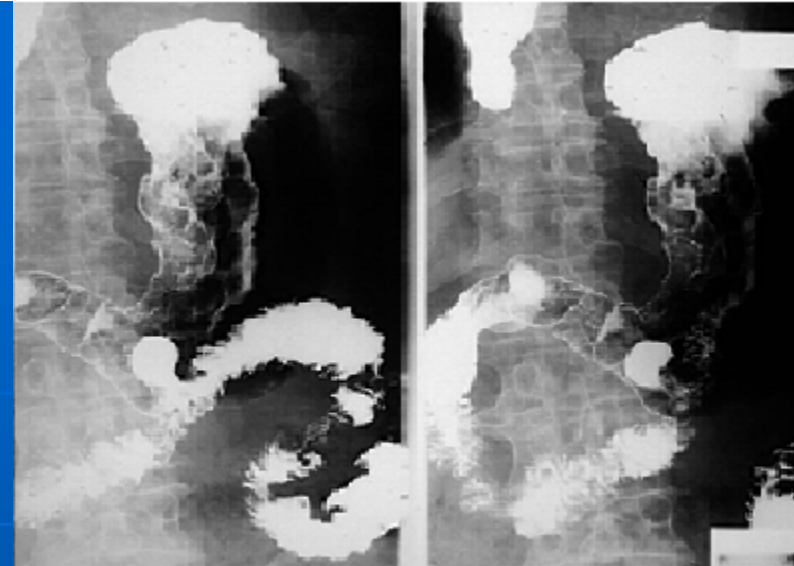
- upper gastrointestinal series

Mass or filling defect -70%

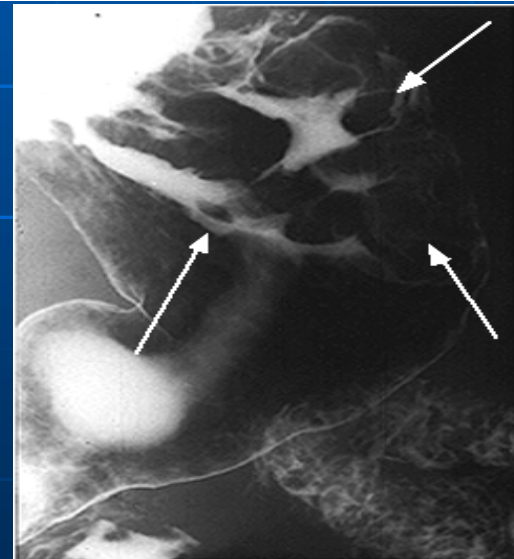
Ulcerated lesion -40%

Diffuse infiltration -20%

- none is diagnostic
- gastric adenocarcinoma, Menetrier's disease, chronic active gastritis, segmental rugal fold hypertrophy and PUD can mimic lymphoma
- patients should undergo gastroscopy with biopsy to confirm the diagnosis



Gastric MALT lymphoma Two air contrast upper gastrointestinal barium radiographs demonstrate diffuse nodular infiltration of the entire gastric body in a patient with a MALT lymphoma.



Gastric lymphoma Double contrast upper gastrointestinal examination shows massive and irregular thickening of the folds in the body of the stomach (arrows). Courtesy of Jonathan Kruskal, MD, PhD.

Gastric Lymphoma

Staging evaluation

- performed once the diagnosis of gastric lymphoma is established
- important prognostic information and dictates therapy
- All patients CT of the abdomen, pelvis, and chest to look for evidence of locoregional lymph node involvement, infiltration of contiguous structures, and distant metastases
- EUS may provide an assessment of the depth of intramural penetration
- both CT and EUS are limited in their assessment of perigastric lymph node status.

Staging evaluation

Laparotomy - mini-laparotomy, laparoscopy

- advantage of allowing direct visualization of the stomach, peritoneum, liver, and regional lymph nodes should probably be reserved only for patients without obvious systemic disease and with equivocal EUS or CT findings

Treatment

Eradication of H pylori

- Complete histologic regression has been demonstrated in 50 to 80 percent of carefully selected patients
- 10 % of patients with gastric lymphoma have localized (stage IE) mucosal disease are candidates for anti-H. pylori therapy
- the majority have aggressive or high-grade histology (ie, diffuse large B-cell lymphoma, see below), extensive mural involvement, or advanced stage (stages IIE to IV).
- even high-grade tumors may regress with antibiotic treatment and may not require more aggressive therapy

Treatment

- Eradication of *H. pylori* infection was achieved in 15 of the 16 patients
 - Gross and histologic tumor regression was evident in 10 subjects at the first follow-up endoscopic examination
 - the remaining six patients were immediately referred for chemotherapy
 - At a median follow-up of 43 months, all 10 patients with responsive disease were alive and free of lymphoma, while five of the six non-responding patients achieved complete remission following CHOP chemotherapy
-
- Chen, LT, Lin, JT, Shyu, RY, Jan, CM. Prospective Study of Helicobacter pylori Eradication Therapy in Stage I(E) High-Grade Mucosa-Associated Lymphoid Tissue Lymphoma of the Stomach. J Clin Oncol 2001; 19:4245

Treatment

- patients who do not respond to, or who relapse following, anti-*H. pylori* therapy still have a high rate of cure. Five-year survival for these patients is as high as 80 to 90 percent following single agent chemotherapy (eg, cyclophosphamide, chlorambucil, cladribine) or radiation therapy, including those positive for t(11;18)
- Multiagent chemotherapy, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), is reserved for patients failing or recurring after other less aggressive therapies, those with advanced stage disease (ie, stage III or IV disease), and those with transformation into diffuse large B-cell lymphoma

CHOP Chemotherapy for Non-Hodgkin's Lymphoma

CHOP-21 chemotherapy consists of four agents, Cyclophosphamide (Cytosan), Doxorubicin (Adriamycin, Hydroxydaunomycin), Vincristine (Oncovin), and Prednisone. One complete course is given every 21 days. Full treatment usually consists of six to eight such courses.

Drug	Dose and Route [†]	Given on day(s)
Cyclophosphamide	750 mg/m ² IV	day 1
Doxorubicin	50 mg/m ² IV	day 1
Vincristine	1.4 mg/m ² IV*	day 1
Prednisone	100 mg/day PO	days 1 through 5

*Total dose not to exceed 2.0 mg (CALGB protocols)

Major CHOP variants include:

CHOP-14, which uses the same four agents and doses as in CHOP-21 (above), but is given every 14 days. In CHOP-14, recombinant granulocyte colony-stimulating factor (G-CSF) is started on day 4 and is continued until day 13

CNOP, in which Doxorubicin is replaced by Mitoxantrone (Novantrone, 10 mg/m² IV, day 1)

CHOPE/CHOEP, in which Etoposide (100 mg/m² PO) is also given on days 1 to 3. CHOPE/CHEOP can be given every 21 days, or given every 14 days along with G-CSF.

CHOP-BLEO (CHOP-B), in which Bleomycin (10 u/m² IM) is also given on day 1

CHOP-R, in which Rituximab (375 mg/m² IV) is also given on day 1. In one version (GELA), rituximab, cyclophosphamide, doxorubicin, and vincristine are all given on day 1. In another version (ECOG), rituximab is given on day 1 and the other infusions are given on day 3.

Abbreviations: CALGB: Cancer and Leukemia Group B; GELA: Groupe d'Etude des Lymphomes de l'Adulte; ECOG: Eastern Cooperative Oncology Group

[†] McKelvey, EM, et al. Cancer 1976; 38:1484.

Treatment

- Historically, surgery was often the initial, and often sole therapy, for gastric lymphomas
- there is ample evidence for NHLs in general, and for gastric NHL in particular, to support the use of gastric conservation and rely more on systemic chemotherapy. This applies to both early stage IE and II/IIIE cases, and those with obvious extragastric spread (stage IIIIE, IV)
- For MALT lymphomas, and perhaps all gastric lymphomas, surgery may be a treatment which is no longer necessary

Koch, P, del Valle, F, Berdel, WE, et al. Primary Gastrointestinal Non-Hodgkin's Lymphoma: II. Combined Surgical and Conservative or Conservative Management Only in Localized Gastric Lymphoma-Results of the Prospective German Multicenter Study GIT NHL 01/92. J Clin Oncol 2001; 19:3874

Treatment

- 589 patients with early stage primary gastric diffuse large B-cell lymphoma were randomly assigned to receive either surgery (S), surgery plus radiation therapy (SRT), surgery plus CHOP chemotherapy (SC), or CHOP chemotherapy alone (C)
- ten-year event free survivals for the S, SRT, SC, and C groups were 28, 23, 82, and 92 percent, respectively
- Late toxicity was more frequent and severe in patients undergoing surgery. It was concluded that chemotherapy alone should be considered the treatment of choice in this setting

Aviles, A, Nambo, MJ, Neri, N, et al. The role of surgery in primary gastric lymphoma: results of a controlled clinical trial. *Ann Surg* 2004; 240:44

Treatment

- The original concern that chemotherapy in a patient with involvement of the stomach might lead to gastric perforation and/or bleeding has not been confirmed in a number of comparative studies

Schmidt, WP, Schmitz, N, Sonnen, R. Conservative management of gastric lymphoma: the treatment option of choice. *Leuk Lymphoma* 2004; 45:1847

- Usual therapy for the aggressive variants of NHL, such as gastric DLBCL includes the four drug CHOP regimen given in standard doses, without dose-reduction for the elderly

Intestinal Lymphoma

Primary small intestinal lymphoma

- uncommon in Western countries
- 75 percent of primary gastrointestinal lymphomas in the Middle East and Mediterranean basin
- in the Middle East, the presentation of small bowel lymphoma depends upon its association with immunoproliferative small intestinal disease (IPSID).

Intestinal Lymphoma

- Most patients with "western-type" intestinal MALT lymphomas have undergone a laparotomy at diagnosis because of perforation or obstruction, or to evaluate an unexplained abdominal mass
- only approximately 30 % of patients with stage IE or IIE disease, regardless of histology, may be cured with en bloc resection of involved bowel and contiguous nodes.

Clinical Features of the Different Types of Small Intestinal Lymphomas[†]

Feature	IPSID-associated lymphoma	Non-IPSID-associated lymphoma
Median age	25 years	37 years
Gender	Primarily males	Slight male predominance
Symptoms and signs	Abdominal pain Chronic diarrhea Malabsorption Severe weight loss Clubbing Ankle edema	Abdominal pain Palpable abdominal mass Bleeding Intestinal obstruction Intestinal perforation
Paraprotein	Usually present	Usually absent

[†]Adapted from Salem, P, El-Hashimi, L, Allam, C, et al, Cancer 1987; 59:1670.

Intestinal Lymphoma

Predisposing conditions - similar to those noted above for gastric lymphoma:

- Autoimmune diseases

- Immunodeficiency syndromes (eg, AIDS)

- Long-standing immunosuppressive therapy (eg, posttransplantation)

- Crohn's disease

- Radiation therapy

- Nodular lymphoid hyperplasia

Symptoms in Gastrointestinal Lymphoma According to Involved Site[†]

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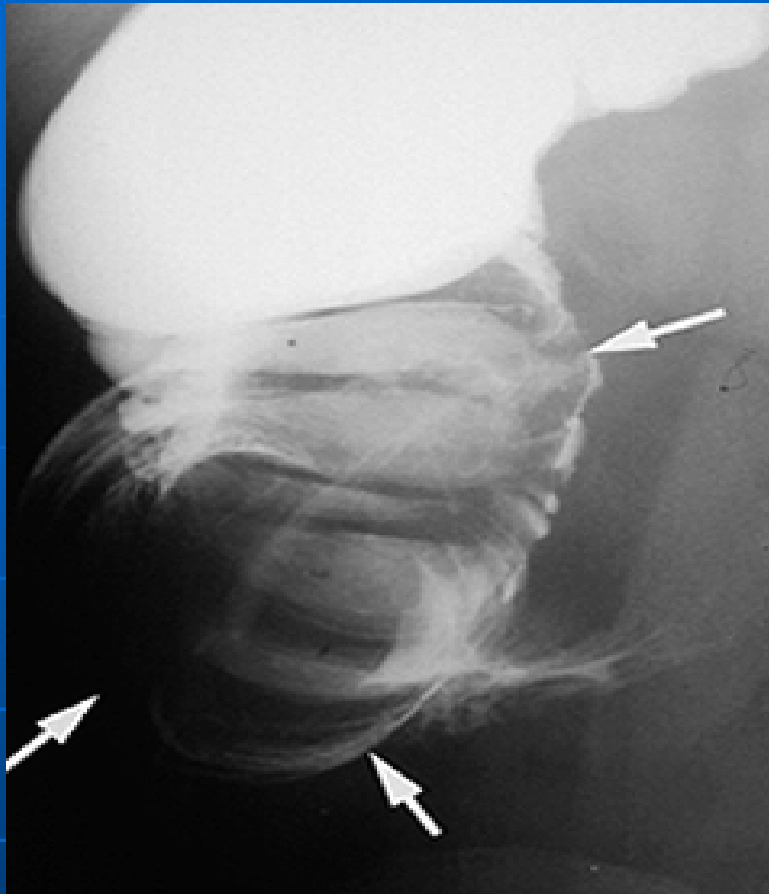
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[†] Data from Koch, P, et al. J Clin Oncol 2001 ; 19:3861.

Intestinal Lymphoma

Diagnostic evaluation

- Contrast radiography - the initial diagnostic modality for detecting small bowel lymphomas
- IPSID-associated lymphomas, more common in the proximal small intestine - diffuse infiltrating lesion, sometimes resembling cobblestoning
- Western-type non-IPSID lymphomas, more common in the distal small intestine - ulcerated, protruding, or infiltrating mass lesions - unifocal but can be multifocal



Intussusception of ileal lymphoma Barium enema shows a large soft tissue mass in the cecum (arrows) caused by intussusception of a lymphoma arising in the terminal ileum. Courtesy of Jonathan Kruskal, MD, PhD.

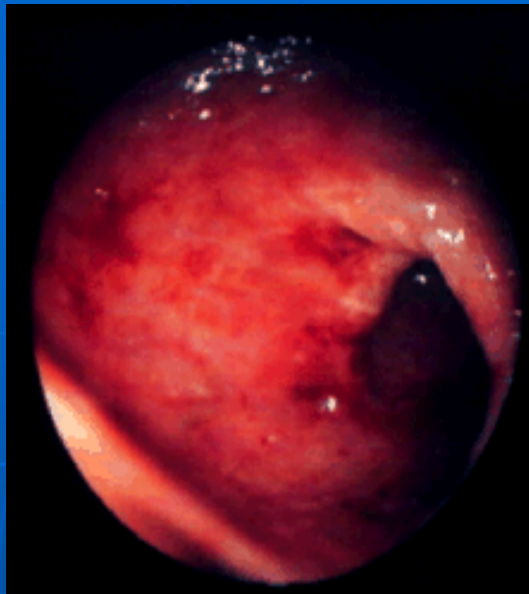


Non-Hodgkin's lymphoma of the colon and terminal ileum Post-evacuation film from a barium enema shows diffuse nodularity of the ileum and entire colon. Histology was consistent with a non-Hodgkin's lymphoma.

Intestinal Lymphoma

Diagnostic evaluation

- Proximal small bowel lesions may be detected by "push" enteroscopy
- Intubation of the terminal ileum during colonoscopy
- Exploratory laparotomy should be performed when the lesion is not accessible via endoscopy or when endoscopic biopsies are non-diagnostic.
- Colonoscopy is the principal diagnostic modality for colorectal lymphomas- diffuse mucosal nodularity, colitis-like changes with induration and ulceration, or a mass with or without ulceration



Non-Hodgkin's lymphoma of the colon Colonoscopic view of a friable, indurated mucosa with scattered areas of ulceration suggestive of inflammatory bowel disease. Histology was consistent with a non-Hodgkin's lymphoma.



Non Hodgkins lymphoma Endoscopic view of the rectum in a 95 year-old patient who presented with weight loss and anemia. The biopsy revealed non Hodgkins lymphoma. Courtesy of Alfonso Sandoval, MD.

Intestinal Lymphoma

Diagnostic evaluation

- Barium enema - may suggest the diagnosis but cannot reliably differentiate lymphoma from other conditions

Mass lesions with mucosal destruction

Mucosal nodularity

Infiltration of the submucosa with associated stricture

Bulky extracolonic masses

Treatment

Surgery

- after attempted curative resection five-year survival rates are only approximately 45 % for stage IE disease and 19 % for stage IIE
- relapses occurring 5 to 10 years after resection are common
- patients most likely to relapse include those with nodal involvement, extension beyond the bowel wall, and high-grade histology
- To improve survival rates, both radiation therapy and chemotherapy are often used postoperatively, although their efficacy is uncertain

Contreary, K, Nance, FC, Becker, WF. Primary lymphomas of the gastrointestinal tract. Ann Surg 1980; 191:593.

Treatment

Radiation therapy

- may reduce local recurrence rates when used in the adjuvant setting
- radiation has little impact on survival, because of high recurrence rates outside the radiation portals
- carries a significant risk of acute and chronic morbidity from radiation enteritis and vasculitis
- Combination chemotherapy may improve both disease-free and overall survival compared to surgery alone

Daum, S, Ullrich, R, Heise, W, et al. Intestinal non-Hodgkin's lymphoma: a multicenter prospective clinical study from the German Study Group on Intestinal non-Hodgkin's Lymphoma. J Clin Oncol 2003; 21:2740

Treatment

Combination chemotherapy

- treatment of choice for patients with advanced (stage III E and IV) disease. Response rates are comparable to those observed for extraintestinal NHLs, but the overall prognosis is poor, with 5-year and 10-year survival rates of approximately 50 and 20 percent, respectively

Fisher, RI, Dahlberg, S, Nathwani, BN, et al. A clinical analysis of two indolent entities: Mantle cell lymphoma and marginal zone lymphoma (including the mucosa-associated lymphoid tissue and monocytoid B-cell subcategories): A Southwest Oncology Group Study. *Blood* 1995; 85:1075

- As in the adjuvant setting, CHOP is the preferred regimen outside of a clinical trial

Palliative

- The role of radiation and surgery in advanced disease is uncertain.
- Radiation therapy provides effective palliation for extensive, unresectable disease, but is unlikely to have an impact on overall survival.
- Palliative surgical resection in patients with extensive or advanced disease prior to chemotherapy may prevent subsequent bleeding or perforation, but this approach remains controversial

Mantle Cell Lymphoma

- 31 cases found the following sites to be involved: stomach (57 percent), duodenum (52 percent), jejunum/ileum (87 percent), colon (90 percent), and rectum (69 percent)
- involvement of multiple sites, particularly the small intestine and colon, is referred to as "lymphomatous polyposis." The mean age at presentation is 55 years, with a male predominance.
- Polyps were found in both the small bowel and colon in 28 of 31 cases
- The unusual distribution of these lesions may be related to expression of the integrin alpha 4 beta 7 which a mucosal homing receptor that mediates lymphocyte migration to the intestinal mucosa by binding to MAd-CAM-1, which is a vascular recognition molecule (addressin) selectively expressed on mucosal endothelium

Mantle Cell Lymphoma

Presenting symptoms

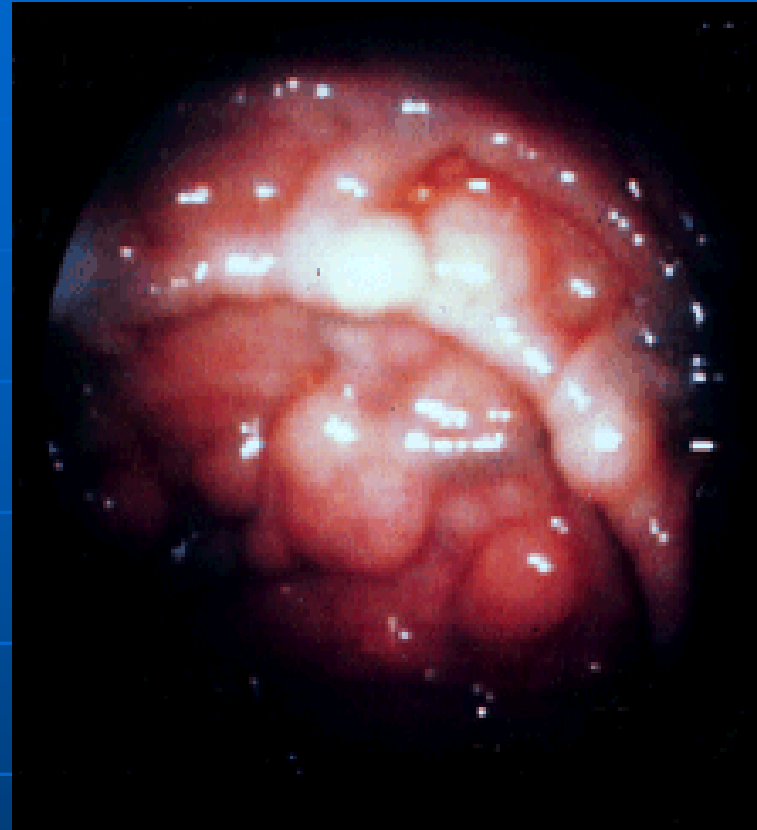
- often reflected the site of disease
- abdominal pain
- Diarrhea
- Hematochezia
- weight loss, fatigue
- Liver involvement occurred in 26 percent of the patients, while malignant cells were seen in the peripheral blood in only one case

Mantle Cell Lymphoma

Diagnostic evaluation —dictated by the clinical presentation.

- Colonoscopy - hematochezia, occult bleeding, diarrhea, or lower abdominal pain
- confirm abnormalities noted on barium enema.
- Endoscopy (esophagogastroduodenoscopy or enteroscopy) - epigastric pain or obstructive symptoms. occult bleeding or lower gastrointestinal symptoms and have negative colonoscopies

- Typical small nodular or polypoid tumors (2 mm to more than 2 cm in size), with or without normal intervening mucosa, can be seen by colonoscopy or enteroscopy
- large cerebroid folds may be seen in the stomach



Mantle cell lymphoma

Colonoscopic view of multiple polypoid lesions in the proximal colon. Histology was consistent with a mantle cell lymphoma.

Mantle Cell Lymphoma

Diagnostic evaluation

- Barium radiographs of the small bowel may show numerous round filling defects in the lumen or a tumor mass in the terminal ileum
- Abdominal CT with oral contrast may reveal ileocecal thickening, an obvious mass which may cause obstruction, retroperitoneal lymphadenopathy, and hepatic or splenic enlargement.

Mantle Cell Lymphoma

- Endoscopy with biopsy - diagnostic procedure of choice.
- colonoscopic intubation of the ileum with biopsies should be performed when barium studies show terminal ileal involvement
- EGD for upper gastrointestinal tract symptoms or when UGIS suggests involvement proximal to the second portion of the duodenum
- push enteroscopy should be performed for proximal jejunal lesions or in patients presenting with major bleeding in whom colonoscopy and standard upper endoscopy fail to identify a source
- CT-guided needle biopsy can be used for an accessible mass

Mantle Cell Lymphoma

Staging evaluation

- Common sites of involvement include bone marrow (52 percent of patients) and Waldeyer's ring (27 percent)
- Approximately 70 percent of patients have advanced disease (ie, stage IV) at the time of diagnosis

Treatment

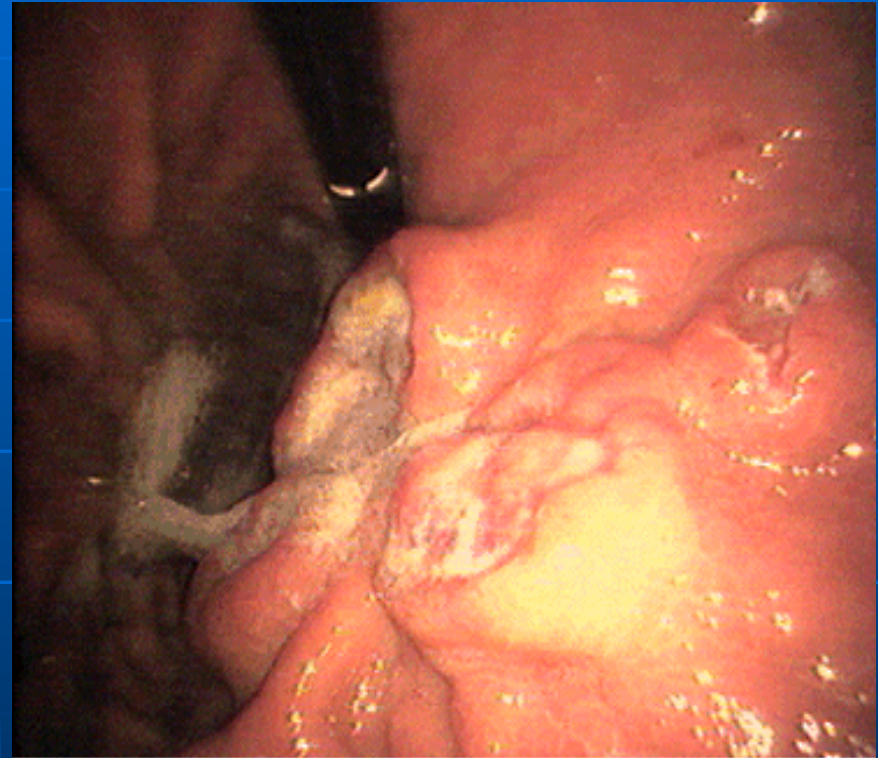
- systemic chemotherapy is the treatment of choice
- presently considered to be an incurable disease, with a median survival of 3 to 5 years
- aggressive chemotherapy followed by autologous stem cell transplantation may benefit younger patients

Khouri, I, Romaguera, J, Kantarjian, H, et al. Hyper-CVAD and high-dose methotrexate/cytarabine followed by stem-cell transplantation: An active regimen for aggressive mantle-cell lymphoma. *J Clin Oncol* 1998; 16:3803

- Surgery has a relatively small role in the management of this disease, but may be of value in patients presenting with bowel obstruction.

Burkitt's and Burkitt-like Lymphomas

- disease of childhood, peak incidence at about 8 yo
- GI manifestations are infrequent but may include obstruction or intussusception
- "Burkitt-like" ("sporadic" Burkitt's) lymphoma exhibits a wider age distribution, only 50% of cases affecting children, often presents with abdominal pain and obstructive symptoms caused by ileocecal involvement



Burkitt's lymphoma Lobulated, ulcerated protuberances seen on retroflexed view during endoscopy in a patient with abdominal pain. Biopsy revealed them to be Burkitt's lymphoma. Courtesy of Eric D Libby, MD.

Burkitt's and Burkitt-like Lymphomas

- may be associated with HIV infection, immunosuppressive therapy, or Epstein-Barr virus (EBV) infection

Burkitt's and Burkitt-like Lymphomas

Diagnostic evaluation

- Small bowel contrast radiography
- CT scan
- laparotomy is often required for confirmation
- colonoscopic retrograde intubation of the terminal ileum and biopsy may be diagnostic
- CT-guided biopsy can be attempted when a mass is present
- examination of the bone marrow and peripheral blood may be diagnostic, and may obviate the need for laparotomy and/or other biopsy procedures

Treatment

- Chemotherapy is the mainstay of treatment
- resection is often required to alleviate symptoms or avoid perforation during chemotherapy

Fleming, I, Turk, PS, Murphy, SB, et al. Surgical implications of primary gastrointestinal lymphoma of childhood. Arch Surg 1990; 125:252

- Autologous bone marrow transplantation is also of value in patients with poor-risk disease
- In adults, tumors can arise at any site in the gastrointestinal system, but are most common in the ileocecal region and the rectum. Treatment options are the same as in children.

Prognosis

- non-HIV associated cases - improved considerably with the use of aggressive, multidrug chemotherapy regimens, and, in selected cases, autologous hematopoietic cell transplantation.
- HIV-associated Burkitt-like lymphomas is related more to the underlying HIV syndrome than the lymphoma itself

Enteropathy-associated T-cell Lymphoma

- sequela of gluten-sensitive enteropathy (celiac sprue)
- ulcerative enteritis, another complication of long-standing celiac sprue, is probably a variant of EATL
- The mean age of patients with EATL is 60 years
- Most patients have a several month to several year history of abdominal pain and weight loss, but only a small proportion have a history of celiac disease dating back to childhood
- Patients often present with acute bleeding, obstruction, or perforation

Enteropathy-associated T-cell Lymphoma

- Clinical deterioration of celiac disease, despite compliance with a gluten-free diet, should raise suspicion of the possible presence of lymphoma
- Conversely, since celiac disease may be undiagnosed at the time of presentation of the intestinal lymphoma, it has been suggested that patients with a T-cell lymphoma and/or a gut primary localization should be tested for the presence of underlying celiac disease

Enteropathy-associated T-cell Lymphoma

- **Diagnostic evaluation**
- Endoscopy with biopsy is the diagnostic test of choice

Large circumferential ulcers without overt tumor masses are found in the jejunum

Biopsies of the involved mucosa demonstrate lymphoma, while biopsies of the normal appearing mucosa usually show villous atrophy characteristic of celiac disease

- laparotomy may be necessary to confirm the diagnosis

Treatment

- the prognosis is poor and is worse than that of intestinal B-cell lymphoma
- Five-year survival is approximately 10 percent
- Favorable outcomes with multidrug therapy occur only in patients who have minimal gastrointestinal symptoms prior to the diagnosis of lymphoma, and can tolerate therapy. Patients should also be maintained on a gluten-free diet.