

Extranodal Lymphomas

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Case: JT

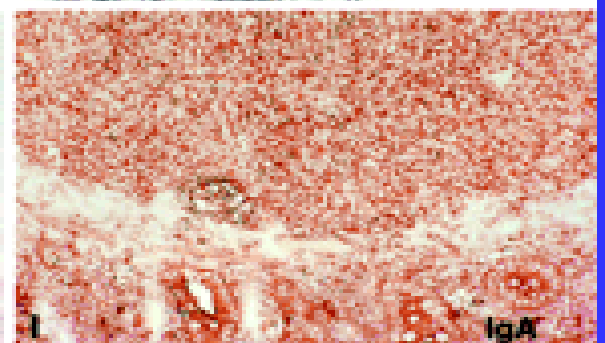
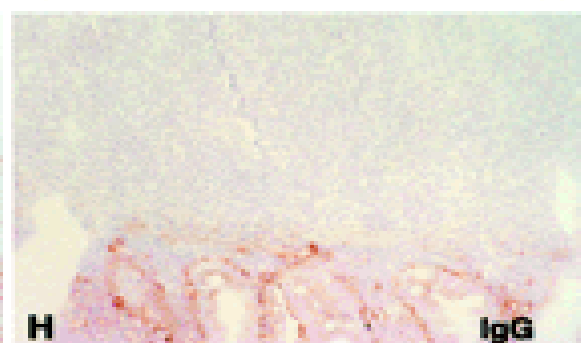
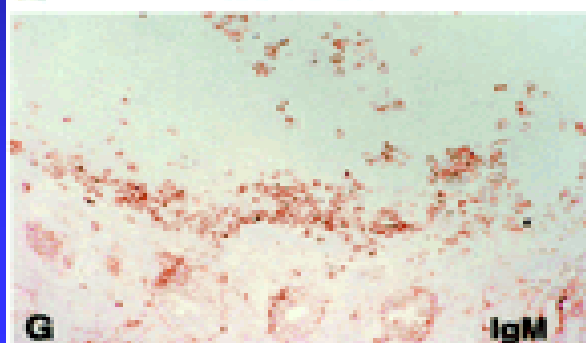
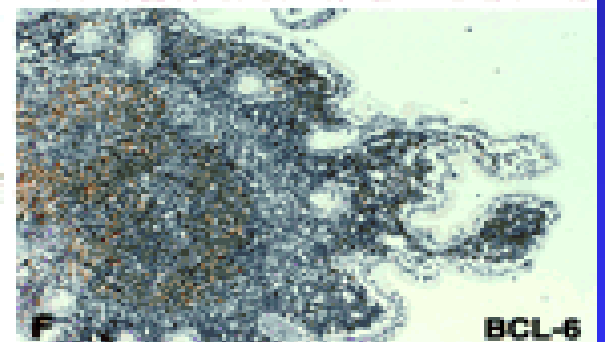
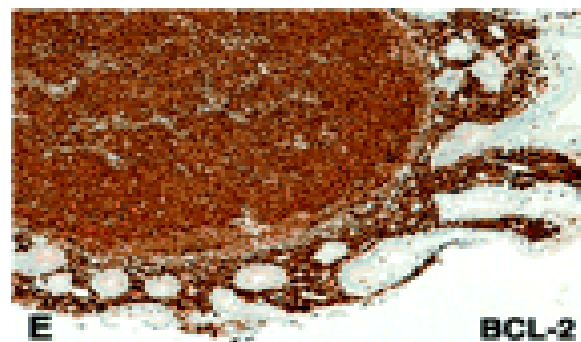
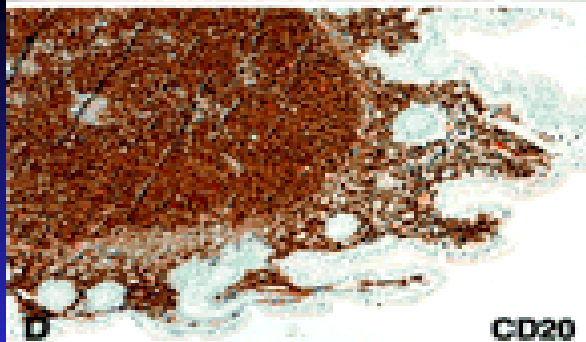
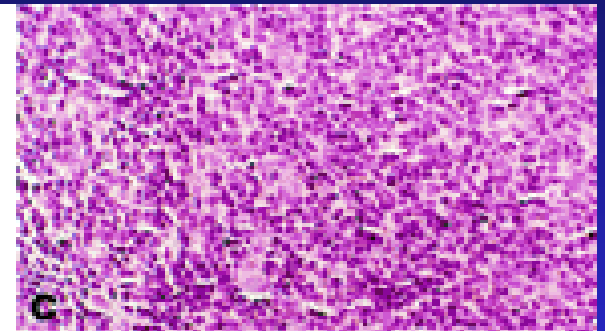
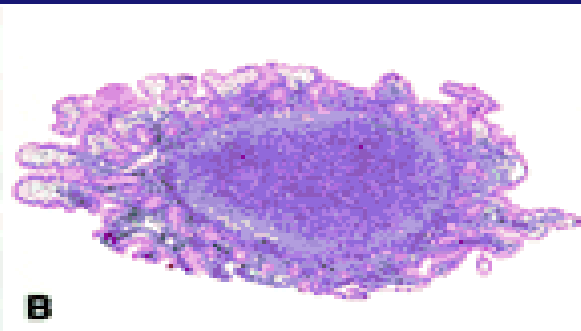
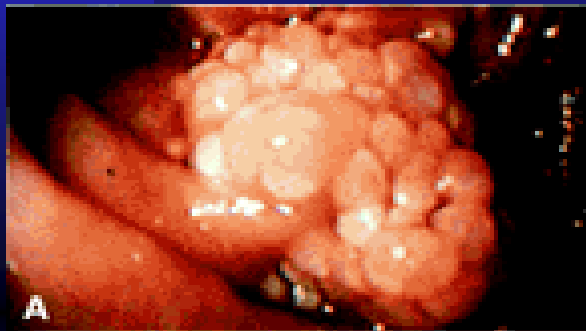
- 69 yo male COO software company
- PMHx: basal cell back, cholesterol
- Presents to ER with severe abdominal pain, bloody diarrhea x 2d
- In ER vomiting x 2
- ROS: RLQ discomfort for years; increased satiety for 1 month
- Sigmoidoscopy internal hemorrhoids
- Colonoscopy: 10 cm polypoid mass Right side of colon distal to cecum with near complete luminal obstruction
- CT scan demonstrates: cecal mass with ileocecal intussusception with moderate SBO; several prominent RLQ mesenteric nodes 9 mm, aortocaval 7 mm
- CT chest negative
- LDH, CBC, Creat, liver profile normal
- Transferred to Gen Sx in Toronto

Case continued..

- Biopsy from colonoscopy: B cell NHL unknown type- looks low grade
- BM biopsy: neg
- How would you treat him?
 1. Surgical excision alone
 2. Surgical excision and XRT
 3. Surgical excision and chemotherapy
 4. XRT alone
 5. CVP-R
 6. CHOP-R
 7. Fludarabine based-R

Patient underwent hemicolectomy:

7 x 4.5 cm intussuscepted segment of ileum in colon - mucosal surface covered by tan polypoid mucosal projections
Bowel: infiltrated by small lymphs with angulated nuclei extending into submucosa
Proximal ileum and distal colon normal



Patient underwent R hemicolectomy....

- Negative for CD10, cyclin D1, CD5 and CD23
- PCR: t(14;18)
- Ki67 5%
- Mesenteric lymph nodes 0.6 cm to 2.5 cm: preserved nodal architecture with reactive pattern but t(14;18) by PCR
- **Diagnosis:** follicular grade 1 involving terminal ileum/ileocecal valve and mesenteric LN's

Primary extranodal lymphomas

- 1/3 of NHL arise extranodally
- Limited data on optimal therapy
- Diagnosis controversial:
 - ◆ Only stage 1-2?
 - ◆ Permit regional lymph node involvement
 - ◆ Permit distant nodal disease as long as EN NHL predominant disease bulk?
 - ◆ EN involvement in disseminated disease may be secondary

IELSG outcome of EN lymphomas

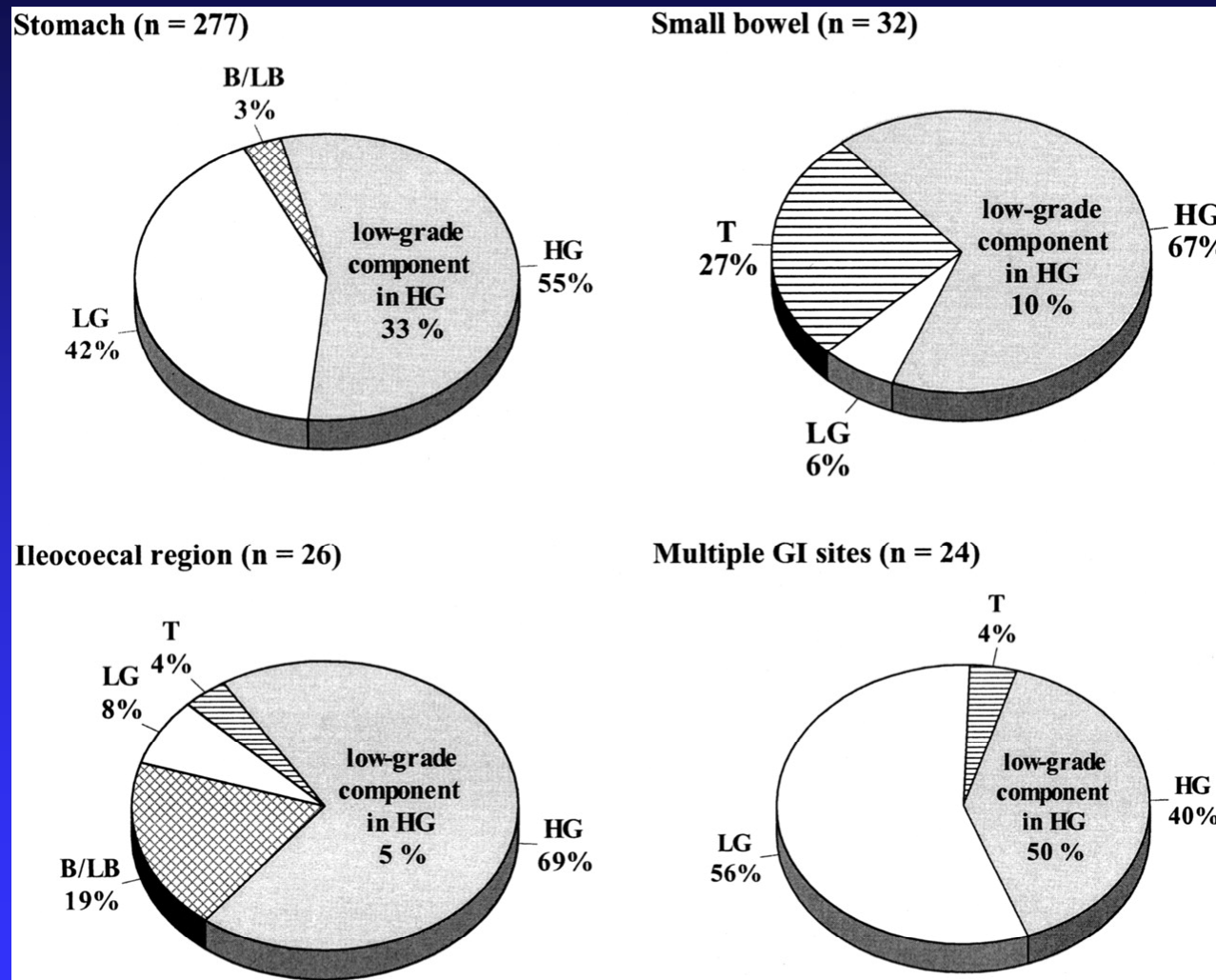
NHL site, histology	# patients Stage 1-2/total	Survival	Reference
Stomach, MALT	100/100	5 yr: 91%	Hancock, 2005
Intestine, MALT	21/35	5 yr: 65%	Cortelazzo, 2002
Non-GI, MALT	131/180	5 yr: 90%	Zucca, 2003
Stomach, DLBCL	219/312	5 yr: 75%	Cortelazzo, 1999
Intestine, DLBCL	40/87	5 yr: 68%	Cortelazzo, 2002
Breast, DLBCL	193/204	5 yr: 63% 10 yr: 47%	Ryan, 2008
Testis, DLBCL	294/373	5 yr: 48% 10 yr: 27%	Zucca, 2003
CNS, DLBCL	370/370	5 yr: 37%	Ferreri, 2003

The GI tract and lymphoma

- Most common site of EN primary NHL
- 4-18% in Western countries and up to 25% in middle east

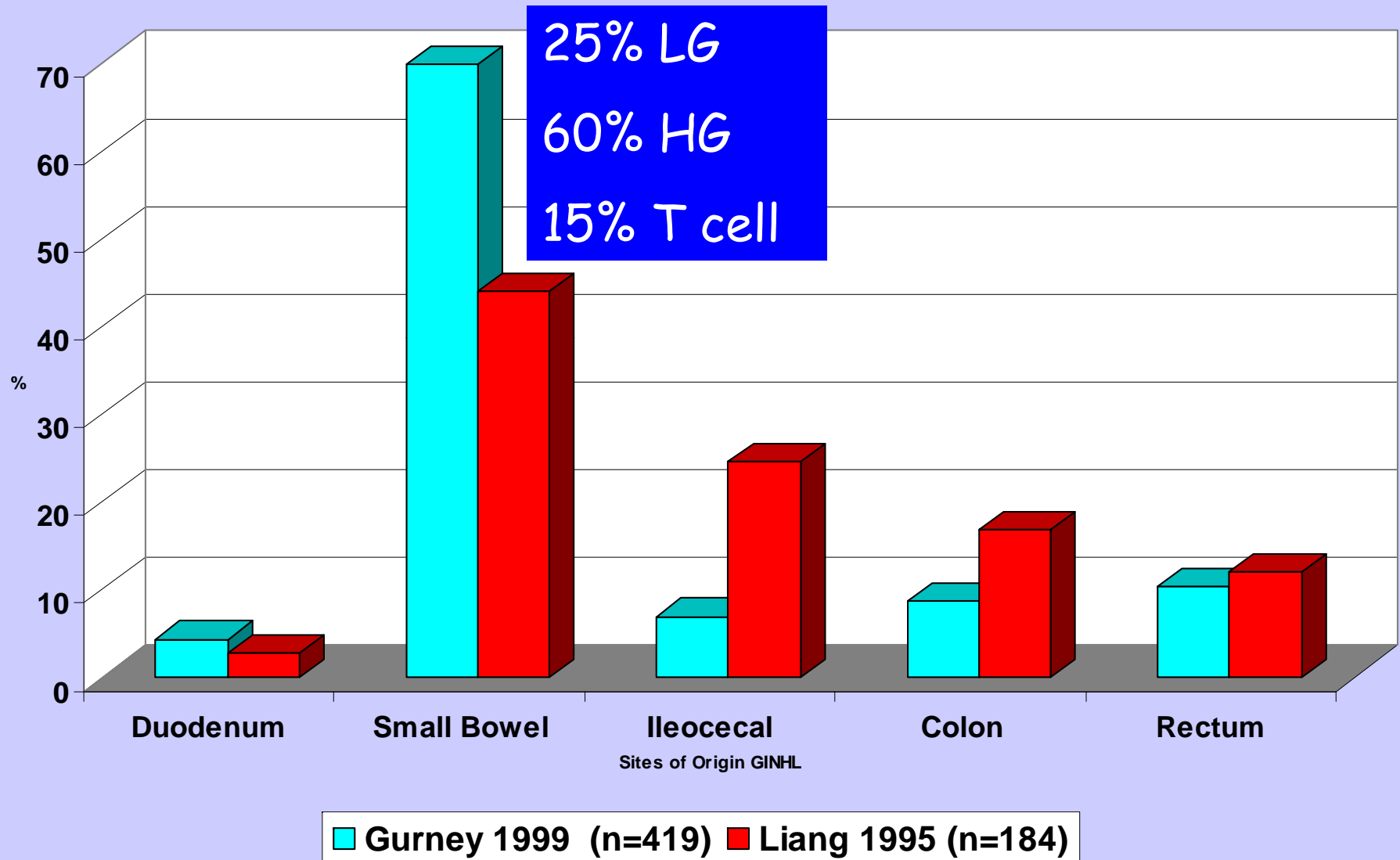
Primary Site	#	%
Stomach	277	75%
Small bowel	32	8.6%
Ileocecal	26	7%
More than 1 GI site	24	6.5%
Other sites	12	3.2%
Duodenum	3	
Colon, diffuse	3	
Rectum	6	
All	371	100%

Fig 1. Distribution of histologic subtypes in primary GI NHL.
 Abbreviations: LG, low-grade; HG, high-grade; B/LB, Burkitt's or lymphoblastic; T, T cell.



Koch, P. et al. J Clin Oncol; 19:3861-3873 2001

Sites of Origin in Primary Intestinal NHL: Literature



Common primary lymphomas of the GI tract according to the WHO classification

B cell

MALT

Mantle cell

Burkitts

DLBCL

Follicular

SLL

Lymphoplasmacytic

Plasma Cell: plasmacytoma

T cell and NK

Adult T cell

EITCL

Nasal type/NK cell

Angioimmunoblastic

ALCL

Hodgkin's

GI-NHL Staging International Workshop

Lugano

Rohatiner et al 1994

<u>Stage</u>	<u>Criteria</u>
I	Tumor confined to GI tract Single primary site or multiple non-contiguous lesions
II	Tumor extending in abdomen from primary GI site Nodal involvement
II1	Local (paragastric or paraintestinal)
II2	Distant(mesenteric, para-aortic, pelvic, inguinal)
III	Penetration of serosa to involve adjacent organs or tissues
IV	Disseminated extranodal involvement of a GI tract lesion with supradiaphragmatic nodal involvement

Symptoms at diagnosis of primary GI NHL

- Pain: 58-73%
- Anorexia: 40-58%
- Weight loss: 15-34%
- Bleeding: 6-18%
- Vomiting: 7-31% (small bowel highest)
- Night sweats: 11-46% (multiple GI highest)
- Diarrhea: 3-30% (multiple GI highest)
- Ileus: 4-37% (small bowel highest)
- B symptoms: 11-25% (multiple GI highest)
- Median time to diagnosis:
 - ◆ Gastric: 93 d
 - ◆ Small bowel: 135 d
 - ◆ Ileocecal: 76 d
 - ◆ Multiple GI: 142 d

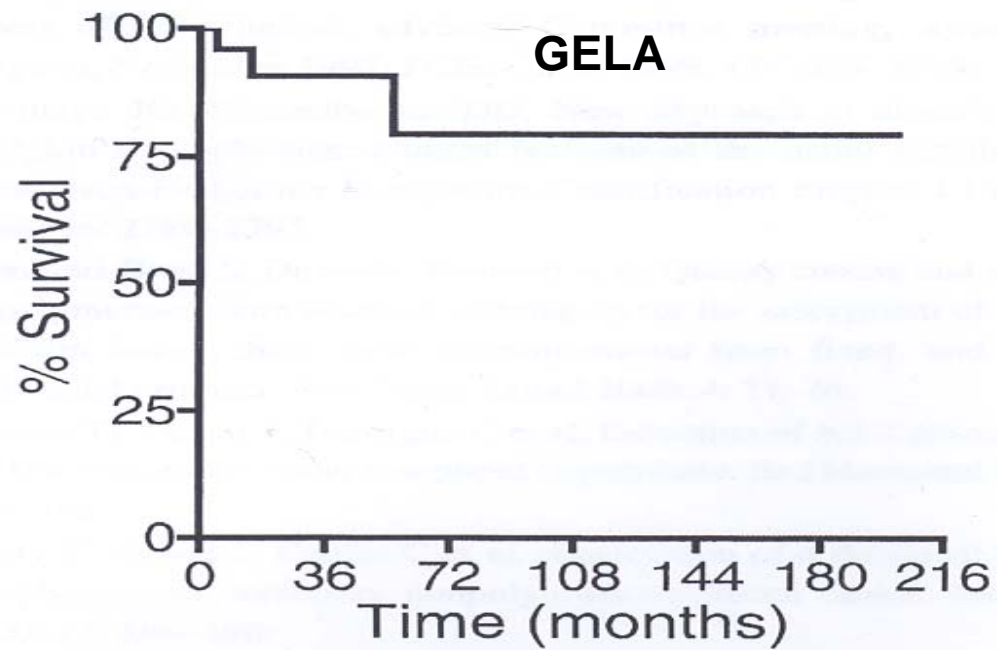
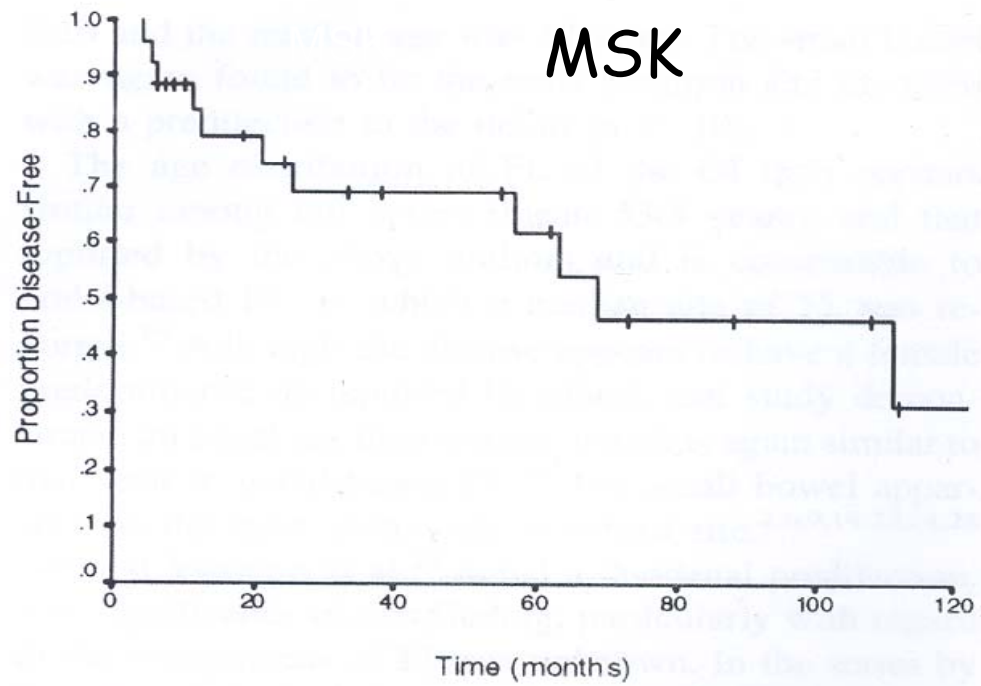
Primary Follicular Lymphoma of GI tract

- 1-6% of lymphomas arising in GI tract
 - ◆ 35% of duodenal lymphomas
- Histologic, IHC and genetic features of nodal FL
 - ◆ Express surface IgA and $\alpha 4\beta 7$ integrin
- 2 major series:
 - ◆ MSK-Shia J. et al Am J Surg Path 2002 (n=26)
 - ◆ GELA-Damaj G et al. Annals of Oncology 2003 (n=25)

*Bende RJ, Am J Pathol. 2003 Jan;162(1):105-13 Shia J. et al 2002. 26(2): 216-224.
Damaj G 2003. Annals of Oncology 14: 623-629*

	GELF: Damaj et al 2003 (n=25)	MSK: Shia et al 2002 (n=26)
Median age	56	55
M: F	1:2	1:1
Abdominal pain	50%	50%
Unifocal/Multifocal	15/10	21/5
Small bowel	60%	84%
duodenum	9	10
ileum	13	6
Colorectal	10	6
Lymphomatous polyposis	7	1
Stage I/II/IV	12/10/3	16/10/0

	GELA: Damaj et al 2003 (n=25)	MSK: Shia et al 2002 (n=26)
Therapy at diagnosis	18/25	22/25
CSR alone	4	7
CTx alone	10	4
CSR + CTx	2	9
CTx + rads	2	1
observation	7 (5 unifocal)	4
CR	83%	68%
Relapse	33% (31m)	33% (46m)
Median follow up	34 months	44 months
Death from lymphoma	1	0
5 yr RFS	N/A	54%
Median DFS	N/A	69 months



Conclusions

- PFLGI rare-6% of all GI lymphomas
 - ◆ Usually localized
 - ◆ Predominance for small bowel
- Prognosis not different from nodal FL
- Can present as lymphomatous polyposis
- Surgery, XRT and/or immuno-chemotherapy: clinical symptoms
- Median time to progression 31-38 months

My patient..

- 3 months post-op:
 - ◆ CT scans clear
 - ◆ CT enteroscopy: negative
 - ◆ FDG PET: neg
- 12 months staging: NAD
- Currently under observation and asymptomatic @ 20 months