Weird and Wonderful Tumours in the GI Tract

GIST
Carcinoid
Lymphoma

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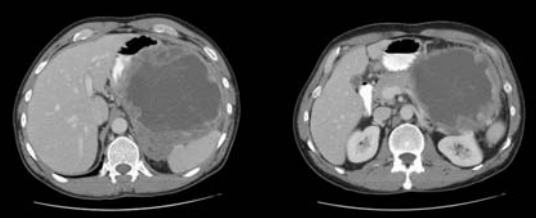
Disclosure

Case I

- 53-year-old male presents with UGI bleed
- Transfused 2 units of blood
- EGD shows gastric ulcer related to apparent extrinsic mass
- Endoscopic biopsies nondiagnositic

CT Scan Abdomen



Management

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US Guided Core Biopsy

- Retroperitoneal approach to avoid peritoneal contamination
- Pathology- consistent with GI stromal tumour, c-kit positive, unable to assess mitotic activity in small sample
- Is biopsy always necessary and what are risks?

GI Stromal Tumours

- 0.2% of all GI tumours but 80% of GI sarcomas
- Peak incidence 40-60 year old
- Originate from interstitial cells of Cajal (ICC)
- Gastric (50%), SI (25%), CR (10%)
- Asymptomatic(1/3), vague pain, bleeding

Management

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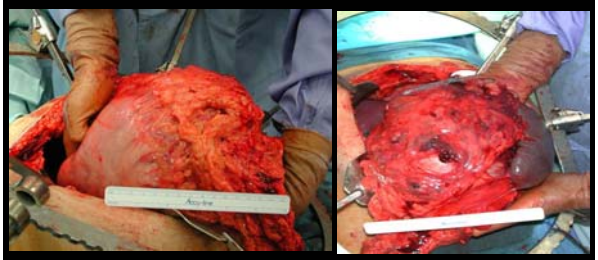
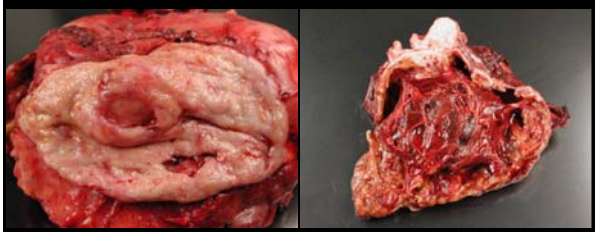
Principles of Surgery

- Complete gross resection with intact pseudocapsule
  - Handle with care!
  - Fragile, hemorrhagic and tend to disseminate if ruptured
- Tend to displace rather than invade organs
- Lymphadenectomy not necessary

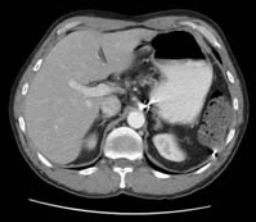
Operation: Partial Gastrectomy and Splenectomy



Postoperative Specimen



Postoperative CT Scan



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Pathology Report

- 20 cm high grade GIST
- Spleen not involved with tumour
- Extensive necrosis and hemorrhage within tumour
- Pseudocapsule intact, gastric margins clear

Follow-up

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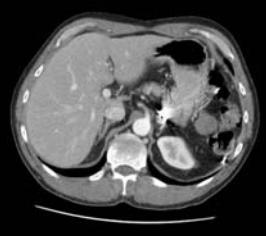
GIST: Malignant Potential

Risk *	Size	Mitotic Rate
High	Any	>10/50 HPF
	>10 cm	Any
	>5cm	>5/50 HPF
Intermediate	5-10 cm	<5/50 HPF
	<5 cm	6-10/50 HPF
Low	2-5 cm	<5/50 HPF
Very Low	<2 cm	<5/50 HPF

Overall Survival by Risk Group

- Overall 5 year survival 50-65% but only 20% for tumours >10cm
- 50% survival after 1.5-2.5 years for high risk /overtly malignant group
- 50% survival after 14 years for the intermediate group
- Note: 35% of GIST patients are high risk

One year later



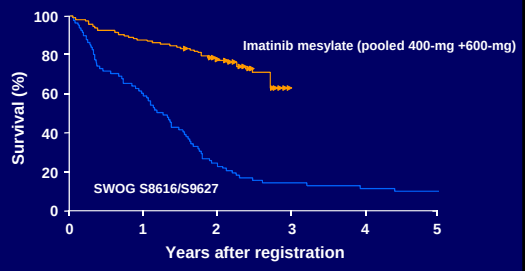
GIST Recurrence

- Depends on site
- Median time is 18 months
- Overall only 10% of patients remain disease free on extended follow-up
- Recurrence is equivalent to metastatic disease
- Primary OR only if fully resectable

Management of Recurrence

- 95% of GIST have mutations in KIT Receptor Tyrosine Kinase (c-kit) which affect proliferation
- Imatinib Mesylate (Gleevac) is a tyrosine kinase receptor blocker
- Effective in the management of recurrent/metastatic GIST

Imatinib Mesylate in GIST: Pivotal Trial—Overall Survival



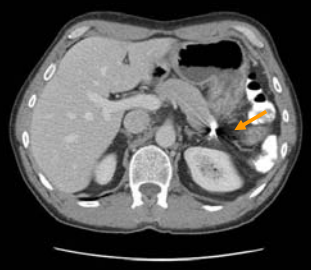
- With a median follow-up of 34 months, median survival has not been reached

Blanke et al. ASCO 2004 Gastrointestinal Cancers Symposium. Abstract 2.

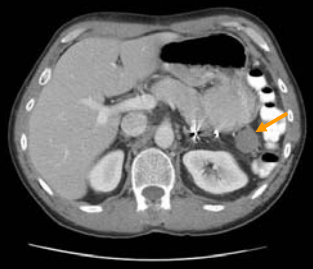
Management of Recurrence

- Treated with imatinib mesylate 400 mg po daily
- No adverse effects and continued to function normally
- Common SE:fatigue, diarrhea, edema, anemia
- Serious SE: hemorrhage, neutropenia

Post-treatment CT Scan after 10 months: Complete Resolution



Tumour Progression During Treatment at 14 months



Resection of Recurrent Focus

- Patient underwent complete excision of this single focus of recurrent disease with negative margins
- Exploration of the rest of the abdomen revealed no other evidence of disease
- At this time remains well on Imatinib (drug should not be discontinued as flare risk)

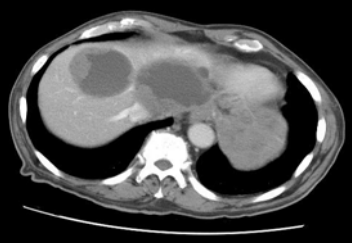
Alternative Option: Adjuvant Therapy

- Given high risk of recurrence current trials under way
- resected high risk tumours (nonrandomized)
- low-medium risk (randomized)

Case II

- 74 year-old male
- Presented in summer 2003 with vague abdominal pain
- EGD revealed a submucosal gastric mass-biopsies negative
- CT abdomen showed liver mets and liver biopsy revealed metastatic GIST

CT Imaging



Management

Patient with unresectable metastatic disease

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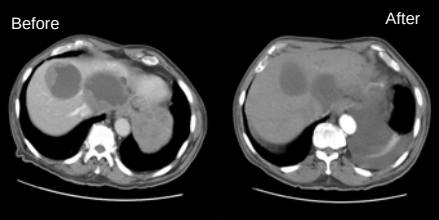
Treatment with Imatinib



Management of Metastatic GIST

- Patients with unresectable metastatic disease and resectable primaries can be managed with imatinib with close medical supervision
- Change in density on CT is seen before change in size
- PET very sensitive to response to treatment (2 weeks)
- Dose escalation indicated in non-responders
- New therapies

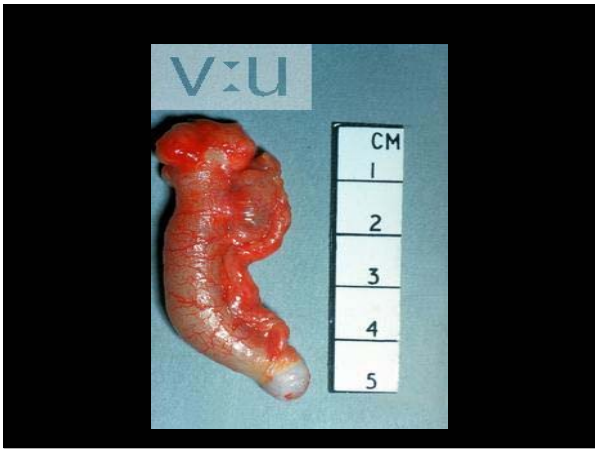
Question Period GIST

Case III

- N.C 40 year old man
- Presents to emergency with 12 hour hx RLQ pain, initially periumbilical
- Anorexic
- Temp 38.2, WBC 13,000
- Tender with guarding at McBurney's point

Operative Findings

- Routine open appendectomy
- Apparent early appendicitis
- Small nodule noted at tip of appendix



Pathology Report

- Early acute appendicitis
- 0.9 mm incidental carcinoid tumour at tip of appendix
- No local invasion
- No lymph nodes in specimen

Carcinoid Tumours

- Neuroendocrine tumours derived from enterochromaffin cells
- 90% are GI origin (bronchus, ovary, thymus)
- Most common site appendix 36%
- 0.3% of appendectomies

Management Appendiceal Carcinoid

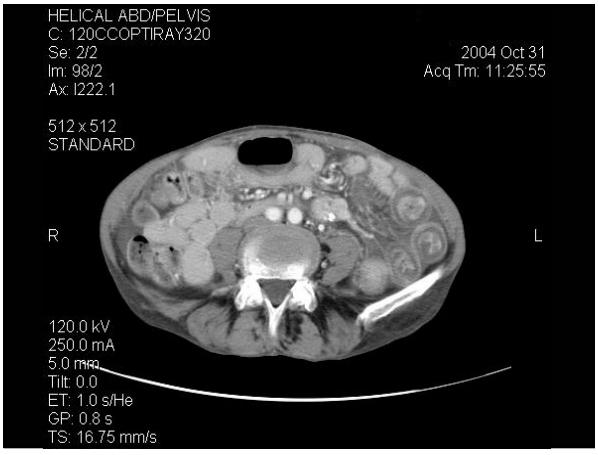
- <1 cm appendectomy alone
- >2 cm right hemicolectomy (20-30% have nodal mets)
- 1-2 cm right hemi if margins positive, subserosal lymphatic invasion, mesoappendiceal invasion
- Survival 99%

Case IV

- M.K. 57 y.o woman
- Presents to emergency department with a small bowel obstruction
- 2 month history of intermittent crampy periumbilical abdominal pain and nausea
- No prior surgical history
- No hernias on physical exam

Investigations

- WBC mildly increased at 12.5
- Typical findings of SBO on plain films
- CT scan of abdomen ordered



Radiology Report

- Dilated thickened jejunal loops on left side
- Free fluid
- Calcified mesenteric mass measuring 3 cm in size in proximal jejunum
- Celiac osteal stenosis
- Mesenteric lymphadenopathy present

Operative Findings and Procedure

- Tumour in distal jejunum
- Tumour in mesentery causing secondary ischemia of distal jejunum over 1.5-2 feet
- Segmental resection including mesenteric mass with primary anastomosis

Pathology Report

- Carcinoid tumour of small bowel with 3 tumour nodules (2cm, 0.5cm, 0.2cm) with transmural invasion
- Mesenteric mass (4.5 cm) is 'soft tissue deposit of carcinoid'
- 2/14 regional nodes positive for metastatic carcinoid, one completely replaced
- Margins of resection clear

Carcinoid Tumours of SB

- 2nd most common site of GI involvement (25%)
- Multiple in 30-50%
- Kinking and angulation of the small bowel
- mesenteric masses, calcified with desmoplastic reaction

- Nodal involvement in 45% with tumours less than 1cm
- Wide excision plus nodes for all cases
- Prognosis 50-60% 5 year survival overall (75% if node negative)

Follow-up Plan

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Carcinoid Syndrome

- Carcinoid tumours secrete serotonin (+)
- Contain dopa decarboxylase which converts 5 hydroxytryptophan (5HPT) in serotonin (5HT) which is metabolized into 5 hydroxy-indoleacetic acid (5HIAA)
- Systemic 5HIAA causes flushing, diarrhea, bronchospasm, and right heart valvular disease

Carcinoid Syndrome

- 18% of patients overall
- rare in appendiceal carcinoid
- Common in small bowel carcinoid
- Associated with large volume disease and liver mets (systemic access)
- 24 hr urine 5HIAA (not sens or spec)
- Serum chromogranin A (100% spec, 80% sens)

Follow up

- 24 hour urine 5HIAA normal at 19 mmol/day
- Serum chromogranin A normal at 34
- Repeat CT Abdomen NED
- Clinically asymptomatic at 3 months post op

6 months post op

- asymptomatic
- 24 hour urine 5HIAA 26 (0-50)
- CgA 20 (<40)

9 months post op

- Brief episodes of flushing at night
- No diarrhea
- No change in blood or urine results
- Single new 1.2 cm hypodense liver lesion
- Indeterminate and not amenable to biopsy

12 months post op

- Flushing and diarrhea
- Urine 5HIAA 37 (0-50)

Management

?

Carcinoid Management of Metastatic Disease

- Tends to be slowly progressive
- Debulking, ablation, embolization improve 70%
- Medical therapy- octreotide reduces flushing in 70%, diarrhea in 60%
- Radiolabeled octreotide decrease symptoms and tumour load in 60%

Question Period Carcinoid

Case V

- 67 y.o. man
- History of GERD for 7 years, takes Ranitidine
- May 2004: anorexia, early satiety and fatigue
- July 2004: Melena, coffee ground emesis. Lost 20 lb over 2 months
- ER: Hgb 70

Management

- Transfused, IV PPI
- Upper GI endoscopy: esophagitis, nodular mass, blood clots.
- Biopsy: Diffuse large B-cell lymphoma (intermediate grade WHO). H.pylori negative.

GI Lymphoma

- GI tract in most freq extranodal site NHL
- Most common GI primary lymphoma (50-65%) are diffuse large B cell
- West –stomach, SI,
- Other places - SI, stomach (immigrants)
- HIV - SI
- SI lymphoma present as emergency in 50%

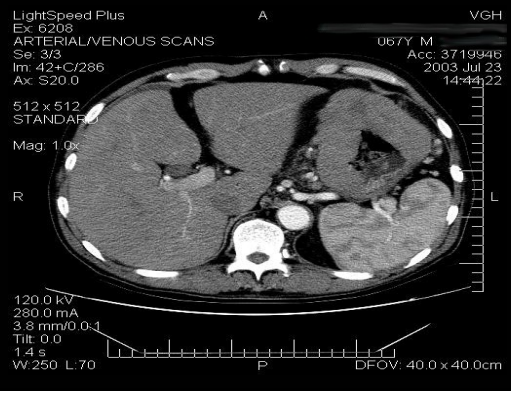
Management of GI B-Cell Lymphoma

- Surgery?
- Radiation?
- Chemotherapy?

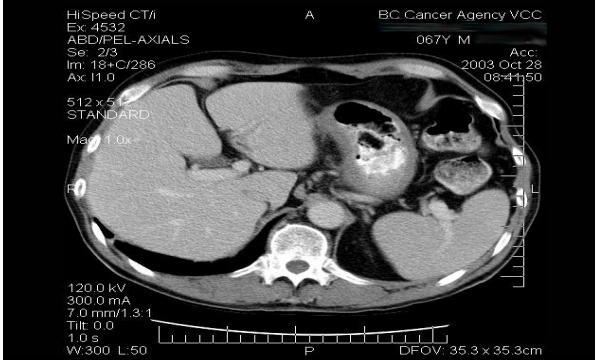
Management

- Surgery- localized disease, young patient, emergency presentation, avoid for diagnosis only, if in OR frozen section and clips
- Radiation –limited by GI toxicity and long term complications if young
- Chemotherapy- mainstay CHOP- doxorubicin,vincristine, cyclophosphamide, prednisone

CT scan before chemo



CT scan after 4 cycles of chemotherapy



Prognosis

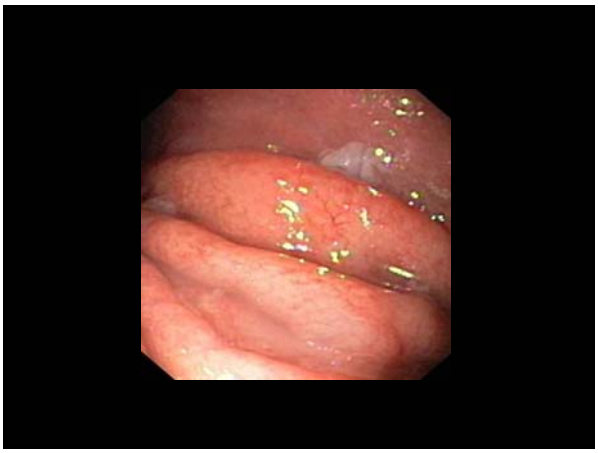
- Function of extent of disease
- 3cm tumour 100% local control cf 60% if >6 cm
- Overall complete response in 50%
- 3 year disease free 46%

Case VI

- 27 y.o. female, no significant medical history
- 1 wk history of epigastric pain and melena.
- Similar pain 1 year ago, had negative barium swallow. Resolved without treatment.
- CBC: Hgb 95, all other blood work normal

UGI Endoscopy

- 2cm ulcer in the gastric antrum
- adjacent area of apparent thickened mucosal folds with increased small vessels



Pathology

- MALT lymphoma
- H. Pylori positive

Gastric MALT Lymphoma

- MALT= mucosa associated lymphoid tissue
- Clonal population of B-cells develop under constant stimulation
- Low grade in 75%
- Associated with H. pylori infection in >90% of cases

Staging and Diagnosis

- CT scan Abdomen/Pelvis normal
- Bone marrow biopsy normal
- EUS (not available at centre)

- Stage IAE gastric MALT lymphoma, associated with H.pylori infection.

Management Issues

- Treatment?
- Evaluation of response?
- Follow up?

Management MALT Lymphoma

- **For stage 1AE eradication of H.pylori my induce prolonged remission**
- **Rescope at 2 months to confirm control**
- **Close follow-up with rescope q 6 mo for two years then annually for 3 years.**
- **Persistant H.pylori- retreat once**
- **Persistant lymphoma or recurrent lymphoma - standard lymphoma rx**

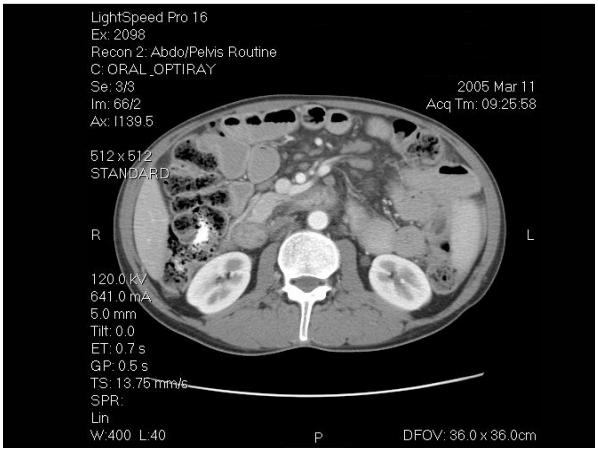
Prognosis

- >95% 5 year survival for stage 1
- 75% 5 year survival for stage 2

Case VII

- 47 year old man
- 10 year history of crampy abdominal pain and diarrhea
- 1.5 years ago diagnosed with celiac disease and also H.pylori positive
- Triple therapy and dietary gluten restriction

- 9 month history increasing upper abdominal pain worse with meals
- Abdominal ultrasound shows mild splenomegaly and peripancreatic nodes
- CT scan of the abdomen ordered by GP



Radiology Report

- Enlarged spleen 15cm
- Mesenteric lymphadenopathy
- 12mm lesion in right love of liver
- Otherwise normal
- Recommend open biopsy of node and US guided biopsy of liver

Surgical Consultation

- Referred for biopsy of mesenteric nodes
- No fevers, night sweats or weight loss
- Normal WBC and LDH and CXR
- Mild anemia 108
- Patient very reluctant to have surgery

Upper GI Endoscopy

- Edematous and erythematous duodenal folds- biopsies taken
- Gastric antrum minimal erythema
- Gastric fundus unusual reticulated pattern of erythema and pallor- biopsies taken

Pathology

- Both gastric and duodenal biopsies show clonal T cell population consistent with a peripheral T-cell lymphoma of the GI tract
- Based on involvement of stomach, duodenum, spleen and nodes – stage 4A

Management

- Referred to BCCA for completion of staging
- No laparotomy required (endoscopic biopsies adequate)
- Bone marrow biopsy-atypical T cells
- CT chest-normal
- Started on CHOP + gemcitabine

Enteropathy- type T cell lymphoma

- Less common compared to gastric and MALT
- Aggressive disease
- 5 year survival 15%

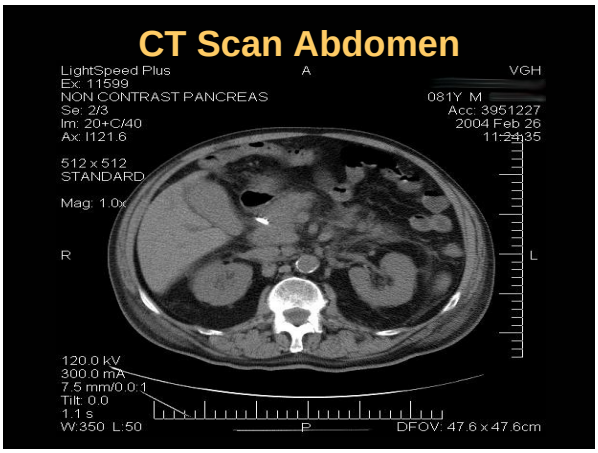
Question Period Lymphoma

Case VIII

- 81 year old man
- Jaundiced 10 days post knee surg
- C/o nausea, epigastric discomfort, 15 lb weight loss
- CBC, lytes normal
- Alkphos 379 AST 125 bili 264 LDH 221 Ca 19-9 74 (normal <37)

- US 4.5 cm mass in head of pancreas, duct dilation
- ERCP with stent insertion
- FNA atypical lymphoid cells
- Core: diffuse large B-cell lymphoma

CT Scan Abdomen



Post Chemo and involved field RT