Weird and Wonderful Tumours in the GI Tract

- GIST
- Carcinoid
- Lymphoma

Facilitator:
Rona Cheifetz

Panel Members:
Carol Swallow, Surgical Oncology
Jamie Appleby, General Surgery
Meg Knowling, Medical Oncology
Abdul Al-Tourah, Medical Oncology
Ursula Lee, Medical Oncology
Don Wilson, Radiation Oncology and Nuclear Medicine

Disclosure

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

CT Scan Abdomen

Management

?
**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**
- ?

**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

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

GIST: Malignant Potential

<table>
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<tr>
<th>Risk *</th>
<th>Size</th>
<th>Mitotic Rate</th>
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<tbody>
<tr>
<td>High</td>
<td>Any</td>
<td>&gt;10/50 HPF</td>
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<tr>
<td></td>
<td>&gt;10 cm</td>
<td>Any</td>
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<tr>
<td></td>
<td>&gt;5 cm</td>
<td>&gt;5/50 HPF</td>
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<tr>
<td>Intermediate</td>
<td>5-10 cm</td>
<td>&lt;5/50 HPF</td>
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<tr>
<td>Low</td>
<td>&lt;5 cm</td>
<td>6-10/50 HPF</td>
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<tr>
<td>Very Low</td>
<td>&lt;2 cm</td>
<td>&lt;5/50 HPF</td>
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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 (Gleevec) 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

**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

**Management**
- Patient with unresectable metastatic disease

**CT Imaging**

**Treatment with Imatinib**

| Before | After |
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.

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 hemicolecetomy (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

**Follow-up Plan**
- ?

**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 tumor load in 60%

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.

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 of 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
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

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- Abdominal ultrasound shows mild splenomegalgy and peripancreatic nodes
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Radiology Report

- Enlarged spleen 15cm
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- Otherwise normal
- Recommend open biopsy of node and US guided biopsy of liver

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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

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**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