“Get the GIST”: Gastrointestinal Stromal Tumor on Multiple Imaging Modalities

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Agenda

- Two case presentations
  - Appearance of GIST on different imaging modalities
- GIST: Pathology, Epidemiology, Clinical Presentation
- Treatment for GIST and role of $^{18}$FDG-PET, PET/CT in monitoring response to chemotherapy
Our Patient YM: Clinical Presentation

- **History**
  - 79 year old woman
  - 2 days of *nausea, vomiting, crampy abdominal pain*
  - 1 small bowel movement, otherwise *no flatus*

- **Physical Exam**
  - Afebrile, vital signs stable.
  - ABDOMEN:
    - Mobile mass palpated in lower abdomen
Patient YM: Transabdominal Ultrasound

- Large, heterogenous mass, multiple echogenicities
- Anechoic, cystic regions

TA US, sagittal
PACS, BIDMC
Patient YM: Transabdominal Ultrasound

Findings

- Large, heterogenous mass, multiple echogenicities
- Anechoic, cystic regions
Highly vascularized mass

Patient YM: Doppler Ultrasound
Patient YM: Doppler Ultrasound Findings

- Highly vascularized mass
Patient YM: Axial Abdominal CT

- With IV and oral contrast
- Arterial phase

C+ CT, axial, arterial phase
PACS, BIDMC
Patient YM: Axial Abdominal CT Showing Dilated Bowel Loops

- With IV and oral contrast
- Arterial phase
- Dilated loops of small bowel

C+ CT, axial, arterial phase
PACS, BIDMC
Patient YM: Axial CT, Abdomen and Pelvis
Showing Mesenteric Swirling

- With IV and oral contrast
- Arterial phase

**Mesenteric swirling**
around a vascular pedicle

- Dilated bowel loops proximal to swirl
- Collapsed bowel loops distal to swirl

- Consistent with a **transition point** signifying small bowel obstruction

C+ CT, axial, arterial phase
PACS, BIDMC
Patient YM: Axial CT, Abdomen and Pelvis

Showing Mass in Mesentary

- With IV and oral contrast
- Arterial phase

- Compressed bowel loops
- Heterogeneously enhancing mass
- Arises from mesentary
- Calcification
Patient YM: Axial CT, Abdomen and Pelvis with Mass Arising From Mesentary Highlighted

- With IV and oral contrast
- Arterial phase

- Compressed bowel loops

- Heterogeneously enhancing mass

- Arises from mesentary

- Calcification
Patient YM: Axial CT, Abdomen and Pelvis
Showing Mass with Multiple Attenuations

- With IV and oral contrast
- Arterial phase

- Large, well circumscribed, heterogeneous mass

- Predominantly hypoattenuated to muscle with areas of hyperattenuation

- Compressed bowel loop

C+ CT, axial, arterial phase
PACS, BIDMC
Patient YM: Axial CT, Abdomen and Pelvis, Heterogeneous Mass Highlighted

- With IV and oral contrast
- Arterial phase
- Large, well circumscribed, heterogeneous mass
- Predominantly hypoattenuated to muscle with areas of hyperattenuation
- Compressed bowel loop

C+ CT, axial, arterial phase
PACS, BIDMC
Patient YM: Axial MRI, Pelvis

- With and without IV gadolinium contrast
- T1 weighted images
- T1 pre-contrast
- T1 post-contrast
Patient YM: T1 Weighted Axial MRI of Pelvis Pre-contrast Findings

- With and without IV gadolinium contrast
- T1 weighted images
  - T1 pre-contrast
    - Large, well circumscribed mass
    - Low signal intensity compared to muscle, soft tissue
  - T1 post-contrast
Patient YM: T1 Weighted Axial MRI of Pelvis Post-contrast Findings

- With and without IV gadolinium contrast
- T1 weighted images

**T1 pre-contrast**
- Large, well circumscribed mass
- Low signal intensity compared to muscle, soft tissue

**T1 post-contrast**
- Internal enhancement in signal intensity on right side of mass
- Peripheral enhancement anteriorly and to the left
- Enhancement consistent with solid regions
- Nonenhancing areas consistent with hemorrhage or necrosis
Patient YM: T2 Weighted Coronal and Axial MRI Pelvis

- T2 weighted images, no contrast

- Well circumscribed
- Heterogeneous
- Regions of hypo and isointensity
- Regions of high intensity signal consistent with fluid, necrotic areas
- Dilated loops of small bowel
Patient YM: T2 Weighted Coronal and Axial MRI
Pelvis Findings Highlighted

- T2 weighted images, no contrast

- Well circumscribed
- Heterogeneous
- Regions of hypo and isointensity
- Regions of high intensity signal consistent with fluid, necrotic areas
- Dilated loops of small bowel
Our Patient YM: Summary

- 79 F with nausea, vomiting, abdominal pain, and palpable abdominal mass

- Imaging:
  - Well circumscribed, heterogenously enhancing, large pelvic / abdominal mass with solid and cystic components, and partial small bowel obstruction

- Differential Diagnosis
  - Gastrointestinal stromal tumor (GIST)
  - Lymphoma
  - Leiomyoma, leiomyosarcoma
  - Submucosal GI lipoma
  - Carcinoid tumor
  - Primary ovarian tumor
Patient YM: Clinical Course

- Underwent laparotomy with tumor and small bowel resection

- Tumor immunohistochemistry consistent with GIST c-kit (CD117) positive

- Tumor involved submucosa, muscularis propria and subserosa; no mucosal invasion.

- Large size, prominent necrosis, high mitotic index suggest high risk of malignant potential
Now let’s review the clinical presentation of Companion Patient 2, another patient who turned out to have GIST.
Companion Patient 2: Clinical Presentation

- History
  - 60 year old man
  - 2 large bowel movements mixed with bright red blood on morning of admission

- Physical Exam
  - No palpable abdominal masses, NG lavage negative, fresh red blood staining anus

- Labs
  - Anemia – Hct 23.1%
Patient 2: GI Bleeding Study with Tc-99m labeled red blood cells

- Dynamic blood pool images
- Immediate activity in LUQ
- Later shown to follow serpiginous course of small bowel (not shown)

Tc-99m tagged RBC scan, coronal PACS, BIDMC
Patient 2: GI Bleeding
Study reveals a bleed near ligament of Treitz

- Dynamic blood pool images
- Immediate activity in LUQ
- Later shown to follow serpiginous course of small bowel (not shown)
- Findings consistent with bleed near ligament of Treitz

Tc-99m tagged RBC scan, coronal PACS, BIDMC
Anatomy review: ligament of Treitz

Ligament of Treitz
(Suspensory muscle of duodenum)

C2: duodenum, descending part
C3: duodenum, horizontal part
C4: duodenum, ascending part

esophagus
SMA
jejunum
Right diaphragmatic crus
celiac trunk

Because Companion Patient 2 had bright red blood per rectum with a positive tagged RBC radionuclide study, but no definite bleeding source identified with colonoscopy, diagnostic angiograms of the celiac trunk, superior and inferior mesenteric arteries were performed.

Let’s review the angiogram of the superior mesenteric artery (SMA)
Patient 2: Diagnostic Angiogram of the Superior Mesenteric Artery

Superior Mesenteric Artery

Patient 2: Diagnostic Angiogram of SMA

- Catheter
- Superior Mesenteric Artery
- Oval shaped area of arterial contrast collection, LUQ
- Consistent with a hypervascular mass
Patient 2: Diagnostic Angiogram of SMA with Findings Highlighted

- Catheter
- Superior Mesenteric Artery
- Oval shaped area of arterial contrast collection, LUQ
- Consistent with a hypervascular mass
The finding of an abnormal arterial contrast collection in the LUQ on diagnostic angiogram of the SMA led to further evaluation of Companion Patient 2 with a contrast-enhanced CT of the abdomen and pelvis.
Patient 2: CT Abdomen and Pelvis, Axial View

- With IV and oral contrast
- Axial view
- Well circumscribed soft tissue density mass
- Homogeneously enhancing
- Located in LUQ
Patient 2: CT Abdomen and Pelvis, Coronal View

- With IV and oral contrast
- Coronal view
Patient 2: CT Abdomen and Pelvis, Coronal View Findings

- With IV and oral contrast
- Coronal view

- **Gallbladder**
- low attenuation liver lesion
  - consistent with simple liver cyst

- **Well circumscribed LUQ soft tissue density mass**
- Homogeneously enhancing
Patient 2: Summary

- 60 M with GI bleed, anemia

- Imaging
  - Well circumscribed, homogenously enhancing, highly vascularized LUQ abdominal mass abutting loops of small bowel

- Clinical Course
  - Underwent diagnostic laparoscopy with tumor and small bowel resection
  - **Immunohistochemistry consistent with GIST**: strongly positive for smooth muscle actin and KIT (CD117).
  - Small tumor size, low mitotic rate, support low risk of disease progression
Now, let’s review the clinical features, imaging features, and treatment of GIST
Gastrointestinal Stromal Tumors (GIST)

Pathology

- Tumor cells share morphologic and immunophenotypic characteristics of interstitial cells of Cajal (ICC)
  - Found within intestinal muscle layers
  - Pacemaker system of intestinal muscle layers coordinating smooth muscle contraction
- Activating mutations in class III tyrosine kinase c-KIT (CD117) and platelet derived growth factor receptor alpha (PDGFRα)
GIST: Epidemiology

- Most common mesenchymal tumor of the GI tract
- Represents ~5% of all sarcomas
- Annual incidence ~14.5 per million, prevalence of 129 million according to a Swedish population-based study
- ~5000 new cases per year in the USA
- ? Slight male predominance
GIST: Epidemiology (Continued)

- Median age of onset 60 yrs (patients rarely younger than 40)
- Rare in pediatric populations
- Majority are sporadic
- Hereditary GISTs -- characterized by multiple GISTs and cutaneous hyperpigmentation

Unusual variants

- **Carney triad**: synchronous or metachronous GISTs, pulmonary chondromas, extra-adrenal paragangliomas. *No mutations in KIT or PDGFRa*
- **GIST associated with neurofibromatosis 1**: younger patients, multiple tumors arising in small bowel, *no mutations in KIT or PDGFRa*. 
GIST: Clinical Presentation

- **Asymptomatic**, incidental finding on imaging, surgery, autopsy
- Tumor-induced **GI bleed, anemia**
- Other symptoms secondary to **mass effect** on GI tract
  - Abdominal discomfort
  - Early satiety
  - Palpable abdominal mass
  - Bowel obstruction and/or perforation
  - Dysphagia
# GIST: Tumor Locations

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>5%</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td><strong>50-60%</strong></td>
</tr>
<tr>
<td><strong>Small Bowel</strong></td>
<td><strong>20-30%</strong></td>
</tr>
<tr>
<td>Large Bowel</td>
<td>10%</td>
</tr>
<tr>
<td>Mesentary, Omentum, other abdominal</td>
<td>5%</td>
</tr>
<tr>
<td>cavity locations</td>
<td></td>
</tr>
</tbody>
</table>
GIST: Risk Stratification

- Malignant potential of GIST depends on:
  - Tumor size
    - $\leq 5 \text{ cm} = \text{low risk of progression}$
  - Mitotic rate
    - $<5 \text{ mitoses per 50 HPF}$
  - Anatomic location
    - stomach lower risk of progression than small bowel / other locations
GIST: Imaging Modalities and General Features

- **Contrast enhanced CT** = best imaging tool for GIST

- **Contour**
  - Round, ovoid, or dumbbell shape

- **Growth pattern**
  - Endoluminal (I)
  - Exophytic (II)
  - Mixed (III)

- **Border**
  - Well defined in 95% of tumors

- **Enhancement Pattern**
  - Depends on tumor size
  - Heterogenous (large)
  - Homogeneous (small)

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Imaging Features of GIST on Contrast Enhanced CT

- **Contrast enhanced CT** = best imaging tool for GIST

- Contour
  - Round, ovoid

- Growth pattern
  - Endoluminal (bulges into gastric lumen)
  - Exophytic (growing out of small bowel wall with no luminal bulge)
  - Mixed

- Border
  - Well defined

- Enhancement Pattern
  - Depends on tumor size
  - Heterogenous (large)
  - Homogeneous (small)

King DM, Cancer Imaging. 2005 Dec 15; 5:150-6
Companion Patient 5: Imaging Features of GIST on Noncontrast CT

- **Companion Patient 5**: 63M with 1 month abdominal pain and weight loss

- **Contour**
  - Large, round, ovoid

- **Growth pattern**
  - Exophytic
    - Derived from small bowel mesentary
  - Mixed

- **Border**
  - Well defined

- **Heterogenous attenuation**
  - Areas of high and low attenuation
Imaging Features of GIST on Plain Film

- **Plain film**
  - No role in diagnosis of GIST
  - GIST detectable on plain film if calcified
    - Calcifications in 25% of cases

GIST with multiple calcifications in sigmoid colon

Plain abdominal radiograph
Imaging Features of GIST on Upper GI / Barium Swallow

• Upper GI / Barium Swallow
  - In stomach: may detect rounded filling defect due to endoluminal submucosal gastric mass
  - Ulcerations common in larger masses

Companion Patient 7

Upper GI Series / Barium Swallow
King DM, Cancer Imaging. 2005 Dec 15; 5:150-6
Imaging Features of GIST on Ultrasound

- **Ultrasound**
  - Typically hypoechoic
  - Variable vascularity on color Doppler
  - Usually difficult to identify organ of origin

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**Our Patient YM**

- TA Doppler US, sagittal
- PACS, BIDMC

**Companion Patient 8**

- Radial endoscopic sonogram of sigmoid colon

- Large hypoechoic mass
- Multiple shadowing calcifications

**Companion Patient 5**

- Biopsy needle
- Mass

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**TA US, sagittal PACS, BIDMC**
Imaging Features of GIST on Angiograms

- **Angiography**
  - SMA angiogram in these examples
  - Hypervascular GIST visualized
  - **Tumor blush on arteriogram**

Digital subtraction angiography of SMA
King DM, Cancer Imaging. 2005 Dec 15; 5:150-6
Imaging Features of GIST on T1 Weighted MRI

- MRI
  - T1 pre-contrast:
    - isointense mass
  - T1 post-contrast:
    - enhancement of solid areas
    - Non-enhancing regions consistent with necrosis or hemorrhage
Imaging Features of GIST on T2 Weighted MRI

- MRI

- T2
  - Hypo to isointense submucosal mass
  - Hyperintense areas consistent with fluid or necrosis

Patient YM

T2W MRI, coronal
PACS, BIDMC
GIST: Metastases

- 15 – 47% of patients present with metastatic disease
- Common sites of metastases: liver, peritoneum, omentum
- Lymph node, bone, and brain metastases are rare

Contrast enhanced axial CT showing low density, cystic intrahepatic GIST metastases
GIST: Treatment

Resectable GIST

- **Surgery** with complete resection (wedge, wide resection, or en-bloc)
- Lymphadenectomy usually unnecessary
- Treatment with adjuvant imatinib for 1 year improves relapse-free survival

Unresectable and/or metastatic GIST

- **Treatment with imatinib**, small molecule tyrosine kinase inhibitor with activity against KIT
- **For imatinib-refractory GIST use sunitinib**, another tyrosine kinase inhibitor with additional anti-angiogenic activity
Metabolic responses to imatinib treatment can be followed using positron emission tomography (PET) using fluorine-18-fluorodeoxyglucose (\(^{18}\text{FDG}\)).

Significant reduction in tumor \(^{18}\text{FDG}\) uptake in imatinib-responsive tumors as early as 24 hours later and by 1 month after initiating imatinib therapy.
18FDG-PET scans of a patient with metastatic GIST prior to and 1 month after imatinib therapy

- Baseline scan obtained prior to starting therapy
- Primary tumor and GIST metastases show intense glycolytic activity on 18FDG-PET
- Reduction of abnormal 18FDG uptake in all tumor sites
  - as early as 24 hours
  - by 1 month after starting imatinib therapy in imatinib-sensitive tumors

Prior to therapy

1 month after therapy

A

B

Companion Patient 11

18FDG-PET scans, coronal
18FDG-PET and correlating CT scans of a patient prior to and 1 month after imatinib therapy

- LUQ mass arising from stomach, liver metastasis, small mass in LLQ
- Metabolic changes precede by weeks or months any significant decrease in tumor size on CT
- FDG-PET resolves ambiguous “new” liver lesions of imatinib-treated metastatic GIST

All images taken from Van den Abbeele, A. D. Oncologist 2008;13(Supplement 2):8-13
Lack of metabolic response on $^{18}$FDG-PET indicates primary or secondary resistance to chemotherapeutic agent.
Summary (1)

- GIST: gastrointestinal stromal tumor
  - Most common mesenchymal tumor of the GI tract
  - Submucosal, derived from interstitial cells of Cajal, pacemaker cells of gut
  - Common **signs & symptoms** secondary to mass effect of bulky tumor; GI bleed
Summary (2)

- Contrast enhanced CT = best imaging tool for GIST
  - Location: stomach > small bowel > esophagus / colon > mesentery
  - Well circumscribed, exophytic or endoluminal lesion with heterogenous or homogenous enhancement
  - \(^{18}\)FDG-PET, PET/CT play critical roles in monitoring response to chemotherapy
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