The Pathology Says What?
GISTs, Carcinoids and Anorectal Squamous Malignancies

Ahmer A Karimuddin, MD, MAEd, FRCSC
Clinical Associate Professor
Conflict of Interests

- None Relevant
- Honoraria Received
  - 3M
  - Sanofi
  - Servier Pharmaceuticals
  - Medtronic
  - Takeda
Carcinoids, GISTs and Anal Canal Lesions

- Carcinoids
  - Rectal Carcinoids
- Gastrointestinal Stromal Tumours (GISTs)
- Anorectal Squamous Cell Malignancies
  - HPV Associated lesions
“Don’t think of me as a Proctologist. Think of me as Colon Tech Support.”
Carcinoids

- 67 year old male
- FIT positive
  - 110
- Normal colonoscopy, until just before withdrawal

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Carcinoids

- Hard, nodular
- Normal appearing mucosa
Carcinoids

- Biopsy
  - 0.8 cm well differentiated carcinoid tumour
Carcinoids

- Otto Lubarsch
  - First described in 1888
- Siegfried Oberndorfer
  - 1907: “Karzinoid”
Carcinoids

• slow growing tumours of neuroectodermal origin
• Belong to the APUD system
• Originate from Kulchitsky cells in the crypts of Lieberkuhn
• Produce very different (> 30) amines and peptides
  – Serotonin
  – Chromogranin
  – Synaptohysin
  – Enolase
  – Other prostaglandins
Carcinoids

- 15% of all carcinoids occur in the rectum
  - Appendix, small bowel and bronchus
Carcinoids

- Taghavi et al (DCR, 2013)
  - Rectal carcinoids are now more common than small bowel carcinoid

![Graph showing comparison of RCs and SICs by year of diagnosis](image-url)
Carcinoids

- Tichansky et al (DCR, 2002)
  - 13% risk of synchronous lesions
  - Colorectal Cancer most common
    - Small Bowel
    - Lung
Carcinoids

• Majority of rectal carcinoids are picked up incidentally
• Symptoms are rare
  – Rectal bleeding
  – Minor change in bowel habits
Carcinoids

- Carcinoid syndrome
  - RARE!
    - Flushing, diarrhea, abdominal pain
  - Only after metastatic disease to the liver, and in the setting of small bowel or lung carcinoids
Carcinoids

- So, pathology is back? Now what?
- Complete Colonoscopy
- CT Chest, Abdomen, Pelvis
- Only in symptomatic patient or patient with high risk pathological features
  - Biochemical Tests
    - 14 h urine 5 HIAA
  - Somatostatin based CT PET
Carcinoids

• What are high risk pathological features?
  – Size > 2 cm
  – Invasion of the muscularis propria
  – Lymphvascular invasion
  – Perineural invasion
Carcinoids

- **< 1 cm**
  - Local excision

- **1-2 cm**
  - Low risk pathology features
  - High risk pathology features

- **> 2 cm**
  - Radical resection
• 76 year old male
• FIT positive
  –85
• Otherwise normal colonoscopy
• 1 cm lesion in low rectum
Gastrointestinal Stromal Tumours

- Most common mesenchymal neoplasm of the GI tract
- First described in 1983
- Arise from interstitial cells of Cajal or other mesenchymal stem cells
Gastrointestinal Stromal Tumours

- Spindle cells
- CKIT positive
- Prognostic Features
  - Size
  - Mitotic Rate
• Rectal GISTs are rare
• 10% of all GISTs
• Slow growing lesions
• Metastatic location
  – Liver, peritoneum
Gastrointestinal Stromal Tumours

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• Workup
  – Colonoscopy
  – ERUS
  – CT Abdomen/Pelvis
  – MRI Pelvis
Gastrointestinal Stromal Tumours

- Resection is necessary for all GIST
- En bloc resection with 1 cm margin
  - Negative margin is key
- No large series are available
- Liu et al (JSO, 2014)
  - Positive resection margin was worse prognostic indicator for recurrence
Gastrointestinal Stromal Tumours

Rectal GIST

Will it require an APR?

No

Local Excision

Low Anterior Resection

YES!

Imatinib, then reassess

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Anorectal Squamous Cell Cancer

- Uncommon malignancy (<2% of GI cancer)
- Almost always associated with HPV
- Risk factors
  - Prior Sexually Transmitted Disease
  - Anal Receptivity
  - Presence of anogenital warts
  - Presence of prior Anal intraepithelial neoplasia
  - Immunosuppression (Transplant/Steroids)
  - HIV positivity, with low CD4 count
  - Smoking
Anorectal Squamous Cell Cancer

- Median Age is 60-65 years
  - Slightly more common in women
- > 1/3 of patients are asymptomatic
- 45% of patients may have painless rectal bleeding
Anorectal Squamous Cell Cancer

- Ulcer or fissure with indurated margins
- Exophytic mass seen on anal spread
- MAY NEED EUA TO EXAMINE
- Sedated colonoscopy may be the only opportunity to assess
Anorectal Squamous Cell Cancer

• Usual spread is to groin lymph nodes
  – Should be assessed on clinical exam
• CT Chest/Abd/Pelvis
• CT PET
  – Anal Canal Squamous Cell Cancer is very FDG avid
### TABLE 12: TNM classification of anal canal tumors

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor $\leq 2$ cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor $&gt; 2$ cm but not $&gt; 5$ cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor $&gt; 5$ cm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor of any size that invades adjacent organs (eg, vagina, bladder, urethra, bladder)(^a)</td>
</tr>
</tbody>
</table>
Anorectal Squamous Cell Cancer

- < 2 cm in size
  - Can you excise it with clear margins?

Chai et al. JAMA Surg. 2017
Anorectal Squamous Cell Cancer

- All other tumours
  - Refer to BCCA for chemoRT
  - 45 Gray radiation over 5 weeks
  - Mitomycin, 5 FU
Anorectal Squamous Cell Cancer

- Ben-Josef et al (JCO, 2010)
  - 20% local failure rate at 5 years, stabilizes out at 1 year

- Ongoing surveillance is important

- If residual disease at 6 months
  - APR becomes necessary
  - ~ 50% 5 year survival (Ghouti et al, DCR, 2005)
Anal Intraepithelial Neoplasia (AIN)

- Dysplastic condition of the anal canal
- Premalignant stage of anal cancer
- Secondary to HPV infection
  - HIV status
  - Anal receptivity
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![Diagram of Anal Intraepithelial Neoplasia (AIN)](image)

**Figure 1. Schematic Representation of SIL**
As shown in this illustration, with increasing severity of SIL of the anus, the proportion of the epithelium replaced by immature cells with large nuclear-cytoplasmic ratios increases. Invasive cancer probably arises from one or more foci of high-grade SIL (HSIL), as depicted in the drawing by epithelial cells crossing the basement membrane below the region of HSIL.
Anal Intraepithelial Neoplasia (AIN)

  - 50% of immunosuppressed patients progressed to cancer
  - 11% of all patients can progress to cancer without surveillance
Anal Intraepithelial Neoplasia (AIN)

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• So you saw a lesion on endoscopy, biopsy came back as AIN?
• Now what?
• Refer to Anal Dysplasia Clinic or your favourite General/Colorectal Surgeon
Anal Intraepithelial Neoplasia (AIN)

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• Anal Dysplasia Clinic
  – Based out of St Pauls
  – Run by family physicians with extra training
  – Perform high resolution anoscopy
  – “Anal Pap Smear”
Anal Intraepithelial Neoplasia (AIN)

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Anal Dysplasia Clinic

A

B

C

D

E

F

Anal Pap Smear
Anal Intraepithelial Neoplasia (AIN)

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- What should the surgeon do?
- Is there a mass or a lump?
- YES!
  - Then excise the lump
  - Ablate all abnormal tissue with cautery
Anal Intraepithelial Neoplasia (AIN)

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• What should the surgeon do?
• Is there a mass or a lump?
• NO!
  – Observe
  – Imiquimod (Aldara)
    • Expensive, burns
  – Topical 5U (free if prescribed by BCCA)
    • Burns
Conclusion

• These diagnoses are rare, but can occur in a large screening program

• Carcinoids
  – Need complete endoscopic assessment
  – If small and good prognostic features, may only need local excision
  – Ask your pathologist for more information if needed
Conclusion

• GISTs
  – Important to remove completely
  – Stage with ERUS and MRI
  – If major surgical procedure or unclear resectability, refer to Cancer Agency or local Colorectal Surgeon
  – Imatinib has changed the landscape completely
• Squamous Cell Cancer
  – If small, local excision can be sufficient
  – If larger
    • CT + CT PET
    • Chemo RT based treatment
    • Watch closely for first year after treatment
Acknowledgements