Handling colorectal polyps

K. Geboes

Colorectal cancer and precursor lesions

Sporadic ca – FAP - IBD

- Polyp – cancer sequence
  - Adenoma – cancer sequence (Morson et al 1984)
- Flat adenoma (Muto et al 1985)
  - Nonpolyloid lesion
  - Height < 3 mm
  - Mucosal thickness is twice or less that of the surrounding mucosa
- Sessile serrated adenoma/polyp/lesion
- Dysplasia
  - Flat
  - Elevated
Polypoid (pedunculated adenoma)
Flat adenoma (668888/1)

Flat lesions
Colorectal cancer and precursor lesions:
Macroscopy

- **Stereomicroscopy - Magnifying endoscopy**
  - Aberrant Crypt focus (micro-adenoma; unicryptal adenoma)
    - With hyperplastic – non-dysplastic epithelial lining
    - With intraepithelial neoplasia – dysplastic type
Flat elevated lesions (FELs)
- Lesions characterized by a slight elevation and a flat upper surface with a reddish colour
- Generally smaller than 10 mm
- Central depression with air insufflation

Histology
- Thickness: less than twice the surrounding mucosa
- Adenoma = Flat adenomas (FAs)
**Histology of Flat elevated lesions**


- 33 FELs less than 10 mm
  - 12 (36.4%) = adenoma
  - 10 = hyperplastic polyp
  - 1 = inflammatory polyp

- **Nonneoplastic lesions**
  - Inflammatory polyps
  - Lymphoid nodules
- **Flat adenomas**
- **Flat serrated lesions**

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**Flat adenoma**

![Flat adenoma image]
Flat adenoma: significance

- Originally difficult diagnosis at endoscopy
- Frequency: 6.8% - 44.4% of all colorectal adenomas
- Flat adenomas at small size demonstrate a higher incidence of
  - Advanced histology (villous aspect...)
  - High grade dysplasia
  - Submucosal cancer
  - Aneuploidy

Small flat colorectal Ca in the UK population (Tweedee e a Colorectal Disease 2007)

1763 surgically resected Colorectal cancers
- 61 small cancers < 20 mm across
- 39/61 (64%) flat morphology
- 20/61 (33%) polypoid cancers
Polyp : mass of tissue that arises from mucous membranes and protrudes into the lumen. *Macroscopy / precise nature unclear*
*Microscopy : neoplasm (= dysplasia); epithelial lesion*

Adenoma : circumscribed benign neoplasm composed of tubular and/or villous structures lined by dysplastic epithelium (WHO)

Other
Colorectal adenomas containing invasive adenocarcinoma that extends through the muscularis mucosae into the submucosa have been defined as “malignant polyps.”

This term encompasses cases in which the entire polyp head is replaced by carcinoma and adenomas with focal malignancy.

But the definition excludes adenomas with high-grade dysplasia (intraepithelial carcinoma) or intramucosal carcinoma (invasive carcinoma limited to the lamina propria or invading no deeper than the muscularis mucosae) because these polyps possess negligible biologic potential for metastasis.

*Arch Pathol Lab Med. 2009*

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**Intraepithelial neoplasia & Malignancy**

- The mucosa of the colon lacks lymphatics
- Therefore “intramucosal cancer” will not disseminate
Colorectal cancer and the pathologist

- Diagnostic biopsies
- Surgical specimens

- Polypectomy
- Transanal Endoscopic Microsurgery (TEM)
  - Surgical «conservative» technique for small rectal lesions, applied more commonly because of less morbidity.

RISK ASSESSMENT FOR RESIDUAL TUMOR
Risk assessment depends
- Upon the patient
- Upon the specimen
What about the specimen?

- Handling the specimen
- Histology

Handling the specimen

- Orientation
- Cutting
Orientation

needle
Stalked lesion  Sessile lesion

Stalked lesion  Sessile lesion
**Histology**

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of cases</th>
<th>Adverse outcome</th>
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<tbody>
<tr>
<td>Colacchio 1981</td>
<td>24</td>
<td>6 (LN)</td>
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<tr>
<td>Lipper 1983</td>
<td>51</td>
<td>2 (1 residual)</td>
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<tr>
<td>Haggitt 1985</td>
<td>64</td>
<td>8 (4=LN)</td>
</tr>
<tr>
<td>Cranley 1986</td>
<td>38</td>
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<td>Richards 1987</td>
<td>80</td>
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<td>Kikuchi 1995</td>
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<td>Cooper 1995</td>
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<td>16 (13=LN)</td>
</tr>
<tr>
<td>Ueno 2004</td>
<td>292</td>
<td>50 (33=LN)</td>
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**Risk factors and adverse outcome**

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Risk factors for residual tumor

- Tumor grade - Poor differentiation
- Vascular invasion
- Positive section margin
- Budding (solitary cells or small groups of cells < 5)
- Haggitt’s classification: width and depth of submucosal invasion

450143
Poorly differentiated CRC
**By convention, signet-ring cell carcinomas, small cell carcinomas, and undifferentiated carcinomas are high grade**

**High grade: Less than 50% gland formation**

**High grade (Grade III) defined by the least differentiated area**

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<th>Treatment</th>
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<tr>
<td>1</td>
<td>II Unassessable Rectum Subtotal colectomy</td>
<td>No residual carcinoma, metastasis, died of disease</td>
<td>Volk e.a. Gastroenterology 109; 1995</td>
</tr>
<tr>
<td>2</td>
<td>II 0 Sigmoid colon Subtotal colectomy</td>
<td>Residual carcinoma</td>
<td></td>
</tr>
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<td>3</td>
<td>III 0 Rectum Subtotal colectomy</td>
<td>Residual carcinoma</td>
<td></td>
</tr>
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<td>4</td>
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<td>Residual carcinoma</td>
<td></td>
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<tr>
<td>5</td>
<td>&lt; 2 Rectum Subtotal colectomy</td>
<td>No residual carcinoma</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>III 0 Rectum Subtotal colectomy</td>
<td>No residual carcinoma, metastasis, died of disease</td>
<td></td>
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<td>7</td>
<td>II 0 Rectum Subtotal colectomy</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
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<td>II 0 Rectum Local radiation</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>III 0 Rectum Local radiation</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>II &lt; 2 Rectum Local radiation</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>III 0 Sigmoid colon Subtotal colectomy</td>
<td>No metastasis, died of disease</td>
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<tr>
<td>14</td>
<td>II &lt; 2 Colon Subtotal colectomy</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>I 0 Rectum Subtotal colectomy</td>
<td>No metastasis, died of disease</td>
<td></td>
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<tr>
<td>16</td>
<td>I 0 Colon Subtotal colectomy</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>II 0 Sigmoid colon Subtotal colectomy</td>
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<td>18</td>
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<tr>
<td>19</td>
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<td>No metastasis, died of disease</td>
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<tr>
<td>21</td>
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<td>No metastasis, died of disease</td>
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<tr>
<td>22</td>
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<td>No metastasis, died of disease</td>
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<td>II Unassessable Sigmoid colon Subtotal colectomy</td>
<td>No metastasis, died of disease</td>
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<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>II &lt; 2 Rectum Local radiation</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>III &gt; 2 Rectum Local radiation</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>I &lt; 2 Sigmoid colon Polypectomy only</td>
<td>No metastasis, died of disease</td>
<td></td>
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<tr>
<td>28</td>
<td>III &lt; 2 Rectum Polypectomy only</td>
<td>No metastasis, died of disease</td>
<td></td>
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<tr>
<td>29</td>
<td>I 0 Sigmoid colon Polypectomy only</td>
<td>No metastasis, died of disease</td>
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<tr>
<td>30</td>
<td>I 0 Colon Polypectomy only</td>
<td>No metastasis, died of disease</td>
<td></td>
</tr>
</tbody>
</table>
Male Patient
°1948
Red blood loss per anum
Polypectomy

Vascular invasion

Low rectal lesion Invades just into the submucosa but has LVI, which is ?? still in the musc mucosae. Margin is clear (wmm)

So Questions.
A) What is the likelihood of any nodes being involved
B) Does she need her nodes removed?
c) If this involves an APR
d) If this involves a TME
Lymphatics in the mucosa (lymphangiogenesis)
Comments (R. Odze)

- nice and difficult clinical decision, here is my view if the patient is young and healthy, and the lvi is real (which it appears to be), then the guidelines say a resection should be strongly considered due to increased risk of lymph node mets, i believe the risk is anywhere from 10-20 percent, to me lvi is lvi regardless if its IN muscularis or BELOW it. They all connect!
- if it means an APR, its a BIG decision. If its a simple LAR, i think its an easier one. Of course, it all depends on the age and health and input and desire of the patient ultimately

Comments (J. Greenson)

- I reviewed a nearly identical case for a lawyer wherein the initial pathologist missed the LVI and the cancer penetrating the muscularis mucosae and stated that the polyp had been completely removed and was just an adenoma. Nothing further was done and the patient presented about 2 years later with a mass invading the sacrum and metastatic disease.
Comments (G Williams)

- I would be more cautious about this. Is this genuine lymphatic invasion?
- This lesion is otherwise a very superficially invasive well differentiated tumour that seems to be miles from the resection margin. So the putative lymphatic invasion is the only indication for radical surgery, and the evidence for isolated lymphatic invasion being an adverse prognostic indicator in the literature is not very convincing.

**Intern Emerg Med.** 2012
Clinical outcome of low- and high-risk malignant colorectal polyps: results of a population-based study and meta-analysis of the available literature.
**Di Gregorio C,** et al

Fifty-five malignant polyps were classified as low-risk lesions and 50 as high-risk.

None of the patients at low-risk died of colorectal cancer.

Of the patients at high-risk, three died of cancer; all three cases showed lymphatic/vascular invasion.
Negative Margin
no consensus definition

• not within the actual diathermy,
• more than one high-power field from the diathermy,
• greater than 1 mm from the margin, and
• more than 2 mm from the margin

Polyp with negative margin

Cancer near the margin
No consensus definition

• cancer cells 1 mm or less from the transected margin,
• cancer cells 2 mm or less from the transected margin, and
• cancer within the diathermy and/or within one high-power field of the diathermy.

Cancer & Polyp with positive margin
**Tumor budding = activity**

- **Definition**
  - Presence of isolated single cells or small clusters (up to four cells) scattered in the stroma at the invasive tumor margins

- **Scoring**
  - Field: X 20 objective lens
  - Number counted in the field with the most frequent tumor budding
  - Counts of 0-9: low-grade
  - Counts of 10 or >10: high grade
Tumor budding is predictive of lymphatic involvement
Ogawa e a Scan J Gastroenterol 2009;44:605-14

- Tumor budding is higher in non-polypoid ca
- Positive link with lymph node metastasis and lymphatic involvement
Invasion or pseudo-invasion

- Glandular pseudo-invasion occurs in 2.5-10% of adenomas
- Diff diagnosis
  - Presence of loosely arranged stroma (lamina propria) between the glands
  - Absence of desmoplastic reaction around the glands
  - Haemosiderin pigment
  - Smooth muscle cells
  - Absence of cytologic and architectural features of high-grade intraepithelial neoplasia.
• **Level 1**: Carcinoma invading into the submucosa, but limited to the head of the polyp.
• **Level 2**: Carcinoma invading to the level of the neck (the junction of the head and stalk) of the adenoma.
• **Level 3**: Carcinoma invading any part of the stalk.
• **Level 4**: Carcinoma invading into the submucosa of the bowel wall below the stalk of the polyp but above the muscularis propria.
Haggitt’s level of invasion

Level 0: Adenocarcinoma
Level 1: Submucosa
Level 2: Muscularis propria
Level 3: Normal
Level 4: Subserosa

Level 3 & 4: 10% risk for lymph node metastasis!
Adenoma with area of invasive carcinoma/malignant adenoma
Colon/cytokeratin stain

Measurement of extent of invasion in the submucosa
(Ueno et al Gastroenterology 2004)
X : width of invasion; Y1 : depth of invasion (when muscularis mucosae is present) Y2 : depth of invasion (within muscularis mucosae)
Maximum diameter (in mm)
- Local recurrence rates at 3 years for tumors 3 cm in size or smaller are significantly lower than for tumors larger than 3 cm (16 vs. 39%; P < 0.03).

Depth of submucosal invasion
- Sm1 superficial third < 0.5mm
- Sm2 middle third 0.5 – 1 mm
- Sm3 deep third > 1 mm (1000 μm)
After endoscopic polypectomy or local resection, 4 patients showed local recurrence and 13 patients showed lymph node metastasis. None of these 17 patients had sm1 disease.

The level of invasion, configuration, and location were significant risk factors for development of lymph node metastasis or local recurrence (P < 0.05), but lymphovascular invasion, histologic grade, and diameter were not risk factors.
Absence of unfavorable tumor grade
- Absence of vascular invasion
- Absence of tumor budding (sprouting)
- Absence of extensive submucosal invasion

Correlation with nodal involvement
- Poor tumor grade
- Vascular invasion (venous & lymphatic)
- Tumor budding
- Absence of these parameters: low risk

Coagulation involving tumor

Risk factors for residual tumor
Ueno et al Gastroenterology 2004; 127

Early colorectal carcinoma
Risk factors (Inoue 2004)
TEM
Low risk

- Size < 3 cm
- Invasion limited to sm1 (recurrence rate 0)
  - Sm2: recurrence rate 17%/ sm3: 30%
- No lymphatic invasion
- Additional surgery needed for
  - Positive vertical margins at the site of submucosal invasion
  - Depth of submucosal invasion greater than 1000 μm
  - Vascular or lymphatic invasion
  - Poorly differentiated adenocarcinoma, signet ring cell carcinoma, or mucinous carcinoma
  - High-grade tumor budding

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**SURGICAL PATHOLOGY CANCER CASE SUMMARY (CHECKLIST)**

Colon and Rectum: Excisional Biopsy (Polypectomy)
Select a Single Response Unless Otherwise Indicated

© Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

*Arch Pathol Lab Med. 2009 October; 133(10): 1539–1551.*
**Polyp Size**
- Greatest dimension: ____ cm
- Additional dimensions: ____ × ____ cm
- ____ Cannot be determined (see Comment)

**Polyp Configuration**
- ____ Pedunculated with stalk
- Stalk length: ____ cm
- ____ Sessile

**Size of Invasive Carcinoma**
Greatest dimension: ____ cm
- Additional dimensions: ____ × ____ cm
- ____ Cannot be determined (see Comment)

**Histologic Type (note B)**
- ____ Adenocarcinoma
- ____ Mucinous adenocarcinoma
- ____ Signet-ring cell carcinoma
- ____ Small cell carcinoma
- ____ Squamous cell carcinoma
- ____ Adenosquamous carcinoma
- ____ Medullary carcinoma
- ____ Undifferentiated carcinoma
- ____ Other (specify): _______________
- ____ Carcinoma, type cannot be determined

**Histologic Grade (note C)**
- ____ Not applicable
- ____ Cannot be determined
- ____ Low grade (well differentiated to moderately differentiated)
- ____ High grade (poorly differentiated to undifferentiated)
Microscopic Tumor Extension (note D)
  ____ Cannot be determined
Invasion (deepest):
  ____ Lamina propria
  ____ Muscularis mucosae
  ____ Submucosa
  ____ Muscularis propria
Margins (select all that apply)
Deep Margin (Stalk Margin)
  ____ Cannot be assessed
  ____ Uninvolved by invasive carcinoma
Distance of invasive carcinoma from margin: ____ mm
  ____ Involved by invasive carcinoma
Mucosal/Lateral Margin
  ____ Not applicable
  ____ Cannot be assessed
  ____ Uninvolved by invasive carcinoma
  ____ Involved by invasive carcinoma
  ____ Involved by invasive carcinoma
  ____ Involved by adenoma

Lymph-Vascular Invasion (notes D and E)
  ____ Not identified
  ____ Present
  ____ Indeterminate
*Type of Polyp in Which Invasive Carcinoma Arose (note F)
*  ____ Tubular adenoma
*  ____ Villous adenoma
*  ____ Tubulovillous adenoma
*  ____ Traditional serrated adenoma
*  ____ Sessile serrated adenoma
*  ____ Hamartomatous polyp
*  ____ Indeterminate
Conclusions

- There is a variety of precursor lesions
- Handling the specimen is important
- Risk factor analysis
  - Size
  - Tumor grade
  - Depth of invasion
    - Haggit's level
    - Submucosal invasion
  - Lymphovascular invasion
  - Budding
  - Margin
- Final conclusion (risk factors – status of patient)

Colorectal neoplasia and treatment

- Intraepithelial neoplasia: low- & high grade – polypoid and non-polypoid
  - Local – endoscopic treatment
  - Follow-up (guidelines)
- Intramuscosal carcinoma - polypoid and non-polypoid
  - Local – endoscopic treatment
  - Follow-up
- Submucosal carcinoma - Early colorectal carcinoma
  - Local – endoscopic treatment
  - Follow-up or colon resection (depending on histology)
Early colorectal carcinoma

- Endoscopic resection
- Histopathological evaluation
  - Detection of risk factors for adverse outcome (presence of residual carcinoma in the bowel wall or in regional lymph nodes) necessitating subsequent colon resection

- Level of invasion
  - 0 = mucosa
  - 1 = head of polyp
  - 2 = neck
  - 3 = stalk
  - 4 = submucosa

- Grading
  - Vascular invasion
  - Carcinoma at or close < 1 mm from the resection margin
Intraepithelial neoplasia is the equivalent of dysplasia and the preferable terminology
Early colorectal cancer is limited to the submucosa and not beyond
Early colorectal cancer can be treated with curative resection (EMR or surgery)
Endoscopic mucosal resection specimens should be handled properly
Risk factors for adverse outcome are poor grade; vascular involvement; tumor budding and coagulation involving tumor