**History**

- 56 y/o man
- >15 year history of currently quiescent CUC
- Surveillance colonoscopy (standard; no chromo):
  - 5 smaller flat polyps left colon (look like HPPs)
  - Largest polyp in rectum, 10 mm, removed by saline lift and hot snare polypectomy and entirely retrieved

<table>
<thead>
<tr>
<th>Location</th>
<th>Size</th>
<th>Removal</th>
<th>Retrieval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Histopathology of 10 mm Rectal Polyp**

- Grossly odd serrated 10 mm rectal polyp. Removed. IIBD.
- This is unrelated to the IIBD.
- This is related to the IIBD.
- I don't know.

**Problem**

- Microvesicular HPP
- SSA/P
- Serrated NOS

**Thought Process**

- Follow
- TEM
- Colectomy
An odd serrated 10 mm rectal polyp. Removed. IIBD.

What is role of:
- Morphology?
- Location?
- Size?
- IHC?
- Molecular?

Usual (non-IBD) consequence: 3 vs 10 yr f/u

Diagnosis or Advice
- Microvesicular HPP
- SSA/P

Thought Process
- This is unrelated to the IIBD.

Problem

The Quintessential Grinders

Morphologic Reappraisal of Serrated Colorectal Polyps

Emma Torlakovic, M.D., Eva Skooglund, M.D., Dale C. Soyer, M.D., Ognen Torlakovic, M.D., and John M. Neelam, M.D., M.B.B.S.

Table 1: Morphologic variables and scoring

Table 2: Provisional classification of the serrated polyps in the colon and rectum

Seeking a diagnosis. Will grinding it out morphologically get us there?

Well-developed serrations – not helpful.
Lots of goblet cells – not too helpful.
At least no dysplasia.
Serrated surface - not helpful

Crypt dilatation, lateral spread marginal; is this enough?

Bettington et al. – “Critical Appraisal of the diagnosis of the sessile serrated adenoma.”

“We found that serrated polyps (MVHPs or SSAs) with any SSA-like crypts had clinical features more in common with the SSA than the MVHP and that this diagnostic cutoff showed good reproducibility between pathologists. This supports the position of a recent consensus publication proposing that polyps with as few as 1 SSA-type crypt should be diagnosed as SSA.”

AJSP 2014; 38(2):158-166

Hmm.

Compelling other evidence of dysmaturation would be helpful – but how would I recognize it?
SSA/P – “Dysmaturation”

- Impaired senescence
- Cells below pile up (sometimes intensely)
- Crypts below may dilate
- Proliferative activity is irregular (basal or mid) +/- expanded
- Migration toward lumen and toward base
- Nowhere to go
- Crypts spread laterally

Basal Maturation – Resemble Gastric Foveolar Epithelium

SSA/P Inverted Growth

- No dysmaturation at base

Back to our case...

The morphology is probably equivocal. Will size or location break the tie?

In my opinion:

<table>
<thead>
<tr>
<th>Size</th>
<th>Right Colon</th>
<th>Left Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5 mm</td>
<td>Mix of SSA/Ps and HPPs</td>
<td>Vast majority are HPPs morphologically</td>
</tr>
<tr>
<td>6-9 mm</td>
<td>Vast majority are SSA/Ps morphologically</td>
<td>Mix of SSA/Ps and HPPs</td>
</tr>
<tr>
<td>10+ mm</td>
<td>Essentially all are SSA/Ps morphologically</td>
<td>Vast majority are SSA/Ps morphologically</td>
</tr>
</tbody>
</table>
“Sidedness” seems to be important in serrated neoplasia (R>>L), but we don’t know why.

<table>
<thead>
<tr>
<th>The Serrated Milieu and Stratified CIMP CA Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Few</td>
</tr>
<tr>
<td>Mary</td>
</tr>
<tr>
<td>Size</td>
</tr>
<tr>
<td>Small</td>
</tr>
<tr>
<td>Large</td>
</tr>
<tr>
<td>Type</td>
</tr>
<tr>
<td>HPPs</td>
</tr>
<tr>
<td>SSAs</td>
</tr>
<tr>
<td>SSA/CD</td>
</tr>
<tr>
<td>Location</td>
</tr>
<tr>
<td>Left</td>
</tr>
<tr>
<td>Right</td>
</tr>
<tr>
<td>Low CA Risk</td>
</tr>
<tr>
<td>High CA Risk</td>
</tr>
</tbody>
</table>


**Table 5. Consensus opinion surveillance intervals after endoscopic resection of serrated lesions** (from Rex et al, 2012)

<table>
<thead>
<tr>
<th>Histology</th>
<th>Size</th>
<th>Number</th>
<th>Location</th>
<th>Interval in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP</td>
<td>&lt;10 mm</td>
<td>Any number</td>
<td>Rectosigmoid</td>
<td>10</td>
</tr>
<tr>
<td>HP</td>
<td>≤5 mm</td>
<td>≤3</td>
<td>Proximal to sigmoid</td>
<td>10</td>
</tr>
<tr>
<td>HP</td>
<td>Any</td>
<td>≥4</td>
<td>Proximal to sigmoid</td>
<td>5</td>
</tr>
<tr>
<td>HPP</td>
<td>&gt;5 mm</td>
<td>≥1</td>
<td>Proximal to sigmoid</td>
<td>5</td>
</tr>
<tr>
<td>SSA/P or TSA</td>
<td>&lt;10 mm</td>
<td>&lt;3</td>
<td>Any</td>
<td>5</td>
</tr>
<tr>
<td>SSA/P or TSA</td>
<td>≥10 mm</td>
<td>1</td>
<td>Any</td>
<td>3</td>
</tr>
<tr>
<td>SSA/P or TSA</td>
<td>&lt;10 mm</td>
<td>≥3</td>
<td>Any</td>
<td>3</td>
</tr>
<tr>
<td>SSA/P</td>
<td>≤10 mm</td>
<td>≥2</td>
<td>Any</td>
<td>1–3*</td>
</tr>
<tr>
<td>SSA/P with dysplasia</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>1–3*</td>
</tr>
</tbody>
</table>

**Stains and MVHP vs SSA/P**
- BRAF not helpful; common in both
- Ki67 – maybe, to identify dysmaturation
- Muc6 – controversial
- Annexin A10 – useful?
- MLH1 – loss occasionally in SSA/P prior to dysplasia developing (new info, C. Rosty presentation USCAP 2017)

I have yet to use stains to help with this DDx. Cost effectiveness unproven. Maybe rarely useful.

**Back to our case:**
The size is more typical of SSA/P, but rectal location is more typical of HPP.

Should I do stain$ or something?

**Problem**

- This is unrelated to the IIBD.

**Thought Process**

- Microvesicular HPP
- SSA/P
- Serrated polyp NOS

** Diagnosis or Advice**

If unrelated to IIBD, what is YOUR vote?
This is related to the IIBD.

**Thought Process**

Why would we even think serrated stuff might be arising in IIBD?

Follow

TEM

Colectomy

**Problem**

An odd serrated 10 mm rectal polyp. Removed. IIBD.

**Diagnosis or Advice**

- "Serrated Epithelial Change" In IIBD – Criteria
  - Random sample (surveillance)
  - IIBD patient
  - Morphology mimics hyperplastic polyp

**“Serrated Epithelial Change” In IIBD – A Patient**

**“Serrated Epithelial Change” In IIBD – Another Patient**

**SEC over time – example**

SEC – Why should we care?

(Is it related to increased risk of dysplasia? Cancer? Death?)
Our Experience (in preparation)

- 94 SEC and @ 187 non-SEC IBD controls; colonoscopic f/u at least one year
- Dysplasia of any type within the colitis:
  - SEC pts. 12.8% vs 4.3% in controls (p=0.013)*
- One cancer in each group

*The difference was not significant in multivariate analysis, contributed to perhaps by closer surveillance employed in the SEC patients.

Year 6 Random Right

SEC – 10/20 fragments
LGD – 1 of 20 fragments

Year 6 – “Random Transverse”

- Expanded crypts (GC HPP-like)
- Low grade dysplasia (in deeper level of same piece)
- Normal to compare

Note – MIXED - same fragment; deeper levels showed different components

Year 3 Surveillance - known SEC Pt.
Rectum – 2 mm Rectal Polyp

HPP-like polyp with unequivocal dysplasia

Year 6.5 - Descending “small polyp and area around polyp”

SEC

Resembles mixed TA/HPP (FSEC with dysplasia)

Normal to Compare

Year 3.5 - Sigmoid

4 mm sigmoid polyp; polypectomy

HPP-like polyp, with deep crypt dysplasia

Subtle SEC in random mucosa around polyp
Normal to compare
SEC and Dysplasia – Observational Studies

- Shen et al – Multiple institutions, 2015
  - 115 IBD patients with serrated polyps (including what others would call SEC among these)
  - mean f/u 56.4 months (no control group)
  - 9% developed dysplasia of some sort within their IBD-effected colorectum but no flat dysplasias or cancers that would have triggered a colectomy.

- Parian – Johns Hopkins, 2016
  - 187 pts, mean of 28 months (no control group)
  - 21% of patients developed dysplasia or cancer (6% were either high grade dysplasia or cancer)
  - SEC seen in follow-up biopsies was a statistically significant risk factor by multivariable analysis.

SEC and Dysplasia – Controlled Studies

- Kilgore – Cleveland Clinic, 2000
  - “hyperplastic-like mucosal change” in 10 of 30 (33%) cases of Crohn’s-related adenocarcinoma compared with 3 of 30 (10%) cases in the control group. \( P = 0.03 \)
  - In the 10 cases of Crohn’s-related adenocarcinoma with HPC, this alteration was found adjacent to the adenocarcinoma in 3 cases, distant to the adenocarcinoma in 5 cases, and both adjacent to and distal from the adenocarcinoma in 2 cases.

- Johnson – Mayo Clinic, 2014
  - 79 IBD and controls
  - Cumulative incidence of colorectal neoplasia:
    - SECs: 12% at 1 year; 30% 3 years
    - Controls: 4% at 1 year; 9% 3 years \( (P = 0.047) \)*

  *statistical difference was not significant after patients were stratified for history of prior or synchronous dysplasia \( (P = 0.09) \).

Batts, get back on track here. We are talking about a polyp and you are talking about random biopsies with SEC.

Observed in our SEC Study . .

In patients being followed for serrated change in random biopsies (“SEC”), unusual lesions were seen endoscopically that look like hyperplastic polyps histologically.
- Lack SSA/P histology
- Too big and irregular for HPPs
- Are these something new (“visible” serrated epithelial change)?

Could THIS explain our patient’s lesion?
Year 7.6 Distal Rectal Lesion

“8 mm area of mucosa different from background mucosa”

Visible SEC?

Year 3 - Descending

In ascending and descending there were “areas a few cm in diameter of mucosal granularity that were slightly raised”

SSA-like

Year 5.5 – Transverse

Transverse colon – “subtle abnormality”

? “visible” SEC

Normal to compare

Year 5 Rectal “Lesions”

“Two, slightly raised, hypopigmented areas were seen in the rectum – possibly serrated changes? – labeled rectal lesion”

Visible SEC?

Year 2.7 – Rectum “Lesions”

“I cm area in rectum looked different”

“Visible” serrated epithelial change?

MN 09-15002 G

1 cm area in rectum looked different

Year 5 Rectal “Lesions”

Visible SEC?

MN09-21237 E

“Visible” SEC?

Year 5 Rectal “Lesions”

Discrete serrated polyp (HPP or SSA/P-like)

Irregular serrated polyp (“lumpy-bumpy”)

Random dysplasia

Discrete polyp-like dysplasia (TA-like)
**Issues with SEC Concept**

- Probably slightly increased risk of dysplasia but not a very scary lesion
- Molecular is largely unknown; might not be part of CIMP/BRAF/MLH pathway
- Endoscopically visible SEC-like lesions will be encountered; remove, debulk if possible to make sure no dysplasia; no colectomy needed
- We don’t know if SEC is truly linked to IIBD, or coincidentally found in IIBD patients

**Diarrhea, normal colon, r/o microscopic colitis**

*Incidental HPP? (favor)*

*SEC in non-IBD??*

**The Serrated Trap**

- When we encounter a serrated polyp, we tend to ignore things that don't fit our paradigms (eg our slow-on-the-uptake history with SSA/P morphology and dysplasia/cancer risk)
- Current traps?
  - “If it is 1 cm or more, it can't be an HPP”
  - “If it has dysplasia arising in it, it must be an SSA”
  - “If there is cancer arising in it, it must be an SSA”
  - “Goblet cell HPPs are only small, left sided polyps”

**Problem** | **Thought Process** | **Diagnosis or Advice**
---|---|---
An odd serrated 10 mm rectal polyp. Removed. IIBD. | Are there more serrated polyps or lesions to be described? (will we have a broader menu in the future?) | Follow
I don’t know. TEM
Colectomy

**16 mm rectal polyp; Polypectomy (continued)**

**5 cm polyp; Desc colon, Biopsy only**

*“Giant” Goblet Cell HPP??*
MVHP with cytologic dysplasia?

“Large” Rectal Polyp; Partial Polypectomy

95% looks adenomatous
5% looks like MVHP

Practical to just call it an “advanced adenoma”. But is it really an MVHP with cytologic dysplasia?

Problem

Thought Process

Diagnosis or Advice

An odd serrated 10 mm rectal polyp. Removed. IIBD.

This is unrelated to the IIBD.

Microvesicular HPP

SSA/P

This is related to the IIBD.

Follow

TEM

I don’t know.

IIBD.

Colectomy

This is unrelated to the IIBD.

My pathway on this case.

Diagnosis: 10 mm Rectal Polyp in an IIBD Patient

- I called it “polypoid serrated epithelial change”, negative for dysplasia (plus a comment)
- I recommended continued IIBD surveillance at usual interval (as long as clinically indicated)