Mesenchymal Tumors of the GI Tract, Part 2

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Disclosure Statement

Dr. Montgomery reports no relevant financial relationships with commercial interests.

Now we will work a bit through the layers of the GI Tract
Let’s start in the mucosa and work our way out

This esophageal mass was pedunculated and shaped like a sausage. The patient presented with a choking episode from regurgitating the lesion.
Sausage-Like Lesion

This SHOULD be a giant fibrovascular polyp of the esophagus/hypopharynx

Rare lesion, well known in radiology literature, consists of fat and fibrous tissue making a polyp that can result in choking

BUT ours is a little different

Liposarcomas in Giant Fibovascular Polyps
Have mostly done well based on presentation as giant polyps (thus equivalent to superficial lesions)
Some examples have required esophagectomy but many managed by polypectomy

A cecal polyp found at the time of screening colonoscopy.
Colon Granular Cell Tumor

Most GI tract granular cell tumors are in esophagus (or anus).

Rare colon examples
Tend to be on right side and often have large nuclei, mineralization, can recur as difficult to totally remove
A single credible malignant example reported to date in colon – rare in esophagus
Anal granular cell tumor with striking pseudoepitheliomatous hyperplasia

Do not panic when you get an anal fibroepithelial polyp (anal tag) with stromal changes....
Anal fibroepithelial polyp - note also the odd surface changes.

This stromal atypia is fine in an anal fibroepithelial polyp.

“Schwann Cell Hamartoma”

Two general settings:
1) Solitary isolated mucosal lesions and
2) Syndromically as multiple lesions either producing multiple exophytic polyps ("ganglioneuromatous polyposis") or poorly demarcated transmural proliferations ("ganglioneuromatosis").
Ganglioneuroma, Solitary

No gender predominance
Adults ages 20-90, peak incidence between the ages of 40 and 60 (mean age of 48 years).
Majority in the colon, usually on the left side, detected during routine colonoscopy.
Solitary lesions are not associated with genetic syndromes.
Intramucosal ganglion cells following mucosal injury

Benign fibroblastic polyps of the colon/perineurioma
Incidental - detected in adult patients undergoing screening colonoscopy.
Mean age in the first reported series 61.5 years.
Small polyps at endoscopy (size range, 0.2 – 1.5 cm).
Lamina propria - Some intimately admixed with hyperpastic polyps.
“Vimentin-only” lesions, lacking CD31, S-100, CD117/c-kit, Bcl-2, and desmin.
A few have focal SMA and CD34.
Similar lesions with EMA/ glut1/ claudin 1 can be regarded as “perineurioma”
Benign fibroblastic polyp/perineurioma associated with hyperplastic polyp – “stromal epithelial interactions”?
Gastric perineurioma
Gastric perineurioma – EMA

Mucosal Nerve Sheath Lesions

Benign
No need to worry about GIST – if is is extension from a GIST it will look ugly
Differ from “Mucosal neuromas” of MEN2B [at right]
Gangliocytic Paraganglioma, Histology

Triphasic (in variable proportions)
1) Spindle cells with the appearance of nerve sheath cells
2) Ganglion-like cells
3) Epithelioid cells arranged in nests (“endocrine” pattern), trabeculae or papillary structures.
Gangliocytic Paraganglioma, Immunohistochemistry

S100 protein in spindle and “supporting/sustentacular” cells.
About half of cases display keratin in the epithelioid cells.
Synaptophysin in ganglion-like cells
Neuron specific enolase staining in all three cell types.
A variety of hormones demonstrated in various fractions of gangliocytic paragangliomas (somatostatin, human pancreatic polypeptide, serotonin, gastrin, glucagon, insulin, and vasoactive intestinal peptide).

Gangliocytic Paraganglioma

Vast majority in duodenum in adult patients (average age, about 54 years).
Rare examples in jejunum or even the pylorus.
The typical presentation - abdominal pain, gastric outlet obstruction, or bleeding.
Most sporadic; reported association with neurofibromatosis.
Typically centered in the submucosa with minor extensions into the mucosa, 3-4 cm with a soft yellowish cut surface, infiltrative borders.
Benign in the majority of cases.
Rare reports of regional metastases – single reported tumor-associated death.
Gangliocytic paraganglioma on crushed biopsy – treacherous!!

- Synaptophysin

- S100 protein
Moving into muscularis propria

Ganglioneuroma, Syndromic
Ganglioneuromatous polyposis - FAP
Diffuse ganglioneuromatosis - MEN type IIB
and with NF1.
Diffuse ganglioneuromatosis is found in virtually all patients with MEN IIB and often antedates the endocrine neoplasms.
Most in colorectum and in younger patients than sporadic isolated ganglioneuromas (mean ages of about 35 years).
GI Glomus Tumors

Rare in the GI tract.
Largest series (AFIP): female predominance, median age at presentation of 55 years.
Majority in stomach
May present with severe bleeding producing melena.
Circumscribed mural masses with a median diameter of 2.5 cm.
Bulge either into the mucosa or externally towards the serosa.
The vast majority behave in a benign fashion.
However, rare examples are lethal with metastases.
Difficult to predict which will have an unfavorable outcome.
Glomus tumor, Collagen type IV

Malignant glomus tumor of GI Tract, "normal area"

Malignant glomus tumor of GI Tract, spindled area
GI Glomus Tumors, Ancillary Studies

Express smooth muscle actin, calponin, and h-caldesmon but lack desmin.
Pericellular net-like positivity is seen with basement membrane proteins (laminin and collagen type IV).
Some cases have focal CD34.
No CD117/C-kit – No KIT mutations, characteristic gene fusion (MIR143-NOTCH).
Occasional cases have focal synaptophysin but these tumors lack chromogranin and they lack keratin.
This gastric mass was resected from a 57 year old woman. The surgeon requested KIT mutational testing at the time of the operation.
Most schwannomas occur in the stomach involving submucosa and muscularis propria. They rarely arise in the esophagus or colon. Lesions classified as GI schwannomas differ from the conventional somatic soft tissue schwannomas histologically by having peripheral lymphoid cuffs, lacking fibrous capsules or vascular hyalinization, and rarely showing degenerative changes.

GI “schwannomas” lack alterations in the NF2 gene found in many sporadic, conventional schwannomas from other sites. Most schwannomas express calretinin – GI “schwannomas” do not.
Gastric Schwannoma

Small bowel schwannoma, very rare but retains lymphoid cuff
Small bowel schwannoma, very rare but retains lymphoid cuff

Gastric GIST

Gastric Schwannoma
Plexiform Fibromyxoma

RARE
Reported only in stomach to date
Antral; usually; no gender or age predominance
Muscularis propria
Plexiform growth of richly vascular nodules –
CD10+, SMA+, KIT-
t(11;12)(q11;q13) – with MALAT1-GLI1 fusion
Case. This patient underwent a resection for bowel obstruction. At operation, an intussusception was noted by the surgeon. This slide was obtained from a firm area near the “lead point”.
Is this an angiosarcoma?

Reactive Vascular Proliferation

A pitfall in diagnosis can be reactive vascular proliferations associated with intussusception
The zone near the lead point can show a florid lobular proliferation of small vascular channels lined by plump endothelial cells extending from the submucosa through the entire thickness of the bowel wall.
Endothelial cells with minimal nuclear atypia, few mitotic figures
Overlying mucosa ulcerated with ischemic-type changes, mucosal prolapse.


Anastomosing hemangioma

An unusual variant of hemangioma.
First described in the genitourinary tract
Primarily in the genitourinary tract and adrenal gland
- can also arise in the gastrointestinal tract/liver, elsewhere
Rare vascular tumor but due to its anastomosing and hobnail features it histologically simulates well differentiated angiosarcoma
This anastomosing hemangioma presented as a colon polyp.

This one was a liver lesion. Look at all the extramedullary hematopoiesis! Here is a megakaryocyte.

Angiosarcoma versus anastomosing hemangioma

Angiosarcoma - Big nasty thing

Anastomosing hemangioma – little dainty thing
Case. A 72 year old woman presented with anemia. A stool test revealed occult fecal blood. At upper endoscopy, the gastroenterologist noted numerous telangiectasias and believed the patient might have hereditary hemorrhagic telangiectasia (Osler Weber Rendu syndrome). This is a biopsy of one of the lesions.
This is an angiosarcoma of the GI Tract

Rare
Usually involve small bowel
Highly aggressive
Usually epithelioid

A real case of "angiodysplasia" of colon - not our case
A real case of angiodysplasia
- not our lesion

**Angiosarcoma Location**
- Cutaneous
- Post-RX
- Deep ST

**Epithelioid Angiosarcoma**
- Hyperchromasia
- Mitotic activity
- Racemose pattern
- Infiltrative borders
- Endothelial stratification
- Necrosis
Cutaneous

M>F

Head/ Neck

Cutaneous angiosarcoma

CD31
Cutaneous angiosarcoma - epithelioid

Cutaneous angiosarcoma - epithelioid

Cutaneous angiosarcoma - epithelioid

Cutaneous angiosarcoma - epithelioid
Deep Soft Tissue

M>F

Extremities > Trunk > Head/ Neck

1 - 15 cm

70% epithelioid

50% mortality at 11 months

Meis-Kindblom et al, 1998

Deep angiosarcoma
Deep angiosarcoma – treacherous on biopsies
Deep angiosarcoma – CD31

Deep angiosarcoma – CD31

Deep angiosarcoma – CD31
**Immunohistochemistry - Endothelium**

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<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>vWF</td>
<td>50-75%</td>
<td>Not specific</td>
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<tr>
<td>FVIIIrA</td>
<td>80%</td>
<td>Least specific</td>
</tr>
<tr>
<td>CD34</td>
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<td>More specific</td>
</tr>
<tr>
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<td>Very specific</td>
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<tr>
<td>Fli1</td>
<td>94%</td>
<td>Most specific</td>
</tr>
<tr>
<td>ERG</td>
<td>96%</td>
<td>Very sensitive/ specific</td>
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Kahn et al. 2002
Miettinen et al. 2011
Folpe et al. 2000

**Lymphatic markers**

- D2-40
- VEGFR-3

**“Special” markers**

- GLUT1
- HHV8

Infantile Hemangioma
Kaposi Sarcoma

Kahn et al. 2002

**Cytokeratins in Vascular Tumors**

- Epithelioid Hemangioma (of bone)
  - Pancytokeratin (100%)
- Epithelioid Hemangioendothelioma
  - K7 (50%), K18 (100%)
- Epithelioid Angiosarcoma
  - K8 (39%), K18 (50%)
Another interesting epitheliod mesenchymal lesion - Perianal skin 6 mm punch biopsy

AE1/3 - skin appendages are internal positive control

NOT sarcomatoid carcinoma - Epitheloid sarcoma-like hemangiendothelioma/pseudomyogenic hemangiendothelioma
Epithelioid sarcoma-like hemangioendothelioma – pseudomyogenic hemangioendothelioma – ERG
Skin is internal negative control

Epithelioid sarcoma-like hemangioendothelioma – pseudomyogenic hemangioendothelioma – INI1 is retained - Skin is internal retained control

Carcinoma
EHE

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<th>CD31</th>
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<tr>
<td>EHE</td>
<td>+/-</td>
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<tr>
<td>Carcinoma</td>
<td>+</td>
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<td>Epi A/S</td>
<td>+/-</td>
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INI1 is only lost in epi sarc
Case. What syndrome is most likely?
Summary
There is a well-differentiated neuroendocrine (carcinoid) tumor
This tumor is actually a somatostatinoma
There is something that is very reasonable for a gastrointestinal stromal tumor

So the syndrome is NF1

GIST and somatostatinoma
A special variant of duodenal neuroendocrine tumor

Somatostatinoma in patients with neurofibromatosis (NF1)
Back to the mesentery once again

Case. This adult patient present with small bowel obstruction. Several similar lesions were identified in the small intestine.
Calcifying Fibrous Pseudotumor
- Initially described in children but now recognized in multiple sites at all ages.
- Soft tissue examples are often pediatric but visceral cases occur in adults.
- Typically circumscribed
- Paucicellular fibroblastic lesion with plasma cells and psammomatous or dystrophic calcifications
- Seldom recurs
Calcifying Fibrous Pseudotumor

- Examples have followed trauma and been associated with Castleman’s disease and inflammatory myofibroblastic tumors/IMT (part of IMT spectrum?)
- CFT always lacks ALK [anaplastic lymphoma kinase] and usually lacks actin, in contrast to IMT
GI Tract Mesenchymal Lesions

Most are diagnosable with a little knowledge of the layers of the bowel and a few syndromes.

Of course mucosal biopsies are only of the mucosa and do not sample most GI stromal tumors!