GISTs & NETs: the other guys

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- No conflicts of interest

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- ”Typical” colorectal cancer usually means adenocarcinoma and less often squamous cell carcinoma

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The Other Guys

- GIST – gastrointestinal stromal tumor
- NET – neuroendocrine tumor

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GIST

- Classic question: arise from the interstitial cells of Cajal, the pacemaker cells of the GI tract.
- These cells are located within the muscular layer of the GI tract
- All GISTs have malignant potential and about 10-30% progress to malignancy

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GIST

- 97% present sporadically at median age 65 with a 1:1 male to female ratio
- No known risk factors unless part of familial tumor syndromes
- 56% in stomach, 32% in small bowel, **5-10% in colon and rectum**

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GIST

- Slow growing
- Usually incidental finding during colonoscopy or imaging
- Symptoms are location-dependent (bleeding, n/v, obstruction)
- 20% of patients have metastatic disease at diagnosis (liver MC)
- Considered high-risk if >10 cm or >5 cm with mitotic rate >5/50 HPF or ruptured

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GIST

- Diagnosis made based on histopathologic evaluation of excised tumor or percutaneous biopsy of tumor and immunochemistry
- Majority stain positive for CD117, a marker for type III receptor tyrosine Kinase KIT
- CT or MRI used as initial imaging modalities

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GIST

- Surgical excision is gold standard; excise with 1-2 cm margin and avoid rupture
- No lymph node dissection necessary; does not drain to nodes
- Tumors of SB or colon and rectum treated with segmental resection
- Some rectal tumors can undergo local excision but have high rates of recurrence

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GIST

- Imatinib mesylate (Gleevec) is a tyrosine kinase inhibitor, binds ATP sites on CD117
- Introduced in 2000 – 1st line therapy and used in neoadjuvant, adjuvant and palliative setting
- Shrinks tumors pre-surgery and improves recurrence-free survival after surgery
- Newer agents available (Sunitinib, regorafenib)

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NET

- Previously called carcinoid (carcinoma-like)
- Arise from differentiated epithelial cells throughout the GI tract and secrete peptides and hormones depending on the organ of origin
- Two major categories include well-differentiated and poorly-differentiated

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- WD appear as smooth, round, polypoid lesion with normal mucosa
- PD are high-grade carcinomas, appear as large tumors with invasion into normal tissue
- Also classified by grade:

1- low grade, 2- intermediate, 3- high grade (based on mitoses)

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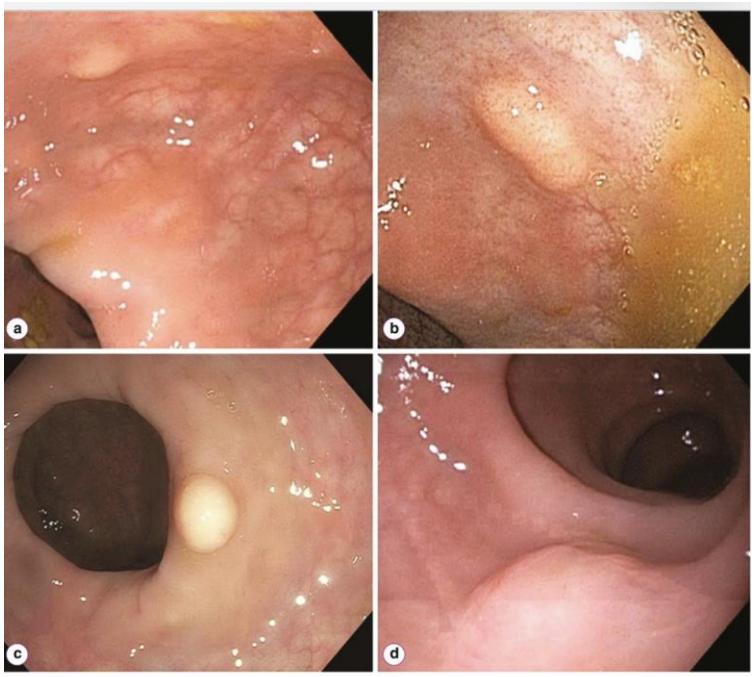

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NET

- SB and CR NETs account for <1% of new cancers
- 52-58% of NETs arise in GI tract
- Most common site is rectum
- Median age is 64 for midgut, 47 for appendix, 65 for colon, 66 for rectal

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NET

- Vague symptoms in midgut (bloating, cramping, diarrhea)
- Advanced disease can have obstruction or ischemia
- Appendiceal NETs usually found after appendectomy
- Rectal NETs usually found incidentally with endoscopy
- Colonic NETs usually present with more advanced disease

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NET

- CR NETs can secrete peptides that are metabolized by the liver
- In setting of liver mets, peptides not metabolized so can experience “carcinoid syndrome” (flushing of skin, watery diarrhea, abdominal pain, palpitations and wheezing)

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NET

- Work up includes colonoscopy, CT of chest/abdomen/pelvis with early and delayed phases, Octreotide scan to look for occult METs, Dotatate scan (similar to PET)

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NET

- Hindgut NETs usually found on endoscopy
- No additional work up for NETs <1cm that are completely resected
- Hindgut NETs 1-2 cm need EUS or rectal MRI
- Hindgut NETs >2 cm need EUS/MRI and CT chest/abdomen/pelvis

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NET

- Biochemical testing includes 5-HIAA, neuron-specific enolase, neurotensin, chromogranin

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Table 34.4: Surgical considerations by tumor site

Primary tumor	Factor	Extent of resection
Midgut	Limited disease	Resection of primary with lymphadenectomy and metastatic tumors
	Extensive disease	Resection with lymphadenectomy or bypass of primary tumor
		Debulking of metastasis
Colon		Colectomy with lymphadenectomy
Rectum	<1 cm	Endoscopic or local excision
	1–1.9 cm	Local excision or proctectomy
	>2 cm	Proctectomy

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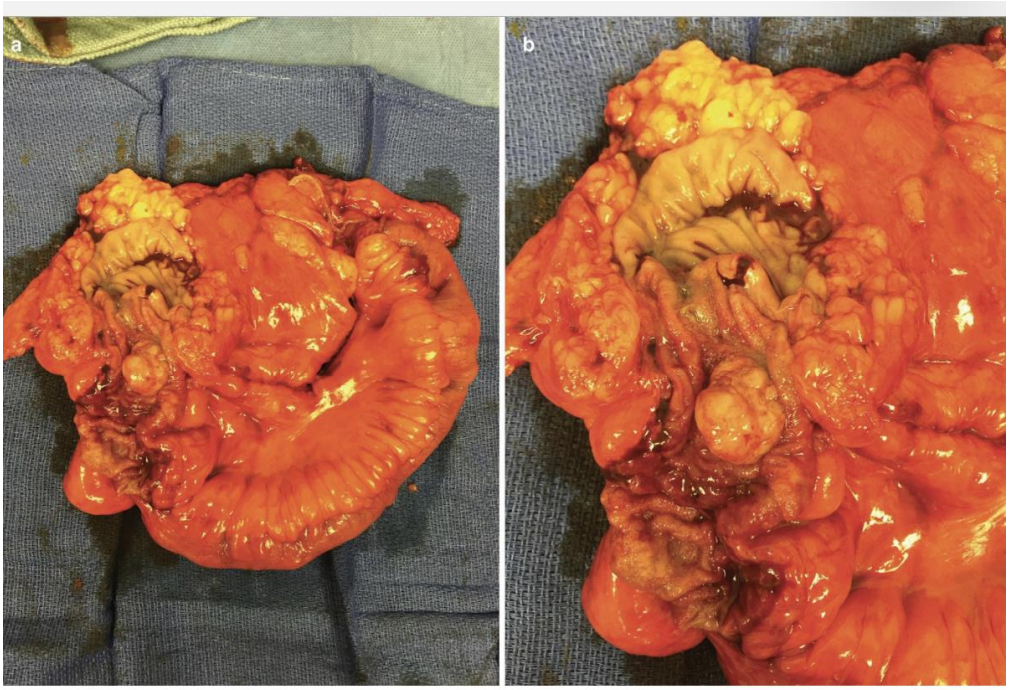

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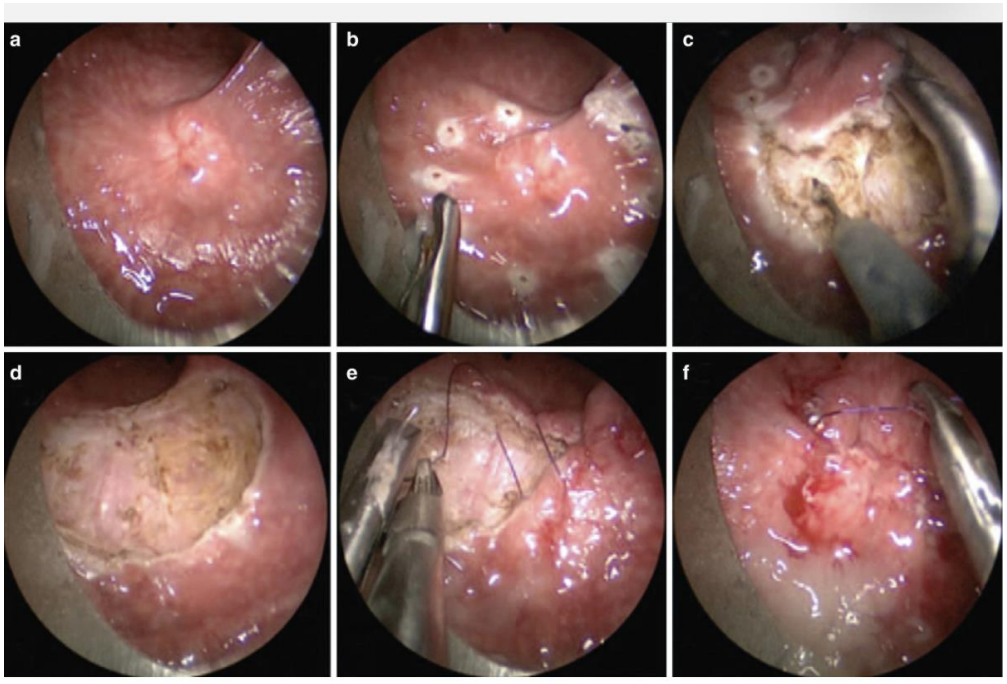

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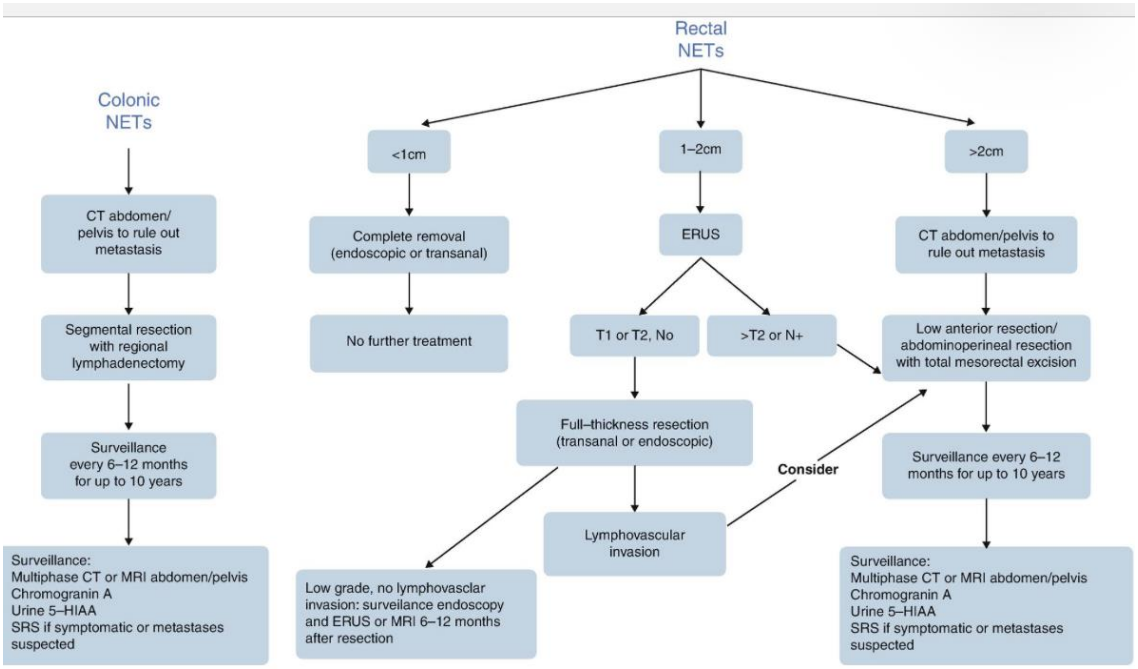

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NET

- Metastatic NETs require multidisciplinary approach and can involve chemo, radiation, hormonal therapy…
- Survival varies widely with location, size, grade, stage

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- Reichardt P et al. GIST I: pathology, pathobiology, primary therapy, and surgical issues. Semin Oncol. 2009;36(4):290-301.

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