

Atypical Colorectal Neoplasms



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KEYWORDS

• Colorectal • Carcinoid • Lymphoma • Neuroendocrine • GIST

KEY POINTS

- Atypical colorectal tumors are rare tumors accounting for less than 10% of all colorectal tumors.
- Primary colorectal lymphomas are primarily of the B-cell lineage, most commonly arising from the right side of the colon, and despite multimodality therapy have a relatively poor prognosis.
- Carcinoids have been reclassified as neuroendocrine tumors (NETs). NETs of the colon and rectum rarely present with carcinoid syndrome and are commonly advanced at diagnosis.
- Appendiceal NETs, depending on size and location, may be treated with appendectomy alone. Larger appendiceal NETs or those with ominous characteristics require an oncologic operation.
- Gastrointestinal stromal tumors are the most common mesenchymal tumor of the gastrointestinal system, possessing gain-of-function mutations in c-Kit. Tyrosine kinase inhibitors have greatly improved their treatment.

INTRODUCTION

Colorectal cancer is the third most common cancer diagnosed in the United States, as well as the third leading cause of cancer related deaths in 2016.¹ Adenocarcinoma is the predominant malignancy found in the colon and rectum. Atypical colorectal neoplasms are rare, and their management is often different than the approach to adenocarcinoma. Although primary colorectal lymphoma (PCL), carcinoids (neuroendocrine tumors [NETs]), and gastrointestinal stromal tumors (GISTs) account for a small fraction of colorectal malignancies, the surgeon needs to be aware of the specific characteristics that dictate their diagnosis and management.

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LYMPHOMA

Introduction: Nature of the Problem

Primary lymphoma of the gastrointestinal system is rare, accounting for approximately 10% of patients with lymphoma.² The most common location is the stomach. PCL accounts for 10% to 20% of gastrointestinal lymphoma and comprises less than 1% of all colorectal malignancies.³ The average age at presentation is approximately 55, with a 2:1 male to female ratio.⁴

Relevant Anatomy and Pathophysiology

PCL can be found throughout the colon and rectum. The right colon is involved most commonly. The cecum accounts for more than 50% and the ascending colon an additional 20% of all PCLs. It is hypothesized that the right colon predominance is due to the greater amount of lymphoid tissue present relative to the rest of the colon.³

A vast majority of PCLs are non-Hodgkin lymphomas of the B-cell lineage.² However, a study from China demonstrated a higher percentage of T-cell PCLs than those found in data from Western studies.⁵ Of the B-cell lineage PCLs, diffuse large B-cell lymphoma is the most common, with follicular, mucosa-associated lymphoid tissue lymphoma, and mantle cell lymphoma, small lymphocytic also identified.^{6,7}

Clinical Presentation and Examination

Patients with PCL present with expected signs and symptoms of colorectal malignancy. Abdominal pain is the most frequent complaint. In addition, patients may have weight loss, a palpable abdominal mass, and hematochezia. Perforation can occur as well, presenting as a surgical emergency.⁶ Apart from weight loss, patients with PCL typically do not demonstrate the symptoms of night sweats and fevers commonly seen with lymphoma in other locations.⁸ Because of the nonspecific nature of the symptoms, presentation is commonly late in the disease course. Immunosuppression, such as with human immunodeficiency virus infection, transplantation, or inflammatory bowel disease, has been linked to the development of colorectal lymphoma. However, a definitive connection has not been elucidated.⁹

Diagnostic Procedures

The diagnostic evaluation is similar for PCL as for other colonic tumors. Computed tomography (**Fig. 1A**) is the imaging method of choice. Findings are typically variable and may include a mass lesion or narrowing of the lumen.¹⁰ Regional lymph nodes may be enlarged. Colonoscopy (see **Fig. 1B**) may show variable morphology as well, with ulceration, infiltration, and a mass lesion.⁵ Colonoscopy also allows for obtaining of tissue for pathologic diagnosis.

Diagnosis

To diagnose PCL accurately, secondary colorectal involvement from another primary site must be excluded. To accomplish this, Dawson and colleagues¹¹ set forth a specific set of guidelines: (1) no peripheral lymphadenopathy, (2) absence of enlarged mediastinal lymph nodes, (3) white blood cell count and differential within normal limits, (4) primary involvement of the bowel with only proximal lymphadenopathy, and (5) lack of involvement of liver and spleen.

On biopsy, the tumor demonstrates findings indicative of non-Hodgkin's lymphoma, with large populations of lymphoid cells present (see **Fig. 1C**). Evaluation of CD20 typically ensures the diagnosis (see **Fig. 1D**). Further evaluation of other markers, such as Bcl-6, Bcl-2, MUM-1, and Ki67 can help to define prognosis.¹²

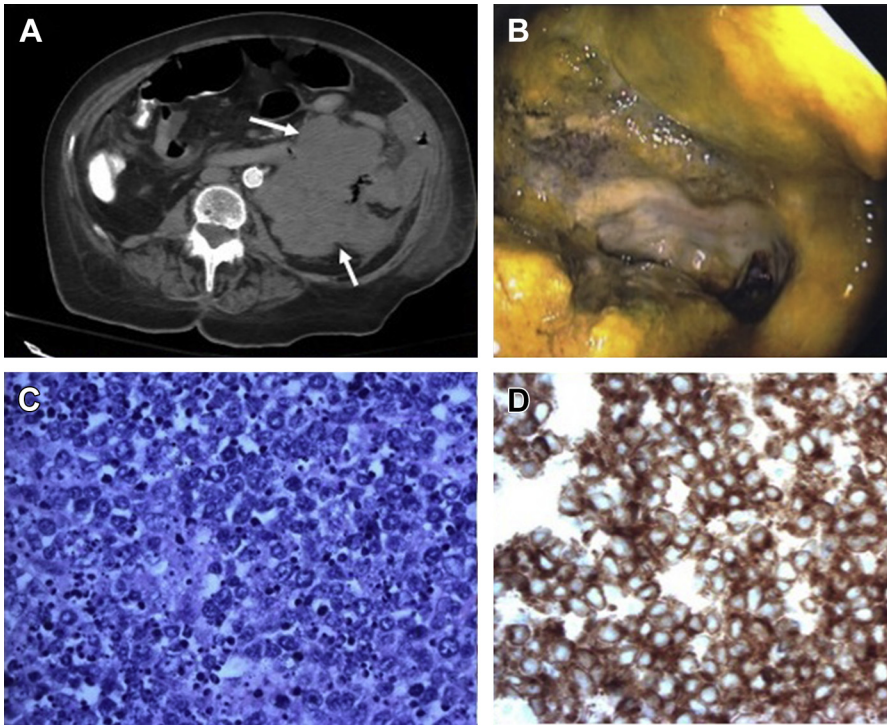


Fig. 1. (A) Computed tomography scan of a patient with a sigmoid primary colorectal lymphoma (PCL) with the mass in the left lower quadrant (*arrows*). (B) Colonoscopy demonstrating a primary colonic lymphoma. (C) Histologic finding of PCL on hematoxylin and eosin staining. (D) PCL stained for CD20.

The Ann Arbor staging system is used to describe the extent of the disease. Stage I is limited to 1 lymph node region. Stage II involves more than 1 lymph node region on the same side of the diaphragm, and stage III involved lymph node regions on both sides of the diaphragm. Stage IV demonstrates diffuse extralymphatic involvement. The designation “E” at any stage indicates extranodal involvement.¹³

Treatment

Owing to the rarity of PCL, to date, the only prospective controlled studies are for the medical treatment of PCL. There are no prospective, randomized controlled studies regarding surgery for PCL. Although chemotherapy and radiation remain the mainstay in the overall treatment regimen, surgery does provide an integral component to PCL treatment.

Surgery for PCL often is performed either in an emergent fashion for bowel perforation or as part of the therapeutic treatment for PCL. Although perforation is not common with PCL, it may occur either spontaneously or after chemotherapy.⁴ Given the predominance of PCL in the right colon, a right hemicolectomy is often performed.¹⁴ Surgery is combined commonly with adjuvant chemotherapy, although no specific guidelines have been defined. Reports show that survival is improved with the combined approach^{15–18} compared with surgery or chemotherapy alone.

Chemotherapy for PCL is very similar to other primary non-Hodgkin’s lymphomas, consisting of the CHOP (cyclophosphamide, hydroxydaunorubicin,

vincristine (Oncovin), and prednisolone) regimen.¹⁹ There are other combinations in use, but less frequently than CHOP. Recently, R-CHOP, with the addition to rituximab, an anti-CD20 monoclonal antibody, to the standard CHOP, has been evaluated. The addition of rituximab provided an additional survival benefit.^{20,21}

Outcomes

The literature regarding PCL is limited primarily to retrospective reviews of patient populations. There is considerable variability in the data presented, such as the chemotherapy regimens used, complication rate, and, in particular, the type and stage of the PCLs examined. One of the more extensive studies, by Kim and colleagues,²² examined 95 patients in Korea and included patients in all stages of disease. Sixty percent of patients underwent combined surgery and chemotherapy, 10% surgery alone, and the remaining 30% receiving chemotherapy and/or radiation. Survival at 1 and 5 years of 78% and 55%, respectively, was reported. The data were evaluated across all patients in the study and were not broken down by treatment regimen. In addition, they failed to comment on the chemotherapy regimens used or complications encountered. Similarly, Aviles and colleagues²³ evaluated 53 patients, all receiving surgery and chemotherapy, with a 10-year survival rate of 83%. All the patients in the study were stage 1E B cell lymphomas, limiting the data to those with early disease.

Survival for PCL is low, with reports indicating long-term survival rates of less than 60% demonstrated in multiple studies. The type/stage of the lymphomas was variable among the studies.^{3,16,22,24} Drolet and colleagues¹⁵ demonstrated survival for rectal lymphoma was even lower than colonic, with a median survival of 42 months versus 110 months. Among variables examined, only age greater than 60 years at time of diagnosis demonstrated a significant difference, with older age having far poorer outcomes. Another group demonstrated that the histologic grade was the only variable that affected outcome.¹⁶

CARCINOIDS (NEUROENDOCRINE TUMORS)

Introduction: Nature of the Problem

Carcinoids were originally described as benign because of their slow growth, but these tumors can behave aggressively. To reduce confusion, "carcinoid" is no longer used to describe these lesions, which are instead referred to as NETs.²⁵ Although these tumors are found most commonly in the bronchopulmonary system, around 25% occur in the gastrointestinal system. NETs account for less than 1% of colonic tumors; 20% of gastrointestinal NETs are found in the rectum, accounting for 1% of rectal tumors.^{25,26} Colorectal NETs are more commonly found in African Americans and Asians than Caucasians.²⁷ Females are more commonly affected than males. Colon NETs primarily present around age 65, whereas rectal NETs are diagnosed 10 years earlier.²⁸

Relevant Anatomy and Pathophysiology

NETs arise from the enterochromaffin cells or Kluchitschky cells within the crypts of Lieberkühn in the colon, whereas in the rectum, they arise from L cells.²⁹ These cells secrete a variety of bioactive molecules, including serotonin, kallikrein, bradykinin, histamine, and prostaglandins. Colonic NETs are primarily right-sided tumors³⁰; in addition, they are the most common tumor of the appendix.³¹ Appendiceal NETs are the most common epithelial tumor of the gastrointestinal system in children, with a majority found at the tip of the appendix.³² Involvement of the base of the appendix, tumor

size greater than 2 cm, and involvement of the mesoappendix or lymphovascular invasion are high-risk features that may require more extensive resection.³³

Clinical Presentation and Examination

Like other colorectal tumors, NETs can present with nonspecific symptoms. These include obstruction, hematochezia, pain, weight loss, and changes in bowel habits.³⁴ Given that most colonic NETs are right sided, they may grow considerably before symptoms appear. Rectal NETs may produce bleeding, constipation, tenesmus, or pain.³⁵

Carcinoid syndrome, characterized by flushing, diarrhea, pain, and cardiac symptoms, is uncommon. Fewer than 5% of patients with colorectal NETs develop this syndrome, usually in the presence of hepatic metastasis.^{27,36,37}

Diagnostic Procedures

NETs are frequently found incidentally during routine endoscopy. Colonic NETs may appear as a discrete polyp (**Fig. 2A**), however, they can appear as large tumors during colonoscopy because they often present late. Rectal NETs may appear as focal thickening or as smooth, round submucosal nodules.³⁶ Higher grade tumors may demonstrate scarring, bleedings, or ulceration.³⁸ Endoscopic ultrasound examination can aid in assessing rectal tumors as well as assisting in evaluation of lymph node status.³⁹

Several imaging modalities are useful in the evaluation of patients with NETs. Computed tomography scanning (see **Fig. 2B**) is used for staging, particularly for evaluation of metastatic spread.⁴⁰ MRI can aid in the determination of invasion of rectal NETs, helping to determine spread of disease.⁴¹ Octreotide scan has been used for localization of NETs in other anatomic locations; however, its usefulness in colorectal NETs has not been determined.

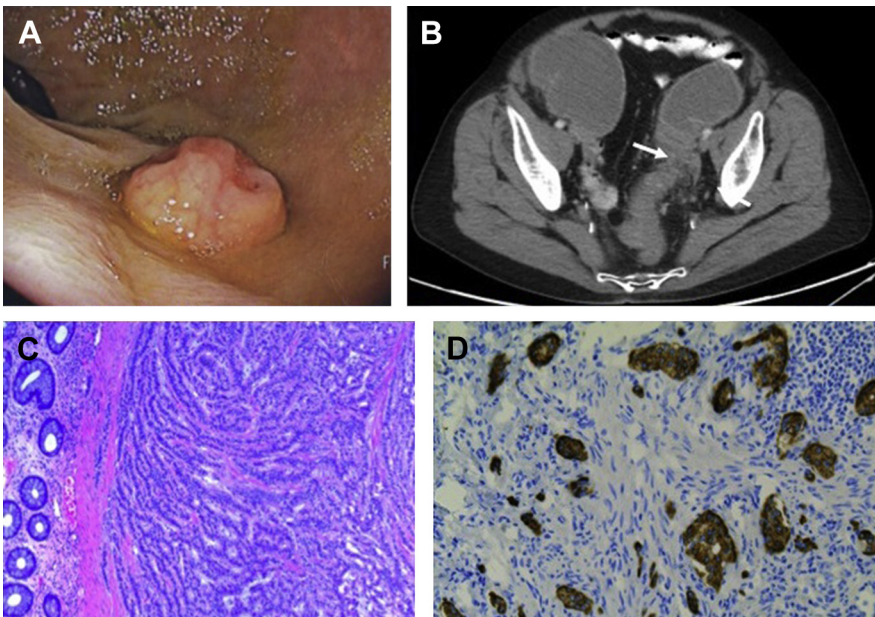


Fig. 2. (A) Colonoscopy demonstrating a mass lesion. (B) Computed tomography scan of a patient with a sigmoid stricture (arrows) resulting from a neuroendocrine tumor (NET). (C) Histologic finding of NET. (D) Appendiceal NET, stained with chromogranin A.

Diagnosis

Although the primary identification of NETs initially is through endoscopy and imaging, laboratory testing also aids in the diagnosis of NETs (see Fig. 2C). Urinary 5-hydroxyindolacetic acid (5-HIAA) is highly specific for NETs, although it lacks sensitivity. Chromogranin A (see Fig. 2D) is a much more sensitive marker than 5-HIAA; however, it lacks specificity.⁴² Rectal NETs may also produce carcinoembryonic antigen and prostate specific antigen. Although these are much less useful in the diagnosis, they could play a role in surveillance after treatment.⁴³

The grade of NETs is determined by microscopic examination of mitotic rate (mitoses per 10 high-power fields) and percentage of Ki67 staining. Grade 1 demonstrates a mitotic count of less than 2 and/or Ki67 of less than 2%. Grade 2 shows a mitotic count of 2 to 20 and/or Ki67 staining of 3% to 20%. Finally, grade 3 has a mitotic count of greater than 20 and/or Ki67 staining of greater than 20%.⁴⁴ If the mitotic count and Ki67 are not concordant for the same grade, the higher grade is assigned. Grades 1 and 2 describe well-differentiated tumors whereas grade 3 tumors are referred to as neuroendocrine carcinomas, which are typically poorly differentiated.⁴¹

There are several tumor, node(s), metastasis (TNM) staging systems for NETs, produced by the American Joint Cancer Committee and the European Neuroendocrine Tumour Society. Table 1 summarizes the 2 TNM systems for colorectal NETs, and Table 2 shows the staging systems. Although the 2 systems differ slightly, both systems have been shown to discriminate in terms of prognosis.^{45,46}

Table 1		
AJCC and ENETS TNM system		
	AJCC	ENETS
TX	Cannot be assessed	Cannot be assessed
T0	No evidence of tumor	No evidence of tumor
T1	Invasion of lamina propria or submucosa and size <2 cm	Invasion of lamina propria or submucosa
T1a	Tumor <1 cm	Tumor <1 cm
T1b	Tumor 1–2 cm	Tumor 1–2 cm
T2	Invasion of muscularis propria or size >2 cm with invasion of lamina propria or submucosa	Invasion of muscularis propria or size >2 cm
T3	Invasion through muscularis propria into subserosa or into nonperitonealized pericolic or perinectal tissue	Tumor invades subserosa, pericolic, or perirectal fat
T4	Tumor invades peritoneum or other organs	Tumor invades other organs and/or perforates visceral peritoneum
NX	Cannot be assessed	Cannot be assessed
N0	No region lymph nodes	No region lymph nodes
N1	Regional lymph node metastasis	Regional lymph node metastasis
M0	No distant metastasis	No distant metastasis
M1	Distant metastasis	Distant metastasis

Abbreviations: AJCC, American Joint Cancer Committee; ENETS, European Neuroendocrine Tumour Society.

From Anthony LB, Strosberg JR, Klimstra DS, et al. The NANETS consensus guidelines for the diagnosis and management of gastrointestinal neuroendocrine tumors (nets): well-differentiated nets of the distal colon and rectum. *Pancreas* 2010; 39(6):770; with permission.

Table 2
AJCC and ENETS staging system

AJCC		ENETS	
I	T1N0M0	IA	T1aN0M0
		IB	T1bN0M0
IIA	T2N0M0	IIA	T2N0M0
IIB	T3N0M0	IIB	T3N0M0
IIIA	T4N0M0	IIIA	T4N0M0
IIIB	T1-4N1M0	IIIB	T1-4N1M0
IV	T1-4N0-1M1	IV	T1-4N0-1M1

Abbreviations: AJCC, American Joint Cancer Committee; ENETS, European Neuroendocrine Tumour Society.

From Anthony LB, Strosberg JR, Klimstra DS, et al. The NANETS consensus guidelines for the diagnosis and management of gastrointestinal neuroendocrine tumors (nets): well-differentiated nets of the distal colon and rectum. *Pancreas* 2010; 39(6):770; with permission.

Treatment

Treatment for NETs depends on the location and size of the tumor. The treatment of appendiceal NETs is based on tumor size and characteristics. Appendectomy alone may be sufficient for treatment of small appendiceal NETs located at the tip of the appendix. However, tumors greater than 2 cm, or those involving the base of the appendix, mesoappendix, or with lymphovascular spread necessitate a right hemicolectomy and regional lymphadenectomy.⁴⁷ Positive margins after appendectomy also requires return to the operating room for a right hemicolectomy. Several studies have evaluated the surgical approach to appendiceal NETs. In the pediatric population, there is a growing consensus that a right hemicolectomy may be too aggressive an approach, despite the presence of the aforementioned ominous findings.^{48,49}

Classically, the treatment for colonic NETs was similar to colonic adenocarcinoma, with segmental resection and lymphadenectomy.⁵⁰ Recent findings indicate that smaller tumors may be amenable to endoscopic mucosal resection.⁵¹ The rate of metastasis for tumors less than 1 cm is less than 5%, indicating that limited resection is feasible.⁵² Similarly, transanal endoscopic microsurgery can be used for rectal lesions, with success even after incomplete excision at the time of endoscopy.⁵³

Chemotherapy and radiation play a minor role in the treatment of colorectal NETs, with the exception of poorly differentiated or metastatic tumors.⁵⁴ The evaluation of molecular targets is limited for NETs, although mammalian target of rapamycin has been studied in the RADIANT-2 and -3 trials (Everolimus Plus Octreotide Long-acting Repeatable for the Treatment of Advanced Neuroendocrine Tumours Associated with Carcinoid Syndrome).^{55,56} No current recommendations for anti-mammalian target of rapamycin agents are available. Sunitinib, a nonspecific tyrosine kinase inhibitor, demonstrated improved progression-free survival in pancreatic NETs, but data for colorectal NETs are limited to a case report for its use in salvage therapy.⁵⁷

Outcomes

The overall survival for NETs is quite variable. The best outcomes are found in pediatric appendiceal NETs, with a 5-year survival of 100% in multiple studies.^{58–60} Historically, survival for nonappendiceal NETs in adults was less than 50%. More recent studies have shown improvement to around 60% for colonic NETs and up to 87% for tumors at the rectosigmoid junction.²⁷

GASTROINTESTINAL STROMAL TUMORS OF THE COLON

Introduction: Nature of the Problem

GISTs, although the most common mesenchymal tumor, are exceedingly rare, with an annual incidence of 7 to 20 new cases per million persons.⁶¹ These tumors originate in the interstitial cells of Cajal, which serve as pacemakers for smooth muscle contraction in the gastrointestinal system.⁶² The average age at diagnosis is 60 years and men are affected more frequently than women.^{63,64}

Relevant Anatomy and Pathophysiology

GISTs arise in the submucosal layer of the gastrointestinal system. The most common location for GISTs is the stomach.⁶⁵ Colorectal GISTs account for 5% to 10%, with colonic GISTs representing 1% of all GISTs.⁶¹ The hallmark of the tumor is gain-of-function mutation in the tyrosine kinase gene c-KIT.^{62,66} These tumors are found most commonly in the transverse and descending colon.⁶⁷ GISTs most commonly metastasize to the liver and peritoneum, with rare metastasis to the lung, bone, and lymph nodes.⁶⁸

Clinical Presentation and Examination

As with other atypical colorectal tumors, the symptoms of GISTs are nonspecific. Most commonly, GISTs of the colon and rectum present with bleeding. Other symptoms include abdominal pain, obstruction, palpable mass, or perforation.^{67,69}

Diagnostic Procedures

Colonoscopy may demonstrate an intraluminal or bulging mass (**Fig. 3A**). If the level of suspicion for GIST is high, biopsy is not necessary and reserved for large or potentially metastatic lesions.⁷⁰ There is concern for potential spillage of tumor during biopsy.

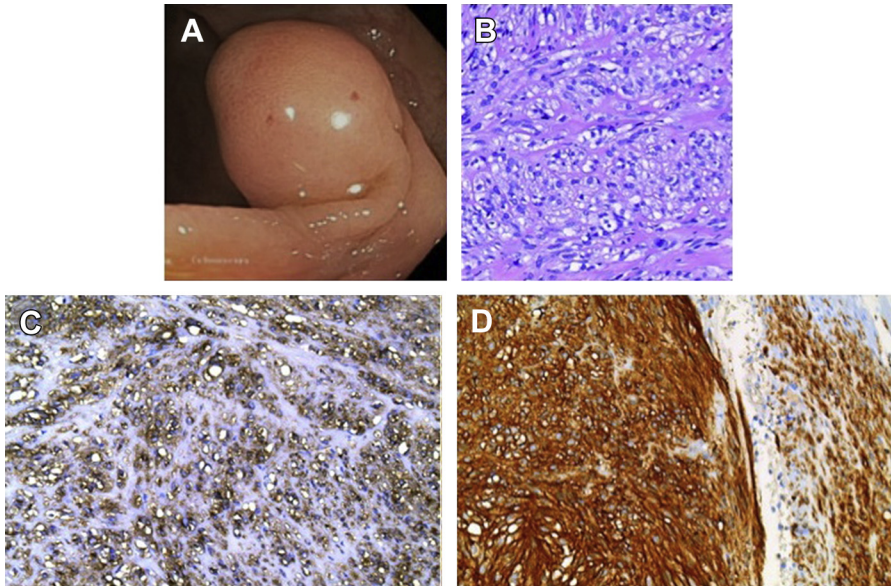


Fig. 3. (A) Colonoscopy of a patient with a polyp found to contain a gastrointestinal stromal tumor (GIST) in the proximal ascending colon. (B) Histologic finding of a patient with GIST. (C) Colonic GIST, with immunostaining for c-KIT. (D) Colonic GIST, with immunostaining for DOG1.

Computed tomography scanning commonly shows a large, exophytic tumor with inhomogenous enhancement.⁷¹ Biopsy primarily is used to rule out other diagnoses of the tumor to plan neoadjuvant chemotherapy. Endoscopic ultrasound examination plays a limited role in the workup.

Diagnosis

GIST tumors demonstrate uniform spindle-shaped cells, small nuclei, and indistinct cytoplasm (see [Fig. 3B](#)). Although c-KIT positivity is a hallmark of GISTs (see [Fig. 3C](#)), it is not 100% specific. Other non-GIST tumors that may harbor c-KIT mutations include melanoma, primary clear cell tumor, sarcomas, and extramedullary myeloid tumor.^{72–74} Similarly, there are tumors that morphologically can be classified as GISTs, but do not express c-KIT. These tumors can be confirmed by other markers, such as protein kinase C-theta or DOG-1 (see [Fig. 3D](#)).^{75,76}

The prognosis for colorectal GISTs is based on tumor mitotic rates. Small tumors (<2 cm) with low mitotic rate (<5 per 50 high-power fields) demonstrate low clinical progression. However, mitotic rates of greater than 5 per 50 high-power fields are associated with a greater than 50% metastasis rate.⁷⁷ [Table 3](#) shows a breakdown of risk based on size and mitotic count.⁷⁸ The TNM classification was updated in 2010 and is summarized in [Table 4](#).⁷⁹ In addition, the risk of progressive disease was formulated by analysis of more than 1800 GISTs, including rectal tumors by the Armed Forces Institute of Pathology (summarized in [Table 5](#)).⁸⁰

Treatment

Treatment for colonic GISTs requires a multimodality approach, with surgery and chemotherapy with tyrosine kinase inhibitors as the mainstays of treatment. Progress has been made in improving the overall survival in patients with GISTs.

The goal of surgery for GIST is removal of the tumor with the pseudocapsule intact. Rupture of the pseudocapsule can lead to spillage of tumor and bleeding. Lymphadenectomy is not necessary because GISTs rarely spread to the lymphatics.⁸¹ The abdominal contents should be evaluated, because GISTs do metastasize to the liver and peritoneum. Depending on the size of the tumor, segmental bowel resection may be adequate. Large tumors, especially those in the rectum may require more aggressive surgical resections, including abdominoperineal resection or possibly pelvic exenteration.⁸² If more than 1 organ is involved, the resection is performed en bloc.

In a study from Memorial Sloan Kettering, colonic and rectal GIST patients, survival was predicated on tumor size, not microscopic margins. Invasion through the bowel

Table 3
GIST NIH risk assessment

Risk	Size (cm)	Mitotic Count per High-Powered Field
Very low	<2	<5/50
Low	2–5	<5/50
Intermediate	<5	6–10/50
	5–10	<5/50
High	>5	>5/50
	>10	Any
	Any	>10/50

Abbreviations: GIST, gastrointestinal stromal tumor; NIH, National Institutes of Health.

From Fletcher CD, Berman JJ, Corless C, et al. Diagnosis of gastrointestinal stromal tumors: a consensus approach. *Hum Pathol* 2002;33(5):459–65; with permission.

Table 4 GIST 2010 TNM classification			
TNM Classification		Staging	
T1	≤2 cm	I	T1-2N0M0, low mitotic rate
T2	2–5 cm	II	T3N0M0, low mitotic rate
T3	5–10 cm	IIIA	T1N0M0, high mitotic rate T4N0M0, low mitotic rate
T4	>10 cm	IIIB	T2-4N0M0, high mitotic rate
N0	No nodes	IV	T1-4N1-2M1
N1	Lymph node metastasis		
M0	No distant metastasis		
M1	Distant metastasis		

Abbreviation: GIST, gastrointestinal stromal tumor.

Data from Agaimy A. Gastrointestinal stromal tumors (GIST) from risk stratification systems to the new TNM proposal: more questions than answers? A review emphasizing the need for a standardized GIST reporting. *Int J Clin Exp Pathol* 2010;3(5):461–71 and Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol* 2006;23(2):70–83.

proper may be more significant than attaining an R0 resection, with complete microscopic removal of tumor.⁸³ Laparoscopic surgery can be used and is ideal for smaller tumors.⁸⁴ Again, careful handling of the tissue to prevent tumor rupture is critical.

Molecular target therapy has made considerable strides over the past decade. Specifically, in the treatment of GIST, the tyrosine kinase inhibitors imatinib mesylate and sunitinib malate have changed the course of chemotherapy for GIST. Previous chemotherapeutic options were poor, because GISTs had a very low response rate to traditional agents.⁸⁵ As mentioned, the vast majority of GISTs contain a mutation in c-KIT. Imatinib mesylate inhibits c-KIT signal transduction, as well as acting on structurally related tyrosine kinases, including PDGFRA and BCR-ABL. However, resistance can develop, and some mutations in c-KIT, especially on exon 9, are especially prone to resistance. Sunitinib malate acts on several tyrosine kinases, including several angiogenesis factors and has been shown to have an effect of some c-KIT mutations that confer resistance to imatinib.⁸⁶

Recent studies have examined the neoadjuvant use of imatinib in phase II studies,^{87,88} with additional studies also confirming tumor shrinkage.^{89,90} By reducing

Table 5 GIST risk stratification		
Mitotic Rate	Size (cm)	Risk for Progression (%)
<5/50	≤2	Low (0)
	2–5	Low (8.5)
	5–10	Insufficient data
	>10	High (57)
>5/50	≤2	High (54)
	2–5	High (52)
	5–10	Insufficient data
	>10	High (71)

Abbreviations: GIST, gastrointestinal stromal tumor.

Adapted from Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. *Semin Diagn Pathol* 2006;23(2):70–83; with permission.

tumor size, a less drastic resection can be undertaken, possibly preserving anal sphincter function in rectal tumors. The optimal dosing regimen has yet to be determined. Therefore, maximal response to treatment is determined by following serial computed tomographic imaging of the tumor.⁹¹

Imatinib was initially approved for treatment of GIST after resection. Two American College of Surgeons Oncology Group trials, Z9000 and Z9001, demonstrated improved recurrence-free survival in phase II and phase III trials, respectively.⁹² Current recommendation is for a treatment course of 1 year after resection for intermediate- to high-risk patients.⁹³ However, the optimal duration of treatment is still under investigation.

Outcomes

Although treatment for GISTs has improved markedly, recurrence is still common and may occur a decade after the initial diagnosis and treatment. Metastases are most common to the liver and peritoneum for colonic tumors; rectal tumors also metastasize to the lung and bone.⁷⁷

SUMMARY

Primary lymphomas, NETs, and GISTs are tumors found throughout the gastrointestinal system, but are quite uncommon in the colon and rectum. Although they may have a similar presentation in terms of symptoms, endoscopic findings, and imaging results to the more common adenocarcinoma, they are important to differentiate because their treatment and prognosis differ from the standard colorectal adenocarcinoma. For each of the atypical tumors reviewed, significant strides have been made in their treatment, with the potential of molecular target therapy, adding to the therapeutic armamentarium.

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