Small Bowel Tumors

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Introduction

Tumors of the small bowel are relatively rare in incidence. They account for only approximately 3-6% of all gastrointestinal neoplasms and 1-3% of all gastrointestinal malignancy. The annual report of cancer statistics in Korea in 2008 reported the incidence of small intestinal cancer is 0.98% of all gastrointestinal malignancy. Several theories to account for the rarity of small bowel tumors have been hypothesized, including rapid intestinal transit time, dilution of carcinogens in chyme, reduced bacterial load limiting conversion of bile acids to carcinogens, rapid turnover of the small intestinal epithelium, conversion of dietary benzpyrene by benzpyrene hydroxylase into less toxic moieties, and protection by high levels of secretory IgA.

Diagnosis is often made using a combination of laboratory, radiologic, and endoscopic techniques. This article describes the general features of small bowel tumors, clinical presentations.

Epidemiology

Epidemiologic studies on small bowel tumors are limited, in part, due to their low incidence. Benign small bowel tumors are usually asymptomatic, which makes the precise incidence difficult to determine. Older studies including 22,810 and 2648 autopsies found 35 and 22 benign small bowel tumors, respectively, for an incidence of 0.15% to 0.83%. Amongst patients with symptomatic benign small bowel tumors, the most common types are leiomyomas, lipomas, adenomas, and angiomas. In autopsy series, benign tumors are far more common than malignant tumors, accounting for up to 75% of all small bowel tumors. However, the latter are more commonly reported in the medical literature.

The global incidence of primary small bowel cancers is highly variable. Incidence rates are highest in North America and Western Europe, lowest in Asia and the Middle East. In most countries, men have a slightly higher incidence compared with women. Incidence increases with age, the mid-60s being the median age of diagnosis. Carcinoids (44.3%) and adenocarcinoma (32.6%) are the most common primary cancers of the small bowel, followed by lymphomas (14.8%) and sarcomas (8.3%). Adenocarcinomas most commonly occur in the duodenum or proximal jejunum, carcinoids and lymphomas in the ileum.

The clinical presentations of small intestinal tumors

The clinical manifestations of small intestinal tumors are generally vague and nonspecific. These symptoms include pain, nausea, and vomiting related to partial or complete bowel obstruction. Bleeding or perforation may occur. OGIB is the most common presentation of small intestinal tumors. In patients presenting OGIB, small intestinal tumors are
diagnosed in around 6%. Weight loss, which occurs in approximately 30% to 50% of patients, should alert the physician to search for underlying organic causes and lead to a more thorough diagnostic workup, especially in patients aged over 50-years-old. Because their clinical presentation is vague, a high index of suspicion is the key to diagnose them.7-10

**Risk factors**

Several medical and genetic conditions are associated with an increased risk for developing small bowel cancer such as familial adenomatous polyposis (FAP), hereditary non-polyposis colorectal cancer (HNPCC), celiac disease, and Peutz-Jeghers syndrome (PJS) are associated with increased incidence of the small intestinal adenocarcinoma. Celiac disease is also associated with the enteropathy associated T-cell lymphoma in the small bowel. Personal history of colorectal cancer and Crohn’s disease increase the possibility of development of small bowel adenocarcinoma. Acquired conditions including biliary diversion, ileostomy stomas, pouches, and conduits increase the risk of small bowel adenocarcinoma.11,12

**Diagnosis**

The nonspecific symptoms of small bowel tumors often result in a long delay in diagnosis. A mean delay of up to 3 years from first symptoms to diagnosis of benign tumors and 18 months for malignant tumors has been reported. Diagnosis is often made using a combination of laboratory, radiologic, and endoscopic techniques. Recent advances in radiologic and endoscopic imaging technologies now enable clinicians to visualize the entire small bowel. Using these new imaging modalities under the correct clinical circumstances has the potential to expedite the diagnosis of small bowel tumors using nonoperative techniques.13,14

**Classification of tumors**

Small bowel tumors are broadly classified as epithelial, mesenchymal, lymphoproliferative, or metastatic. The more common tumors are described in the following sections.

1. **Adenomas and Adenocarcinomas**
   
   Adenomas and adenocarcinomas arise from mucosal glands. Adenomas in the small intestine develop into adenocarcinoma in the same sequence as in the colon with mutations in k-ras, p53, and mismatch repair proteins. Approximately one third of solitary small bowel adenomas will transform into invasive carcinoma. Small bowel adenocarcinoma is staged by the tumor-node-metastasis method. Most patients present with pain, obstruction, or bleeding, and 35% have metastatic disease at the time of diagnosis. Proximal tumors are much more common with about 70% occurring in the duodenum and jejunum.

   The detection of primary small bowel adenocarcinomas is usually by radiologic imaging or CE when presenting as obscure GI bleeding. However, even fungating intraluminal lesions may be missed by CE due to compression or cincturing of the bowel wall by tumor or intraluminal blood that obscures visualization. Therefore, balloon enteroscopy, with the overtube as a straightener, may be needed for detection of even proximal small bowel tumors.15,16

2. **Carcinoid tumor**

   Carcinoid tumor is the most common histological subtype in primary malignant small intestinal tumors, accounting for 20% to 50% of the total. It is divided into two groups: tumors of the duodenum and upper jejunum and tumors
of the distal jejunum and ileum. In the former group, gastrin-cell (G-cell) tumors predominate, followed by somatostatin-cell (D-cell) tumors, gangliocytic paraganglioma, and rarely, enterochromaffin-cell (EC-cell), serotonin-producing tumors. The majority of small intestinal carcinoid tumors occur in the terminal ileum within 1 m from the ileocecal valve. Up to one third of patients have multiple tumors and patients with carcinoid tumors of the small bowel are at risk of a second gastrointestinal malignancy including gastric, colorectal, and pancreatic cancers. Because the majority of carcinoid tumors is small in size and grows very slowly, they are usually asymptomatic and are found incidentally during exploratory laparotomy or autopsy. Occasionally patients complain of episodes of abdominal pain consistent with intermittent bowel obstruction. When the primary carcinoid tumor reaches a size of 2 cm, the risk of metastasis to the liver increases substantially.

Diagnosis of carcinoid syndrome is made by a history of flushing, diarrhea, and measuring an elevated level of 5-hydroxyindoleacetic acid (5-HIAA) in 24-hour urine. Somatostatin analog scintigraphy (octreotide scan) is extremely useful for detecting primary and metastatic tumors as 80% to 90% of carcinoids express high levels of high-affinity receptors to somatostatin. Combined endoscopic and radiologic imaging techniques are usually needed to localize and stage the tumors. It is sometimes difficult to determine whether abdominal lesions are inside or outside the small bowel. CE is useful in detecting small bowel carcinoids. However, it does not allow tissue sampling and is poor at localizing lesions particularly deep in the small bowel. Balloon-assisted enteroscopy of the entire small bowel may be necessary to detect, take a sample for biopsy, and tattoo multifocal lesions for surgical resection. Biopsies are not always diagnostic if tumors are deep in the submucosa.

3. Primary gastrointestinal lymphomas

The gastrointestinal tract is the most common extranodal site of lymphoma with the small intestine accounting for approximately one third of these cases. Most gastrointestinal lymphomas are of B cell origin, including B cell lymphoma of mucosa-associated lymphoid tissue (MALT) type, diffuse large B cell lymphoma, mantle cell lymphoma, follicular lymphoma, Burkitt lymphoma, and immunoproliferative lymphoma. T cell lymphomas are less common and are usually associated with celiac disease. Ileum is the most common site (60-65%) involved, followed by jejunum (20-25%), duodenum (6-8%) and other sites (8-9%). Macroscopically, small intestinal lymphomas present as polypoid, ulcerative (including stricturing, non-stricturing and aneurysmal forms on radiography), multiple lymphomatous polyposis, diffuse, or other types.

4. Gastrointestinal Stromal Tumor (GIST)

GISTs can develop throughout the entire GI tract and are most common in the stomach (60%) followed by the jejunum and ileum (30%), duodenum (4%-5%), rectum (4%), colon and appendix (1%-2%), and esophagus (<1%). Risk of an aggressive clinical course is based on tumor size and mitotic count: low for tumors less than 2 cm with a mitotic count less than 5 per 50 high power fields, and high for tumors greater than 10 cm with a mitotic count greater than 10 per 50 high power fields. GISTs in the small bowel can grow to a large size with no clinical symptoms. With large tumors, diagnosis is easily made on abdominal CT scan. In patients presenting with obscure GI bleeding, these tumors may be missed at CE due to incomplete studies. Reaching these lesions by balloon-assisted enteroscopy may also be difficult as the weight of the tumor may fix the bowel and limit endoscope advancement.

5. Vascular Tumors

Benign vascular tumors of the gastrointestinal tract are most commonly found in the small bowel. They present from infancy to elderly adult life. Hemangiomas and angiosarcomas arise from the vasculature and may be capillary,
cavernous, or mixed. Hemangiomas appear as well circumscribed or encapsulated submucosal mass lesions, sometimes with an exudative surface. They can involve skin, subcutaneous tissue, and the GI tract as in the blue rubber bleb nevus syndrome. Bleeding is the most common presentation. Detection of vascular tumors has improved since the introduction of CE and DBE. Balloon-assisted enteroscopy has the advantage of tattoo placement for laparoscopic or open surgical resection. There are two reports of successful endoscopic management of blue rubber bleb hemangiomas using snare polypectomy and argon plasma coagulation, one in the setting of intraoperative enteroscopy and the other using DBE.24,25

**Conclusion**

Although rare, small bowel tumors may cause significant morbidity and mortality if left undetected. New endoscopic modalities allow full examination of the small bowel with improved diagnosis. However, isolated mass lesions may be missed by CE or incomplete balloon-assisted enteroscopy. Therefore the use of radiologic imaging and intraoperative enteroscopy for diagnosis should not be forgotten.

**References**


