Primary neoplasms of the small bowel at CT: a pictorial essay for the clinician

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Abstract. – OBJECTIVE: Primary small intestinal neoplasms are uncommon tumors that are often small and difficult to identify. The aim of this paper is to describe CT technique and features in detecting and characterizing the tumors of the small bowel.

MATERIALS AND METHODS: This paper focuses on radiological characteristics of benign and malignant primary neoplasms of the small bowel at CT, with special reference to multidetector-CT techniques, type and modality of administration of contrast agents (by oral route or CT-enterography and by nasojejunal tube or CT-enteroclysis). This paper will also provide pictures and description of CT findings of benign and malignant primary neoplasms using examples of CT-enterography and CT-enteroclysis.

RESULTS: Among CT modalities, CT-enterography has the advantage of defining the real extension of wall lesions, possible transmural extension, the degree of mesenteric involvement and remote metastasis. Other useful modalities for the diagnosis of such lesions like capsule endoscopy and enteroscopy, provide important information but limited to mucosal changes with lower accuracy on extension and bowel wall involvement or submucosal lesions.

CONCLUSIONS: Multidetector-CT, performed after distension of the small bowel with oral contrast material and intravenous injection of iodinated contrast material, is a useful method for the diagnosis and staging of small bowel neoplasms.

Key Words:
Small intestine, Neuroendocrine cancer, GI stromal tumor, Radiology/imaging, Oncology-diagnosis, Carcinoid.

Introduction

Primary small intestinal neoplasms are extremely rare. Introduction of multidetector-CT technique has modified the diagnostic workup of patients with suspected small-bowel disease as well as the detection of small neoplastic lesions[1-6]. This paper focuses on the specific features of different small bowel neoplasms using CT, with special reference to multidetector-CT techniques, type and modality of administration of contrast agents (by oral route or CT-enterography and by nasojejunal tube or CT-enteroclysis).

Epidemiology and Clinical Features of Small Bowel Tumors

Small bowel tumors are rare but their incidence is rising, particularly due to the increasing incidence of small bowel carcinoid tumors[7-10]. In the United States, they represent approximately 0.5% of all cancers and 3% of all gastrointestinal tumors[11-12]. The mean age of diagnosis is 65 years old with a higher incidence in males and blacks over whites[7-13].

It is unknown why tumors occur less frequently in the small bowel than the large; however several theories have been proposed, such as a rapid transit of a more liquid stool thereby resulting in a shorter exposure to carcinogens and less mucosal irritation, and a lower conversion of bile acids by the anaerobic bacteria, in addition to a protective effect by the abundant presence of lymphoid tissue and secretory IgA[7,8,11-14].

There are many predisposing conditions and risk factors that may be involved in the development of this neoplasia (Table I): chronic inflammation, especially Crohn's disease[15,16] and celiac disease[17-19], alcohol, red meat, smoked food, refined sugar, salty or fatty food[10,14,20,21], tobacco[20,22], HIV infection, inherited syndromes such as HNPC (Hereditary non-polyposis colorectal cancer), FAP (Familial adenomatous polyposis),

Peutz-Jeghers syndrome and MEN (Multiple endocrine neoplasia) type 1[23-28].

Patients with colon adenocarcinoma are known to have a higher risk of small bowel adenocarcinoma[29]. Additionally, patients with small bowel adenocarcinoma have an increased incidence of multiple cancers including those of the colon, rectum, ampulla of Vater, endometrium, and ovary[30,31].

Small bowel tumors are often clinically silent or have nonspecific symptoms so that an early diagnosis is usually difficult and only made when patients develop an advanced stage of the disease. The most common manifestations are abdominal pain, typically intermittent, nausea, vomiting, weight loss, jaundice, gastrointestinal bleeding, obstruction, and perforation[32-35]. Symptomatic tumors are more commonly malignant.

Nowadays, the most common diagnostic techniques are CT scan, which we will focus on, MR enterography, positron emission tomography and endoscopic techniques, such as enteroscopy and wireless video capsule endoscopy. Many studies demonstrat higher rates of detecting small bowel lesions by capsule endoscopy compared to single balloon enteroscopy in the setting of obscure gastrointestinal bleeding[36], Peutz-Jeghers syndrome and familial adenomatous polyposis[37,38]. In contrast, capsule endoscopy is inferior to standard endoscopy in the detection of duodenal and periampullary polyps in FAP[39]. Enteroscopy facilitates biopsies for a histological diagnosis, marking of a lesion before surgery and therapeutic procedures such as polypectomy, stenting of obstructions and hemostasis.

Double balloon enteroscopy has the highest diagnostic yield in patients with positive findings on previous radiology studies, octreotide scans or capsule endoscopy[40]. Although enteroscopy and wireless capsule endoscopy are highly sensitive for mucosal abnormalities, particularly vascular lesions, they are far less sensitive and specific for submucosal lesions and may miss subtle abnormalities, particularly sub-mucosal lesions.

Materials and Methods

The primary requirements of small bowel imaging using CT are the visualization of the entire small bowel and adequate visceral distension.

The small bowel is most commonly opacified with positive (1-2% barium sulphate suspension or a 2-3% water-soluble iodinated solution) (Figure 1) or negative contrast agents (oral water, oral
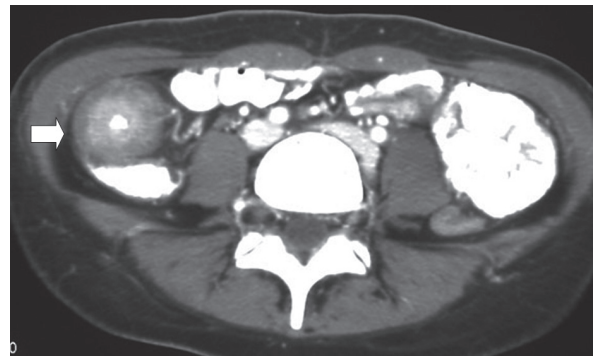

Figure 1. CT Enterography performed after oral administration of water-soluble iodinated solution shows mural thickening of the last ileal loop due to small bowel inflammation (*arrow*). It is not possible to evaluate the wall of the small bowel loops near it due to the high density of the enteral material.

oil emulsions, air, low-density barium suspension solutions, polyethyleneglycol solution or PEG) (Figure 2), administered by mouth or by nasojejunal tube.

Oral contrast agents have the disadvantage of an inadequate non-uniform distension of all small bowel loops, particularly jejunal loops (Figure 3); in contrast, the CT-enteroclysis has the ability to overcome this by using nasojejunal tube administration of the contrast (Figure 4).

The i.v. administration of iodinated contrast agent is necessary to evaluate the extent and pattern of wall enhancement. The amount of
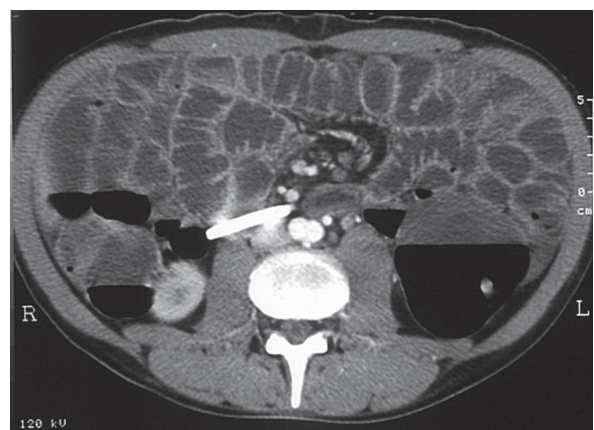

Figure 2. CT Enteroclysis performed after administration of methylcellulose. There is good visualization of the normal wall of the small bowel loops showing a linear and homogeneous hyperdense appearance between endoluminal low-density solution and extraparietal hypodensity of the peritoneal fat.
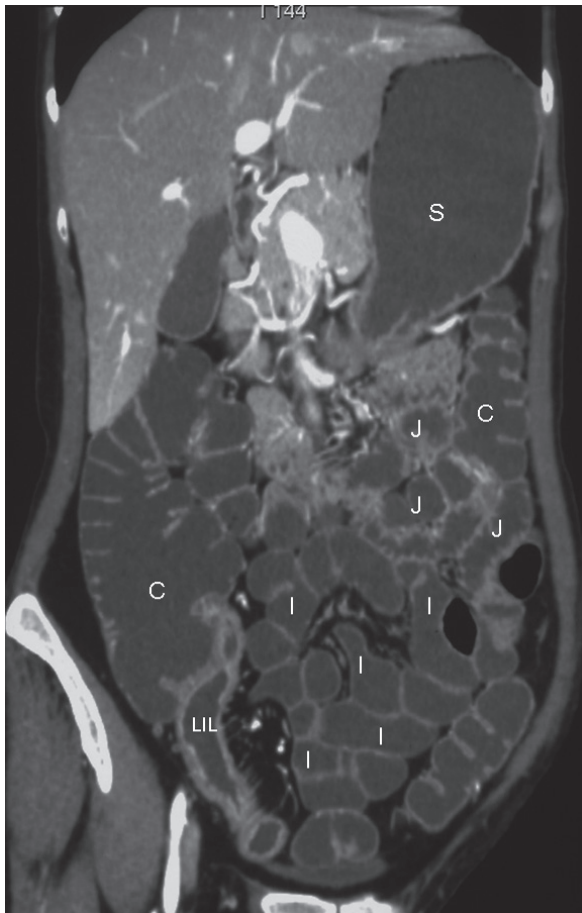
Figure 3. CT Enterography performed after oral administration of hypodense contrast material (PEG) shows inhomogeneous distension of the small bowel loops. In particular, a good distension of the ileum (I) is evident, while jejunum loops (J) show incomplete luminal distension. C: colon; S: stomach; LIL: last ileal loop (pathological).

Figure 4. CT Enteroclysis with methylcellulose shows homogenous distension of jejunal (J) and ileal loops (I).

contrast medium depends on infusion rate and time, which are 120-130 ml at 3 ml/sec with scans usually starting after 70 seconds.

A delay in contrast ingestion or scan initiation can result in incomplete bowel distension and a limited study interpretation[41].

A metanalysis from Boudiaf et al[42] performed in 2013 showed a pooled sensitivity and specificity of helical CT-enteroclysis in the detection of small-bowel tumors, of 92.8% and 99.2% (95% CI 94.2-99.9%) respectively. The mean small-bowel tumor prevalence in the study population was 22.6% (range 7.7-45.8%). Subgroup analysis revealed that small-bowel preparation, more than one imaging pass and larger volumes (≥ 2 L) of enteral contrast agent did not improve tumor

Table I. Predisposing factors for small bowel cancers.

Environmental factors	Diseases	Genetics
Tobacco, alcohol, smoked food	Chronic inflammation (especially Crohn's disease)	Peutz-Jeghers syndrome
Refined sugar, salty or fatty food	Celiac disease	MEN (multiple endocrine neoplasia) type 1
Red meat	Colon adenocarcinoma	HNPC (hereditary non-polyposis colorectal cancer) and FAP (familial adenomatous polyposis)

Table II. Small bowel cancers.

Benign tumors	Malignant tumours

Leiomyoma
  • Intramural
  • Intraluminal (or submucosal)
  • Bidirectional (or dumbbell-shaped)
Adenomas
  • Villous
  • Tubular adenomas
	Adenocarcinomas
	  • Mucinous
	  • Signet-ring cell
	  • Undifferentiated adenocarcinomas
	Gastrointestinal stromal tumours (GIST)
	  • Stomach (60%)
	  • Jejunum or ileum (30%)
	  • Duodenum (4-5%)
	  • Rectum (4%)
	  • Colon or appendix (1-2%)
	  • Esophagus (< 1%)

Lipomas	Carcinoid tumours

	Lymphoma
	  • MPrimary of the GI tract
	  • Secondary to widespread or systemic disease process

detection rate. Incomplete distension, intestinal spasm or functional invaginations were shown to give false-positive readings[43].

Results

We describe below the specific features of different classes of small bowel tumors (Table II) diagnosed by CT, showing key images able to differentiate them from each other.

Benign Tumors

Leiomyoma. These originate in the circular or longitudinal muscle layers and rarely in the muscularis mucosa. Four types have been identified depending on their pattern of growth: intramural, intraluminal (or submucosal) that is the most common, extraluminal (or subserosal) and bidirectional (or dumbbell-shaped)[44,45]. Usually they are asymptomatic, but they can cause intraluminal bleeding when their size outgrows their blood supply causing necrosis and ulceration[46]. On CT leiomyomas typically appear as sharply defined spherical or ovoid masses ranging from 1 to 10 cm. They display homogeneous soft-tissue density and uniform contrast medium enhancement (Figure 5). Calcifications can occasionally be present. It can be difficult to distinguish benign from malignant leiomyomas based on imaging alone. Marked contrast enhancement in the absence of metastases or mesenteric changes is compatible with benign leiomyomas[44,45].

Adenomas. Adenomas are the most common benign small bowel tumors, accounting for 14-20% and consisting of glandular epithelium. They can be divided in two main histologic groups: villous and tubular adenomas. Villous adenomas have a higher potential for malignant transformation than tubular adenomas. The adenoma-carcinoma sequence is comparable to their counterpart in the colon and it has been estimated that approximately one-third of solitary small bowel adenomas will transform into invasive carcinomas[47]. Polyposis syndromes are a significant risk factor and should be suspected when multiple lesions are observed[48]. Additionally, patients with a sporadic duodenal adenoma should be screened for colorectal cancer because of an increased risk of colorectal neoplasia[49,50]. Small bowel adenomas can be
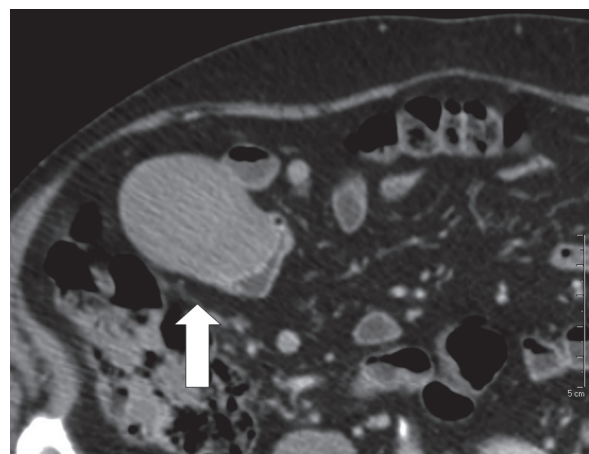

Figure 5. 78-year-old woman. CT Enterography with PEG shows an ovoid mass *(arrow)* with homogeneous soft-tissue density and uniform contrast medium enhancement. Surgical report: leiomyoma.
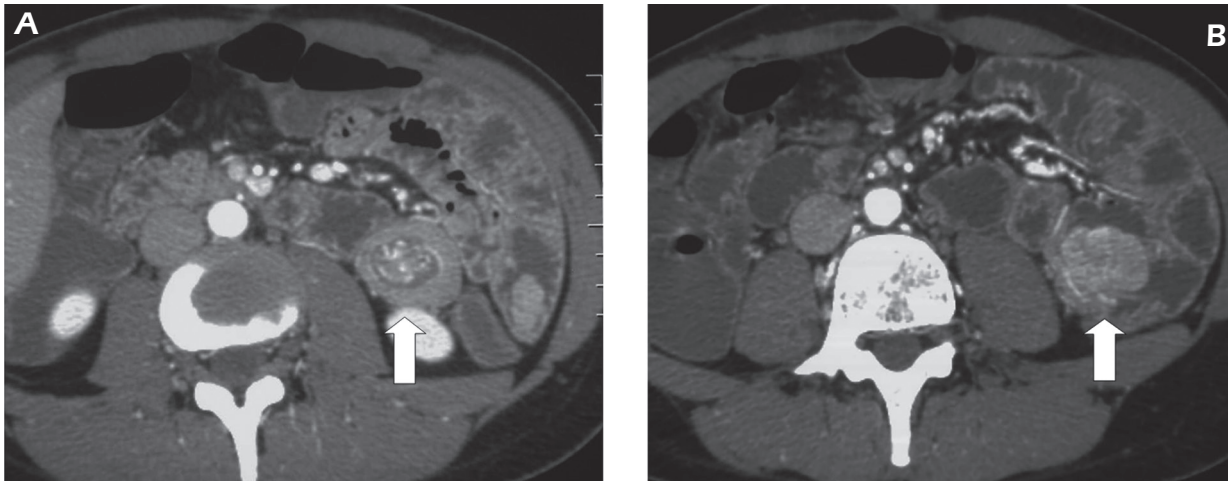
Figure 6. 32-year-old woman. CT Enterography with PEG shows intussusception (*arrow*) of an jejunal loop *(A)* due to a small well-defined, soft tissue mass *(B)* surrounded by a thin rim of oral contrast that shows moderate enhancement after intravenous contrast administration (*arrow*). Surgical report: adenoma.

clinically silent or cause bleeding, obstruction, jaundice (if they involve the ampulla of Vater) and intussusception (Figure 6). On CT they appear as a sessile or pedunculated well-defined, soft tissue mass surrounded by a thin rim of oral contrast showing moderate enhancement after intravenous contrast administration. MPR (Multiplanar reconstruction) images can help to differentiate adenomas from adenocarcinomas by identifying smooth margins, lack of mesenteric invasion and clear fat planes around the tumor[44,45].

Lipomas. Lipomas are the second most common benign tumors of the small bowel and consist ina well-circumscribed proliferation of adipocytes. They are mostly solitary, may grow to a large size and can undergo necrosis, cystic degeneration or calcification[44,45]. CT characteristically demonstrates the fat content of these tumors (values of -40 to -100 HU) (Figure 7)[44,45].

Malignant Tumors

Adenocarcinomas. Adenocarcinomas typically arise from glandular epithelium composed of tubular or villous structures. Gland formation and production of mucin are criteria for their classification as mucinous, signet-ring cell and undifferentiated adenocarcinomas. They are moderately to well-differentiated carcinomas[44,45]. They represent 25-40% of small bowel malignancies[7,8,13,32], with a median age of onset between 50 to 70 years, often lower in patients with predisposing conditions, including pol-

yposis syndromes and Crohn's disease[23,25,51,52]. They most commonly involved the duodenum, especially peri-ampullary, and their incidence decreases progressively more distally in the small intestine. Clinical presentation is generally vague, represented by abdominal pain, nausea, vomiting, anemia, bleeding, jaundice and weight loss, with the non-specificity of

Figure 7. 61-year-old man. CT Enterography with PEG shows an intraluminal mass with fat density (*arrow*). Surgical report: lipoma.
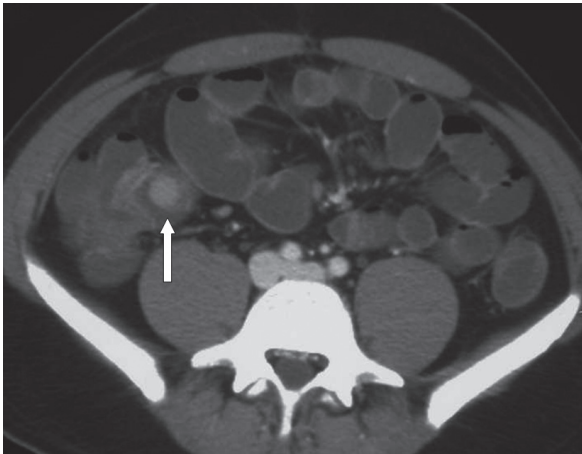
Figure 8. 29-year-old man. CT Enterography with PEG shows a small polyp (*arrow*) of the last ileal loop in patient with Peutz-Jeghers syndrome.

symptoms often causing a delay in diagnosis. On CT they may appear as a solitary soft-tissue mass with annular or eccentric luminal narrowing (Figure 9). They can also appear as a discrete tumor mass or ulcerated lesion, usually involving a short segment and may cause partial or complete bowel obstruction. CT typically demonstrates heterogeneous attenuation and moderate enhancement. Metastases to lo-
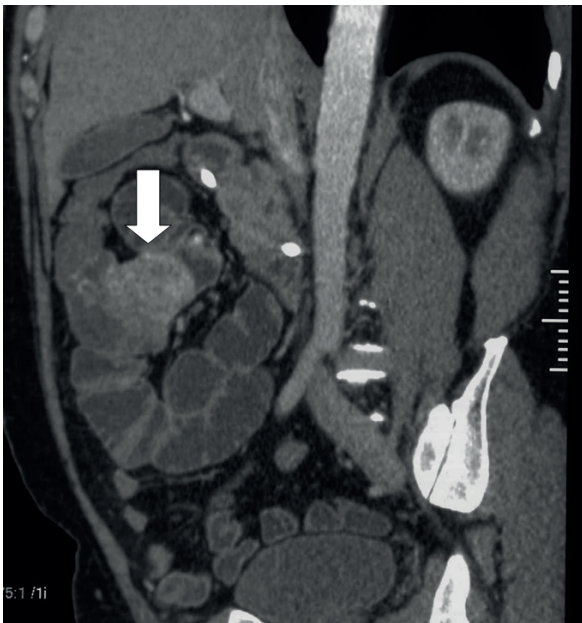

Figure 9. 51-year-old man. CT Enteroclysis with methylcellulose shows a large parietal mass with intraluminal growth in a small bowel loop (*arrow*). Surgical report: adenocarcinoma.

cal lymph nodes, liver, peritoneal surfaces and ovaries can occur, however lymph node enlargement is not as marked as in lymphomatous disease[44,45].

Gastrointestinal stromal tumors (GIST). These are the most common mesenchymal tumors of the gastrointestinal tract originating in the interstitial cell of Cajal (an intestinal pace-maker cell in normal myenteric plexus)[53] and characterized by mutations in the KIT gene. They are most common in the stomach (60%) followed by the jejunum or ileum (30%), duodenum (4-5%), rectum (4%), colon or appendix (1-2%), and esophagus (< 1%)[54]. The clinical course is mainly influenced by the size of the tumor and the mitotic count: tumors greater than 2 cm a mitotic count higher than 10 per 50 high power field are correlated with a poorer prognosis[55]. Common presenting symptoms include pain, weight loss, bleeding, obstruction, and perforation[56,57]. GISTs may be intraluminal, submucosal or subserosal in location and appear as smooth, well-defined masses. After intravenous administration of contrast media, GISTs are typically enhancing masses with areas of low attenuation from hemorrhage, necrosis, or cyst formation. A homogeneous pattern of attenuation is less common. GISTs with malignant transformation can appear as an irregular, lobulated mass (Figure 10) with low attenuation, central liquefactive necrosis, ulceration, direct extension, vascular enhancement, or liver metastases. However, it can be difficult to distinguish benign from malignant GISTs based on imaging alone[44,45,58].

Carcinoid tumors. Up to 40% of small bowel tumors may be carcinoids[7]. They are well differentiated neuroendocrine tumors, arising from argentaffin cells, which usually occur in the ileum. They stimulate a fibrotic reaction in the surrounding tissue that can lead to functional obstruction or vascular compromise[59]. The typical carcinoid syndrome usually arises when the carcinoid tumors have metastasized to the liver, meaning that the secretory products of these tumors gain direct access to the systemic circulation avoiding the liver's metabolism[60-62]. Symptoms are characterized by flushing, diarrhea, abdominal pain, bronchospasm and rarely with pruritus due to histamine excess. Carcinoids < 1 cm rarely metastasis, while lesions > 2 cm have 30 % risk of lymph node metastases[63]. Carcinoids vary in appearance from small submucosal lesions
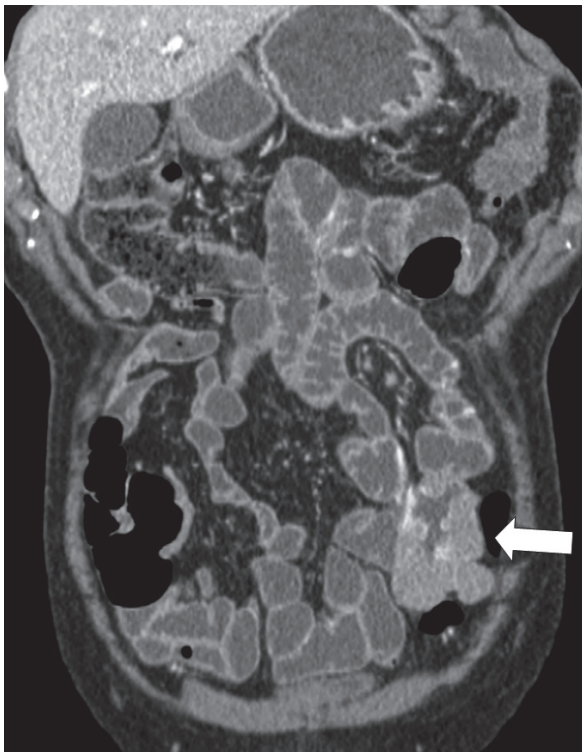
Figure 10. 55-year-old woman. CT Enterography with PEG shows a large inhomogeneous parietal mass in an ileal loop (*arrows*). Surgical report: GIST.

to large ulcerating masses. It can be difficult to differentiate primary carcinoid tumors from other lesions of the small bowel; however, the desmoplastic reaction produced by these tumors is characteristic. A soft-tissue mass with calcification, desmoplastic reaction, and avid contrast enhancement is almost pathognomonic for carcinoids (Figure 11A, Figure 11B). Lymphadenopathy and metastases to the liver, to omentum and ascites may be demonstrated. Small bowel obstruction secondary to the desmoplastic reaction or serosal disease is a recognized complication[44,45].

Lymphoma. The small intestine can be site of malignant lymphoma either as a primary neoplasm, arising focally from lymphoid tissue, or as a part of a widespread or systemic disease process. Primary gastrointestinal tract lymphoma is the most common extranodal form of lymphoma and its diagnosis requires no peripheral or mediastinal lymphadenopathy, a normal white blood cell count and differential on peripheral blood smear, and tumor involvement predominantly in the gastrointestinal tract without liver or spleen involvement[64]. Histologically, these are non-Hodgkin

lymphomas (high or low grade), B-cell (mucosal associated lymphoid tissue type (MALT), diffuse large B-cell, mantle cell, Burkitt and Burkett-Like variants) or T-cell origin. Of these, MALT type lymphomas often occur in the stomach, mantle cell lymphomas usually
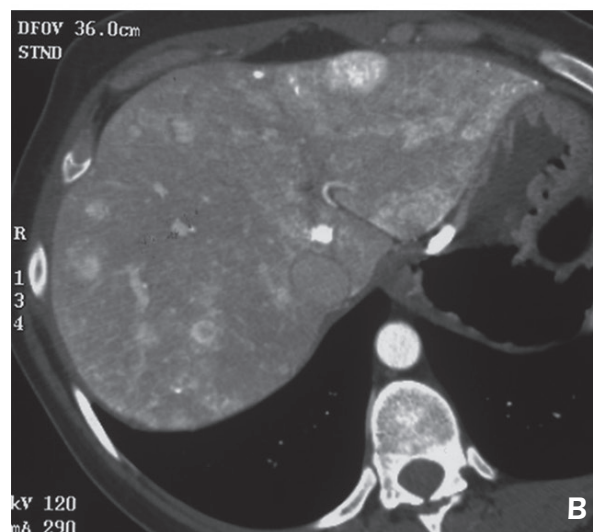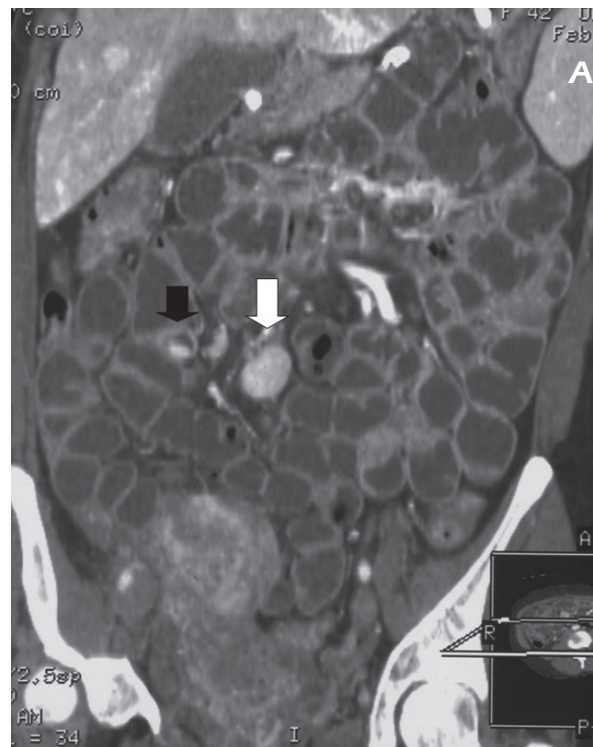

Figure 11. 42-year-old woman. CT Enteroclysis with methylcellulose shows a small hyperdense intraluminal mass (*black arrow*); a hypervascular lymphadenopathy is noticeable in its proximity (*white arrow*) *(A)*. Hypervascular hepatic metastases are also evident *(B)*. Surgical report: carcinoid tumour with hepatic metastases.

occur in the small bowel or colon, and T-cell lymphomas are often jejunal[65]. A primary or secondary involvement of the small bowel by Hodgkin lymphoma is extremely rare[66]. Small bowel lymphomas have a peak incidence in the seventh decade and occur predominantly in males[67]. Predisposing conditions include autoimmune diseases, immunodeficiency syndromes, immunosuppressive therapies, Crohn's disease, radiation therapy and nodular lymphoid hyperplasia. These tumors are characterized by a vague clinical presentation of abdominal pain, anorexia, and weight loss. The spectrum of radiological presentations of small bowel lymphoma includes a circumferential or cavitatory mass, aneurismal dilatation of the bowel, mesenteric nodal disease with secondary small bowel involvement and polypoidal disease[44,45]. Dilatation of the bowel lumen is characteristic of intestinal involvement and is recognized as a central or eccentric collection of gas or contrast within a usually ulcerated mass (Figure 12A, Figure 12B). Mural infiltration presents as intestinal wall thickening, nodular or concentric, and appears relatively homogeneous in density showing a moderate peripheral enhancement after intravenous contrast administration (Figure 12C). Mesenteric involvement is frequently present. It may appear as bulky mesenteric or retroperitoneal adenopathy or ill-defined confluent mesenteric masses encasing loops of intestine. Ulceration, necrosis and fistulous tracts to adjacent bowel loops are also clearly demonstrated[44,45].

Discussion

Small bowel tumors are rare but their incidence is rising, particularly due to the increasing incidence of small bowel carcinoid tumors. They could be benign or malignant lesions, with a large variety of symptoms: from asymptomatic to acute abdomen and major complications.
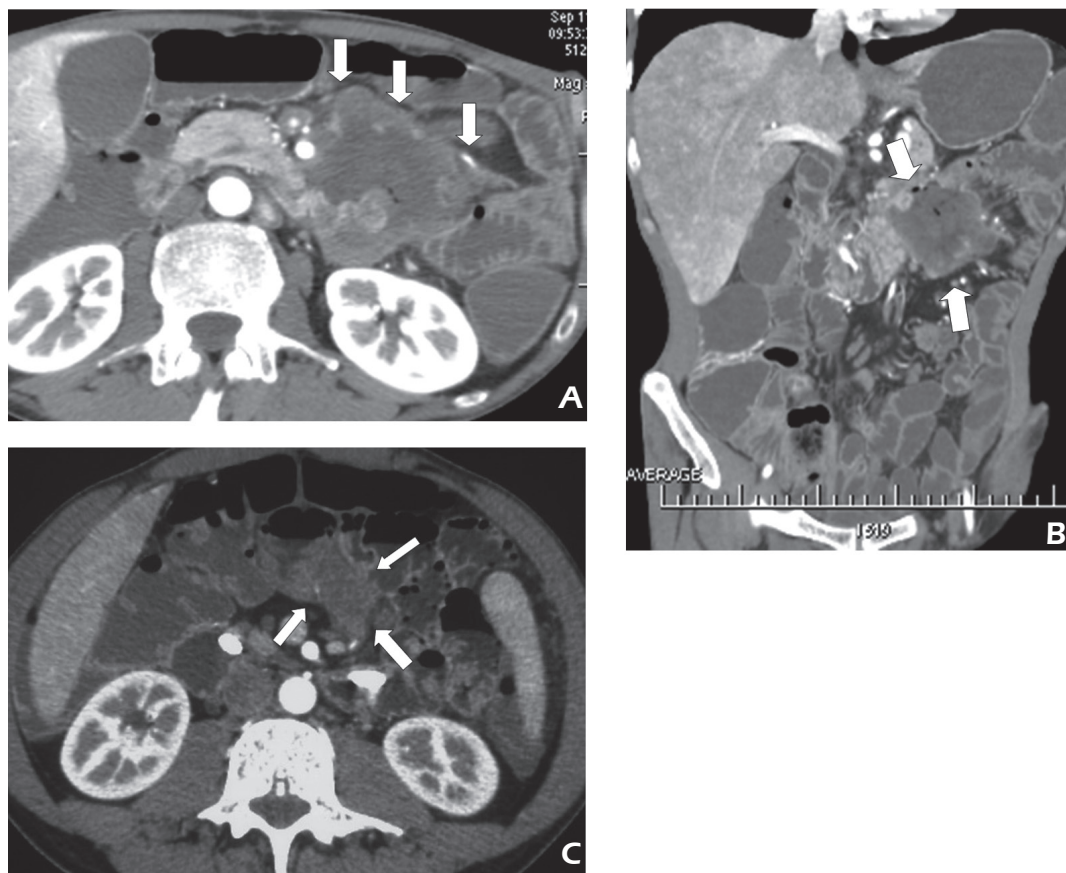

Figure 12. 51-year-old man. Axial *(A)* and coronal *(B)* CT Enterography with PEG image shows a large jejunal mass with ulceration and air bubbles (*arrows*). *(C)* 33-year-old man. CT Enteroclysis with methylcellulose shows an asymmetrical and hypodense thickening of one ileal loop (*arrows*). Surgical reports: lymphoma.

Multidetector-CT, performed after distension of the small bowel with low-density contrast material and after intravenous infusion of iodinated contrast material, is a useful method for the diagnosis and staging of small bowel neoplasms. CT has the advantage of defining the real extension of wall lesions, possible transmural extension, the degree of mesenteric involvement and remote metastasis in a single investigation. Other useful modalities for the diagnosis of such lesions, like capsule endoscopy and enteroscopy, provide important, informations but limited to mucosal changes with lower accuracy extension, bowel wall involvement or submucosal lesions[68,69].

A better approach for the diagnosis and prognosis of small bowel tumors requires a multidisciplinary approach and a close follow-up.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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