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Duodenal and Small Intestinal Tumors and its Classification Treatment Methods, Advances in Diagnosis

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A B S T R A C T

Benign and malignant small intestinal tumors are uncommon. Literature reports that the small intestine constitutes about 75% of the total GI tract. Small intestine malignancies account for less than 2% of gastrointestinal malignancies. Malignant small intestinal tumors constitute 0.1% to 0.3% of all malignancies [1-3]. Benign tumors usually seen are adenomas, lymphangioma, lipoma, leiomyoma, desmoids tumors, and hamartomas. They are usually asymptomatic but can present with complications [3,4]. Malignant lesions of the small intestine, on the other hand, are usually symptomatic. These include adenocarcinoma, leiomyosarcoma, lymphoma, and carcinoids [5].

CLASSIFICATION

Benign Epithelial Tumors

- Benign intestinal epithelial polyps
- Adenomas
- Hamartomas (Peutz-Jeghers syndrome, Cronkhite-Canadasyndrome, juvenile polyposis, Cowden disease, Bannayan- Riley-Ruvalcaba syndrome)
- Brunner gland lesions

Malignant Epithelial Lesions

- Carcinoid tumors (neuroendocrine tumors)
- Primary adenocarcinomas
- Secondary carcinomas (metastases)

Lymphoproliferative Disorders

B-cell

- Diffuse large-cell lymphoma
- Follicular lymphoma
- Immunoproliferative small intestinal disease
- Mantle cell lymphoma (multiple lymphomatous polyposis)
- Marginal B-cell lymphoma (MALT cell lymphoma)

T-cell

- Enteropathy-associated T-cell lymphoma

Mesenchymal Tumors

- Fatty tumors (lipoma, liposarcoma)
- Gastrointestinal stromal tumors (benign and malignant)
- Neural tumors (gut autonomic tumors, schwannomas, neurofibromas,
- ganglioneuromas, granular cell tumors)
- Paragangliomas
- Smooth muscle tumors (leiomyoma, leiomyosarcoma)
- Vascular tumors (hemangioma, angiosarcoma, lymphangioma,
- Kaposi sarcoma)

DUODENAL TUMORS

Benign Tumors

Duodenal Adenomas

Adenomas are the second most frequent benign tumors of the small intestine after leiomyomas. The most prevalent site of involvement in the duodenum and the most common lesion is a villous adenoma. Villous adenomas account for 45% of all benign duodenal lesions. Common symptoms of villous adenomas are jaundice, abdominal pain, anemia or melena, weight loss, and fever (Figure 1). Mucous passing with dyselectrolytemia, as found in colorectal villous adenomas, is uncommon in duodenal adenomas. Adenomas of the duodenum can be found in a variety of syndromes, including familial adenomatous polyposis (FAP), Gardner's syndrome, Peutz-Jeghers syndrome, etc. Invasive tumors of the duodenum can coexist with duodenal villous adenomas [6]

A villous adenoma that is larger than 4 cm is considered malignant. Malignant polyps in the duodenum, particularly villous adenomas, should be screened since they may require drastic surgery. Carcinoma in situ (CIS) and invasive carcinoma (INV) [7] are considered malignant histologically, but an adenoma with or without cellular atypia is considered benign.

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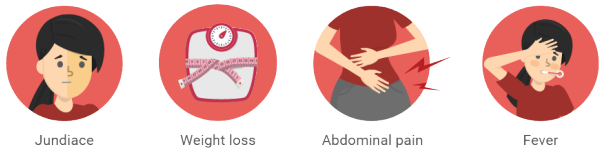

Figure 1: Symtoms of Villous Adenoma .

Brunner's Gland Adenomas

These are extremely uncommon, accounting for only 10.6% of benign duodenal tumors. Brunner's gland adenomas are usually benign, and Brunner's gland primary carcinomas are extremely rare. Brunner's gland hyperplasia is asymptomatic or can present with abdominal pain, upper gastrointestinal hemorrhage and may be associated with chronic pancreatitis. The diagnosis is confirmed after a thorough examination using contrast-enhanced computed tomography (CECT), endoscopic ultrasound (EUS), and biopsy to rule out duodenal malignancy.

Other Benign Tumors

The duodenum can be affected by lipomas, hyperplastic polyps, lymphangiomas, and hemangiomas. It is difficult to make a precise preoperative diagnosis. After symptomatic tumors have been resected, pathological diagnosis can be established.

Malignant Tumors

Duodenal adenocarcinomas are uncommon, accounting for only 0.5% of all gastrointestinal cancers. The duodenum accounts for about 45% of all adenocarcinomas, whereas the jejunum and ileum account for 55%. The chance of having proximal small bowel cancer increases 50 to 300 times in people who have FAP.

Diagnosis

The best way to diagnose suspected adenomas is through an endoscopy. Adenomas are surgically removed and biopsied. In villous adenomas, the rate of false-negative biopsy might be considerable (25-56%); hence a wide excision must be performed with caution.

Treatment

Endoscopic resection of large lateral adenomas is now possible. If endoscopic excision fails, surgical excision can be performed in the form of transduodenal excision, sleeve duodenectomy, or segmental duodenectomy. A more radical excision (pancreaticoduodenectomy) should be recommended in tumors that are invasive on imaging, large (> 4 cm), recurring, associated with lymph nodes (LNs), or when the ampulla is involved. Pancreaticoduodenectomy with peripancreatic node excision is the treatment for biopsy-proven resectable duodenal carcinomas. Although some centers perform this procedure laparoscopically, long-term survival data is still awaited. Segmental duodenectomy with lymphadenectomy is frequently used to treat cancers of the distal third and fourth portions of the duodenum. Tumors in the third portion of the duodenum or at the duodenojejunal flexure should be carefully assessed. The proximity of the superior mesenteric artery (SMA) and superior mesenteric vein (SMV) makes radical resection difficult. If the patient's performance status and clinical circumstances allow advanced-stage small intestinal tumors that cause significant hemorrhage or obstruction should be resected.

Prognosis

While benign polyps have a favorable prognosis, patients with syndromic polyps should be monitored lifelong. Malignant lesions of the duodenum can have a 5-year survival rate of 50% after radical resection, which is better than other periampullary tumors.

SMALL INTESTINE TUMORS

Adenocarcinoma

Small bowel adenocarcinoma is a rare disease that is difficult to diagnose. Due to the inaccessibility of the small intestine, there is generally a delay in diagnosis [8].

Clinical Features (Figure 2)

- Abdominal pain
- Nausea
- Vomiting
- Fatigue
- Anemia
- Upper or lower gastrointestinal tract bleeding
- Jaundice

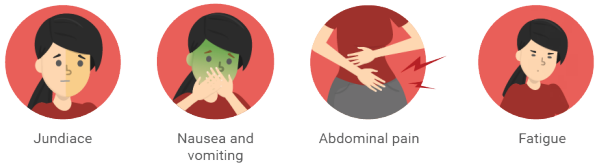

Figure 2: Clinical Features of Adenocarcinoma .

Risk Factors

The important risk factors for small bowel adenocarcinoma are a pre-existing adenoma, either single or along with one of the multiple polyposis syndromes and Crohn's disease. Other risk factors are cystic fibrosis, celiac sprue, peptic ulcer, and dietary factors like smoked and salt-cured foods and red meat.

Diagnosis

Unlike conventional enteroclysis, cross-sectional imaging studies can demonstrate intraluminal, mural, and metastatic lesions simultaneously. The overall accuracy of contrast-enhanced and water-enhanced multidetector computed tomographic (CT) enteroclysis for detecting small intestine neoplasms is 84.7%. Conventional CECT, on the other hand, cannot detect minor mucosal or bleeding lesions or polyps that result in obscure gastrointestinal hemorrhage. Comparing small bowel follow-through, push enteroscopy, and CT for such lesions, capsule endoscopy (CE) has a higher sensitivity, but it is time-consuming and expensive, with no therapeutic or biopsy potential.

Because the capsule retention rate in stricturing or malignant disease is 1.5-5%, CT enteroclysis/magnetic resonance (MR) enteroclysis is the primary investigation of choice. Double balloon enteroscopy (DBE), on the other hand, has the advantage of allowing for biopsy or therapeutic intervention. After initial diagnostic imaging utilizing capsule endoscopy, DBE could be used as a supplement. Endoscopic or percutaneous biopsy is not required for diagnosis because resection is the better option for all patients who are able to safely undergo surgery. Furthermore, a percutaneous biopsy of palpable small intestinal tumors might be harmful since it can result in bile leak, hemorrhage, and peritoneal metastatic dissemination. Intraoperative endoscopy is the last choice if advanced investigative procedures fail or are unavailable.

Treatment

Complete radical resection remains the optimal treatment for small bowel adenocarcinoma. Segmental duodenectomy with or without distal pancreatectomy is often an option for carcinomas of the distal third and fourth portions of the duodenum. Resection of jejunal and ileal carcinomas should be done with at least 10 cm of normal bowel proximally and distally, as well as sufficient mesentery to remove any involved lymph nodes. If a formal right colectomy is not performed, distal ileal tumors are usually resected with at least part of the right colon. Most jejunal or ileal carcinomas can be resected laparoscopically or openly. Although laparoscopic resection is possible, most pancreaticoduodenectomies for D2 malignancy are still performed as open surgeries. When the patient's performance status and clinical circumstances allow, advanced-stage small intestinal tumors that cause significant hemorrhage or obstruction should be resected.

Peter MY Goh, Jorge E Lenzi, (2022) Epidemiology and Clinical Features of Immune Thrombocytopenia Purpura in South-West Nigeria. Int J Med Healthcare Rep:1-4

For Locally Advanced Disease

Endoscopic implantation of self-expandable metallic stents under fluoroscopy for the palliation of patients with inoperable malignant duodenal obstruction is a safe and effective treatment.

For Metastatic Disease

Although no data exists to prove that this aggressive therapy is as effective as colorectal, hepatic metastasectomy, resectable hepatic metastases should be considered for resection, especially for jejunal and ileal adenocarcinomas. Chemotherapy prolongs survival for patients with either unresectable or metastatic cancer. Because of its mobility and the risk of radiation enteritis, radiotherapy for small intestinal malignancies is difficult. Duodenal cancers with a positive resection margin are treated with radiation alone or with 5-fluorouracil (5FU) [10]. Palliative radiotherapy may help control chronic blood loss in advanced unresectable duodenal cancer.

Lymphomas

Lymphomas constitute about 5-10% of gastrointestinal tumors, with 20-30% of them occurring in the small intestine. The second most common tumor of the small intestine is primary gastrointestinal lymphoma. Lymphomas can be sporadic or associated with autoimmune and immunodeficiency syndromes, inflammatory bowel disease, and post-transplant status.

Carcinoids

In 1907, Oberndorfer introduced the term Karzinoide (carcinoma-like). Carcinoid tumors affect approximately 1 to 2 people per 100,000. The most usually affected organs are the gastrointestinal tract (64%) and the lungs and bronchi (28%). Within the gastrointestinal tract, carcinoids are most commonly found in the small intestine (41.8%), rectum (27.4%), stomach (8.7%), and appendix (5%) [11,12].

Classification

mbryologically carcinoids are classified as:

Foregut

- Bronchus
- Thymus
- Stomach
- Duodenum
- Pancreas

Midgut

- Small bowel
- Appendix
- Right colon

Hindgut

- Transverse and descending colon
- Rectum

Carcinoids in the midgut are argentaffin-positive and have a high content of 5-hydroxytryptamine (5-HT). They also secrete prostaglandins, tachykinins, and bradykinins into circulation.

Clinical Features

Carcinoids of the small bowel commonly appear in the sixth or seventh decade, accompanied by pain and obstruction of the small bowel. Carcinoid syndrome symptoms such as flushing (90%), diarrhea (80%), wheezing, or carcinoid heart disease (40-50%) may be the presenting feature in 20-30% of patients [12].

Biogenic amines released by carcinoid tumors are deactivated by the liver. As a result, patients with hepatic metastases, retroperitoneal disease, liver dysfunction, or a substantial tumor burden are likely to develop carcinoid syndrome. Patients frequently have symptoms for 4-5 years before being diagnosed due to the indolent nature of the disease.

Pathology

Carcinoid tumors usually involve the terminal ileum, unlike adenocarcinomas, which affect the proximal small bowel. They arise in the submucosa and are usually small (1-2 cm). At the time of diagnosis, these tumors are progressed, with 70% having lymph node metastases and 50% having liver metastases. 30% may have multiple small intestine tumors.

Treatment

- Surgery

In localized disease, radical resection of the affected small intestine combined with lymphadenectomy and wide excision of the mesentery (fibrosed part) is curative, with 5-year and 10-year survival rates of 73 and 65%, respectively. To avoid leaks or strictures caused by suboptimal mesenteric flow at the ends, a wide side-to-side anastomosis may be preferred. Even in metastatic disease, surgical resections relieve symptoms and improve survival.

The supply of hormones that stimulate the growth of secondaries in the liver may be reduced if the primary is resected. Cytoreductive surgery for liver metastases can be done concurrently with primary tumor excision or subsequently. This can be in the form of anatomical/non-anatomical liver resections or liver transplants. Anatomical/non-anatomical liver resections or liver transplants are two options. Hepatic artery embolization, radiofrequency ablation (RFA), and cryoablation are other treatment options for liver metastases.

Medical Therapies

Long-acting octreotide analogs, such as lanreotide, sandostatin, and somatuline depot have been used to treat carcinoid syndrome. They effectively reduce symptoms in 50-75% of somatostatin receptor-positive tumor metastasis, but true tumor response (reduction in size) is uncommon. Interferon-alpha has also been used to treat symptoms of carcinoid syndrome, but it has been linked with myelosuppression. In poorly differentiated carcinoids, cytotoxic chemotherapy is effective. Up to 60% of patients respond to a combination of etoposide and cisplatin.

Two randomized controlled trials (RCTs) employing a combination of 5FU and streptozocin showed response rates of 22-33% but no survival benefit. Long-acting somatostatin analogs have been combined with radioactive agents such as lutetium (177Lu) and yttrium (90Y) and utilized as adjuvant therapy.

BENIGN TUMORS AND POLYPS

Other tumors that can develop in the duodenum and small bowel are hyperplastic polyps, lipomas, lymphangiomas, and hemangiomas. It is difficult to make a precise preoperative diagnosis. After resecting the tumor in symptomatic patients, a pathological diagnosis can be established.

Small Bowel Polyposis

Polyps in the small intestine can be sporadic or related to a variety of polyposis syndromes. The hamartomatous polyposis syndromes are a group of autosomal dominant disorders. These include familial juvenile polyposis syndrome, Peutz-Jeghers syndrome, MEN syndrome type 2B, basal cell nevus syndrome, phosphatase, and tensin homolog gene hamartoma (Cowden's and Bannayan-Riley-Ruvalcaba syndromes), hereditary mixed polyposis syndrome, Cronkhite-Canada syndrome, and neurofibromatosis type 1.

Juvenile polyposis can be diagnosed when any one of the following criteria is fulfilled:

- Five juvenile polyps in the colorectum
- Juvenile polyps throughout the gastrointestinal tract
- Any number of juvenile polyps with a family history of juvenile polyposis

Classification

Juvenile polyposis is classified based on clinical presentation and location of polyps:

- Juvenile polyposis coli
- Juvenile polyposis of infancy with a very early age of onset, severe hypoalbuminemia, and failure to thrive
- Generalized juvenile polyps of both the upper and lower gastrointestinal tract

Clinical Features

Intestinal obstruction, intussusception, and rectal bleeding are common symptoms of polyposis. Hypokalemia and protein-losing enteropathy are common in patients with multiple juvenile polyps, resulting in hypoalbuminemia and hypoproteinemia. Solitary juvenile polyps are most commonly found in the colon or rectum and appear with rectal bleed and usually present at 4-5 years of age. These have a tendency to prolapse or autoamputate. Patients with hamartomatous polyposis have a higher lifetime risk of gastrointestinal and extraintestinal malignancies. Juvenile polyposis coli is linked with an increased risk for colorectal, gastric, and pancreatic cancer. The cumulative chance of developing any cancer was 93% in a meta-analysis of Peutz-Jeghers syndrome patients.

Management

Double balloon enteroscopy can be used to diagnose and treat small bowel hamartomas. Screening should begin soon after birth in patients with genetically proven syndromes. All small intestinal polyps (> 5 mm) must be cleared as far as possible. The gold standard of management is prompt removal of all small intestinal polyps and thorough screening. Intraoperative endoscopy with polypectomy aids in diagnosis and excision without multiple enterotomies in patients undergoing surgery or when DBE is not available.

In patients with a diagnosis of small bowel malignancy, radical resection with intraoperative endoscopic polyp removal is recommended. To prevent short bowel syndrome, massive resections of the small bowel should be avoided. Chemo prevention for intestinal polyposis with sirolimus (rapamycin) and cyclooxygenase-2 (COX-2) inhibitors is under research.

CONCLUSION

Small intestinal tumors, both benign and malignant, are rare. Benign tumors are usually asymptomatic but can present with complications, while malignant lesions of the small intestine are usually symptomatic. The most common symptoms include nausea and vomiting, abdominal pain, bleeding, and weight loss. The small intestine may also be a location of metastasis, with contiguous, hematogenous, or peritoneal spread. In most lesions, operative resection is the mainstay of treatment, and the prognosis is determined by the disease stage and aggressiveness.

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