Perforated Ileal GIST Associated with Meckel Diverticulum – A Rare Pathological Entity of Surgical Acute Abdomen

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Rezumat

GIST ileal perforat asociat cu diverticul Meckel - o entitate patologică rară de abdomen acut chirurgical

Introducere: Tumorile GIST sunt entități rare (<1% din totalul tumorilor). Își au originea în celulele interstițiale Cajal, care fac parte din sistemul nervos autonom al intestinului. Cea mai frecventă localizare a lor este stomacul, urmată de intestinul subțire. Scopul acestei lucrări este de a prezenta un caz foarte rar de GIST ileal perforat, asociat cu diverticul Meckel.

Prezentare de caz: Pacient în vârstă de 71 de ani, cu comorbidități, este internat în urgență pentru simptome și semne de abdomen acut chirurgical. Laparotomia exploratorie relevă peritonită acută generalizată prin tumoră ileală perforată și diverticul Meckel. Se practică enterectomie segmentară, cu evoluție postoperatorie favorabilă. Examenul histologic al piesei de rezecție arată aspect de GIST, confirmat imunohistochimic.

Concluzii: Tumorile GIST ale intestinului subțire sunt tumori neobișnuite, iar perforația spontană și hemoragia care pun în pericol viața reprezintă o raritate. Tratamentul principal pentru această formă de GIST este rezecția, cu un rezultat clinic favorabil.

Cuvinte cheie: GIST, diverticul Meckel, abdomen acut

Abstract

Introduction: The GIST tumors are very rare entities (<1% of all

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tumors). They originate in the Cajal interstitial cells, which are part of the autonomic nervous system of the intestine. Their most common location is the stomach, followed by the small intestine. The aim of this paper is to present a very rare case of perforated ileal GIST, associated with Meckel diverticulum.

Case report: A 71 years old patient with comorbidities is admitted in emergency for symptoms and signs of acute surgical abdomen. The exploratory laparotomy reveals generalized acute peritonitis due to perforated ileal tumor and Meckel's diverticulum. A segmental enterectomy is performed, with favorable postoperative evolution. The histological examination of the resection piece shows the appearance of GIST, confirmed immunohistochemically.

Conclusions: The GIST tumors of the small intestine are unusual tumors and the spontaneous perforation and life-threatening hemorrhage are a rarity. The main treatment for this form of GIST is the resection, with a favorable clinical outcome.

Key words: GIST, Meckel diverticulum, acute abdomen

Introduction

The primary neoplasms of the jejunum and ileum are only < 2% of gastrointestinal malignancies, the incidence being 1.4 / 100,000 compared to 35.7 / 100,000 for colorectal cancer and 92.9 / 100,000 for breast cancer (1-3).

The term of gastrointestinal stromal tumor (GIST) was first mentioned by Mazur and Clark in 1983, failing to provide ultrastructural evidence of smooth muscle differentiation or nerve sheath in several gastric tumors (4). It is the most common mesenchymal neoplasm of the gastrointestinal tract, found in less than 1% of all tumors (5), belonging to the class of rare tumors (6,7). It has its origins in the Cajal interstitial cells, which are part of the autonomic nervous system of the intestine (8).

GISTs usually occur in the muscular mucosa or in the own layers and they have an endophytic growth profile. The estimated frequency of GIST tumors is 10-20 / 1,000,000 population (9-11) in patients in the sixth decade of life and can develop anywhere in the gastrointestinal tract from the esophagus to the rectum. The perforations of these tumors are extremely rare in the literature (12-14). Clinical signs at presentation include: palpable abdominal mass (5-50 % according to different reports), obstruction (about 5%), gastro-intestinal bleeding and perforation (only 0,8 %) (9,15).

The surgical treatment is the only one that can assure the healing. A complete removal of the tumour is needed. When GISTs present with perforation, we must always have in mind a possible recurrence of the tumor. An abundant peritoneal lavage must be practiced, in order to prevent peritoneal tumor spillage (16,17). GIST tumors respond very poor to conventional chemotherapy (18). A study showed that oral imatinib at doses > 300 mg per day can lead to curative results (19).

Some possible prognostic factors of these tumors can be: the patient's age, the size of the tumor and its anatomic location and also the immunohistochemical characteristics (20). It is considered that small tumors with low mitotic rate usually have a benign behavior (21).

Fletcher made a prognostic classification of GISTs (*Table 1*).

The aim of this paper is to present a very rare pathological situation: the case of a patient who presented with the image of a surgical acute abdomen, resulting from an ileal tumor perforation.

Case Report

The patient H.G., 71 years old, coming from a rural area, known for his history of insulin-requiring diabetes type II, atrial fibrillation, was admitted to the emergency department for diffuse abdominal pain, bilious vomiting,

Table 1. GISTs' classification according to Fletcher et al. (22)

Risk of malignancy	Size of tumor (cm)	Mitotic counts (/50HPF)
Very low	< 2	< 5/50
Low	2-5	< 5
Intermediate	< 5	6-10
	5-10	<5
High	> 5	> 5
	> 10	Any counts
	Any size	>10

intestinal transit disorders, which had a sudden onset 48 years before the admission.

At the objective examination of the abdomen, generalized muscular defense was found. The abdominal ecography reported free intraperitoneal fluid in medium amounts and the abdominal radiography revealed low hydroaerial levels.

The laboratory results showed WBC = 12,660/mm³, hemoglobin = 9.10 g/dl, urea = 104 mg/dl, creatinine = 1.41 mg /dl, blood sugar level = 68 mg /dl, AST = 30 U/L, ALT = 29 U/L.

An emergency laparotomy for exploratory purposes has been decided and it revealed acute generalized peritonitis by perforated ileal tumor and also a Meckel's diverticulum (*Fig. 1*).

A segmental enterectomy with entero-enteroanastomosis and multiple peritoneal drainage was performed. The subsequent evolution was marked by the appearance of

cardio-respiratory complications, following the therapeutically neglected associated diseases, which led to exitus on the 16th postoperative day.

The histological examination of the operative piece described macroscopically a small intestine fragment of 11 cm, with the presence of a tumor formation of 3/3.5/5 cm, white-gray, vegetative, stenotic, of increased consistency, affecting the entire intestinal wall, with ulceration of the mucosa, with excision edges at 3 cm and 4.5 cm from the tumor, respectively.

The microscopic appearance was: malignant stromal tumor of the small intestine (malignant GIST), with the appearance of fibromyosarcoma, affecting the entire intestinal wall, up to serous, with ulceration of the mucosa, with moderate lymphoid reaction of the stroma and excision edges in apparently healthy tissue (*Fig. 2*).

The immunohistochemical examination pleaded to confirm the diagnosis: CD34 - positive in tumor proliferation (cytoplasmic and membrane), C-KIT - positive in tumor proliferation (predominantly cytoplasmic), DOG1 - positive in tumor proliferation (predominantly membranous), Ki67 - positive

Figure 1. Perforated ileal tumor and Meckel's diverticulum – intraoperative aspect

Figure 2. Fascicular and storiform tumor proliferation, covered by small intestine type mucosa. HEx20 (2x lens)

in relatively rare tumor nuclei (about 15%) (Fig. 3, 4, 5).

Discussions

GISTs were previously difficult to define due to the lack of specific markers (KIT protein expression). Therefore, most GISTs have been misdiagnosed as smooth muscle tumors (e.g., leiomyoma and leiomyosarcoma) or as tumors of nerve sheath origin (e.g., Schwannoma and malignant tumors of the nerve sheath). The advances made in immunohistochemistry, molecular technology and identification of the KIT oncogenic mutation in over 80% of GISTs have improved the rate of diagnosis and accelerated the understanding of GISTs. Probably as a result of better histological diagnosis, we have also noticed an increased incidence of GIST in recent years (23).

The immunohistochemical diagnosis is mainly based on CD117 (immunoreactivity for KIT) and several other markers: DOG1, CD34, h-caldesmon, S-100, desmin and cytokeratins 8 and 18. The differential diagnosis should be made with leiomyoma, leiomyosarcoma, schwannoma, fibromatosis, inflammatory myofibroblastic tumor, matrix fibroid polyp, carcinoma and melanoma (for the latter condition HMB-45, Melan-A or S-100, easily helps to resolve the difference) (24).

The mitotic index Ki-67 is well known as a poor prognostic factor, a value over 10% has been cited by most studies, indicating a poor result and affecting long-term survival (25).

Although, specifically, the signs and symptoms are absent (20), most GISTs (70%) are symptomatic, with vague abdominal pain (26). Other symptoms include nausea, vomiting, early satiety, and abdominal fullness. The rest (30%) are asymptomatic and accidentally diagnosed. These tumors are usually small tumors (<2 cm) (8,10,11).

The most common site for GIST is the stomach (60–70%), followed by the small intestine (25–35%) (10). GISTs involving the esophagus, the appendix, the colon and the rectum are rare and tumors from the omentum, the mesentery or the retroperitoneum have

Figure 3. CD34 - positive in tumor proliferation (cytoplasmic and membranous)

Figure 4. C-KIT - positive in tumor proliferation (predominantly cytoplasmic)

Figure 5. DOG1 - positive in tumor proliferation (predominantly membranous)

Figure 6. Ki67 - positive in relatively rare tumor nuclei (about 15%)

been mentioned; but most of these have been found metastatically in primary gastric or intestinal tumors (20). GISTs, mainly tumors larger than 4 cm, can present as abdominal

emergencies, including hemorrhage, usually due to necrosis under pressure and ulceration of the affected mucosa, intestinal obstruction or perforation (13,27). Ileal perforation of GIST is a very rare pathological entity, being found only in 4 cases, cited in the literature (9,28-30).

The mechanism of GIST secondary intestinal perforation is unclear. Possible suggested mechanisms include increased intraluminal pressure due to tumor obstruction, replacement of the intestinal wall with tumor cells followed by necrosis and intestinal ischemia due to tumor embolization (31).

In order to make a correct diagnosis, a high index of suspicion is required, combined with appropriate imaging methods, such as tomography or MRI of the abdominal cavity (32).

The main treatment is the complete (R0) surgical excision. Systemic lymph node dissection is not recommended by some authors (3,33).

The prognostic factors include the anatomical location of the primary tumor, the patient's age, the histomorphology, the molecular genetics and the immunohistochemistry, of which the tumor's size is the most important factor (33,34).

Conclusions

The GIST of the small intestine is an unusual tumor and its spontaneous perforation and life-threatening hemorrhage is an extremely rare initial presentation. Perforation can be attributed to the increased intraluminal pressure and also to the replacement of the small intestine's wall by tumoral cells.

The clinical diagnosis of these GISTs can only be based on an index of suspicion, because specific signs are absent. The diagnosis of certitudine is pathological and immunohistochemical.

The main treatment for these emerging presentations of GISTs of the small intestine is the R0 resection, with complete tumour removal and clear surgical margins.

Conflicts of Interests

The authors declare no conflicts of interests.

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