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Diagnostics and treatment of small intestine tumors in our own experience

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Introduction. Small intestine cancers are a difficult oncological problem. Lack of specific symptoms and difficulties with accessing the location even for advanced diagnostic techniques delay the diagnosis and implementation of appropriate treatment.

Aim. Analysis of incidence, clinical symptoms, diagnostic methods and results of treatment of small intestine tumors in the material of the Maria Skłodowska-Curie Institute — Oncology Center (MSCI) in Warsaw.

Material and method. A retrospective analysis of 54 patients undergoing surgery for small intestine tumor in the years 2006–2015. The evaluated group consisted of 26 (48%) males, 28 (52%) females, median age was 63.5 ± 13.5 years (23–86).

Results. In the study group 18 (33%) cases of sarcomas were found, including 16 (30%) cases of GIST. The remaining cases were diagnosed as: adenocarcinoma — 13 patients (24%), neuroendocrine tumor (NET) — 8 (15%), malignant melanoma — 6 (11%), lymphoma — 3 (6%) and benign tumors — 6 (11%). Symptoms included gastrointestinal bleeding (55.5%), abdominal pain (48%), weight loss (31.5%), nausea (30%), vomiting (24%), flatulence (24%), intestinal passage disturbances (15%). In 70% of patients anemia was diagnosed, which in 33% required an average of 4.5 packed red blood cells (PRBC) units (range 1–100) to be transfused before treatment. The test that led to diagnosis was in 26 (48%) cases computed tomography, in 8 (15%) cases capsule endoscopy and in 5 (9%) cases double-balloon enteroscopy. Partial resection of the small intestine with regional lymph nodes was performed in 38 patients (70%), local excision in 5 (9%) patients and anastomosis gastric pass in 4 (7%) patients. So far, 17 (31%) deaths have been reported in this group of patients. 5-year survival was 93.8% for sarcomas, 53.9% for SIC, 66.7% for GEP-NET.

Conclusions. Partial resection of the small intestine remains the basic method of radical surgical treatment. Both diagnostics and treatment should be carried out in reference centers.

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Key words: small intestine tumor, small intestine cancer, GIST, GEP-NET

Introduction

Small intestine tumors (SITs) are rare and represent about 2% of malignant tumors of the gastrointestinal tract [1]. Low incidence, late, non-specific symptoms and technical diagnostic difficulties cause that they are most often diagnosed in emergencies, such as gastrointestinal obstruction, gastrointestinal bleeding or peritonitis. In 2010, malignant SITs in Poland accounted for 0.5% of all cancers and the standardized incidence rate was $0.4/10^5$ for men and $0.3/10^5$ for women [1]. The incidence rates increase with age, reaching a peak in the eighth decade of life. In relation to the average for the European Union countries, in 2010 the incidence in

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Poland was twice as high [1]. In the USA, malignant SITs account for 0.6% of all new cancer cases [2], with an incidence of 2.3 per 100 000 people. The aim of the study was to analyze the prevalence of clinical symptoms, diagnostic methods and results of SIT treatment in MSCI material.

Material and method

In the years 2006–2015, 4463 patients were operated in the Department of Oncological Gastroenterology, Maria Skłodowska-Curie Institute — Oncology Center (MSCI) in Warsaw. The database of patients undergoing surgical treatment was searched for diagnoses, choosing: duodenal, jejunum and ileum tumors, excluding ampulla of Vater's tumors. Complete disease histories of 54 (1.2%) patients, including 26 men (48%), 28 women (52%), aged between 23 and 86 years (median 63.5 ± 13.5), were extracted and analyzed.

On the basis of the available data, the following parameters were analyzed:

1. Type of neoplasm.
2. Dominant symptoms of the disease.
3. Nutrition status.
4. Anemia and transfusion of blood.
5. The time from the first symptom to the beginning of treatment.
6. Imaging and endoscopic examinations performed.
7. The type of examination leading to the diagnosis.
8. Type and scope of surgery.
9. Postoperative complications.
10. Duration of hospitalization.
11. Disease-free survival time.

Results

Characteristics of the tumor

Among 54 SITs, 48 (89%) were malignant and 6 (11%) were benign lesions. Among cancers 6 (11%) metastatic tumors (metastases of melanoma) were found. Out of 42 primary malignant tumors, 18 (33%) sarcomas were reported, including 16 (30%) GISTs, 13 (24%) adenocarcinomas, 8 (15%) neuroendocrine tumors and 3 (5%) lymphomas. Among 6 benign lesions, two angiomas were diagnosed histopathologially, one lipoma, one adenoma, one myoma and one muscle and one Brunner's gland hamartoma — an extremely rare type of tumor representing only 5% of duodenal tumors. The most frequent SITs were located in duodenum 19 (36%), jejunum 18 (33%) and ileum 17 (32%), (Tab. I).

Table I. Characteristics of lesions

Type of tumor	n = 54 (%)
Malignant	48 (89%)
Benign	6 (11%)
Histopathological type	
Sarcoma	18 (33%)
Adenocarcinoma	13 (24%)
GEP-NET	8 (15%)
Melanoma	6 (11%)
Lymphoma	3 (5%)
Benign	6 (11%)
Location of the tumor	
Duodenum	19 (36%)
Caecum	18 (33%)
Ileum	17 (32%)

GEP-NET — gastroenteropancreatic neuroendocrine tumors

Symptomatology

The most frequently observed symptoms were gastrointestinal bleeding in 30 (55.5%) patients and recurrent abdominal pain in 26 (48%) cases. Less frequent were: weight loss (31.5%), nausea (30%), vomiting (13%), flatulence (24%), recurrent symptoms of obstruction (15%). The most common symptom that initiated the diagnosis was gastrointestinal bleeding — 27 (50%) cases. In 19 (35%) patients bleeding and in 5 (9%) patients pain were the only symptoms of the disease. The remaining patients (56%) presented more than one symptom. The time elapsed from the first symptoms to surgery ranged from 0 to 2190 days (median 90 ± 379.56 days). In four cases (7%), the disease remained asymptomatic, and in one patient (2%) the first symptom was gastrointestinal perforation leading to an urgent surgical treatment.

Pain, nausea and weight loss are symptoms presented in the vast majority of cases in patients with primary malignant SITs and metastatic tumors. In patients with benign lesions, bleeding to the gastrointestinal tract was more frequent, resulting in anemia, often requiring repeated transfusion of blood products. Characteristics of symptoms are presented in Table II.

Diagnostics

Most of the tumors were diagnosed by radiological imaging and endoscopy. Only in 2 (4%) cases the diagnosis was made during laparotomy. Computed tomography (CT) was the most frequent examination leading to the diagnosis of SIT, which was decisive for the further treatment in 26 (48%) cases. Capsule endoscopy (CE) turned out to be the basic examination in 8 (15%), double-balloon endoscopy (DBE) in 5 (9%) and gastroscopy in 5 (9%) patients. Endoscopic ultrasound (EUS) showed the presence of SIT in 3 (5%) patients, positron emission tomography (PET CT) in one (2%), (Tab. III).

The results of the laboratory tests showed a decrease in hemoglobin levels, of which 23 (43%) required transfusion of packed red blood cell (PRBC) (range 1–100), median 4 ± 19.12. The highest number of PRBC transfusions

Table II. Symptomatology of small intestine tumors

Symptom	Frequency n (%)			
	Malignant tumors n = 48	Benign tumors n = 6	Total n = 54	Initial symptom
GB	24 (50%)	6 (100%)	30 (56%)	27 (50%)
Abdominal pain	25 (52%)	1 (17%)	26 (48%)	16 (30%)
Weight loss	17 (35%)	–	17 (32%)	–
Nausea	16 (33%)	–	16 (30%)	–
Vomiting	13 (27%)	–	13 (24%)	–
Flatulence	12 (25%)	1 (17%)	13 (24%)	–
Obstruction	8 (17%)	–	8 (15%)	6 (11%)

GB — gastrointestinal bleeding

was observed in the group of patients with benign tumors, 8–100 individuals, median 19 ± 42.3. In patients with primary malignant SIT, relatively small volumes of blood products were transfused compared to patients with benign tumors, 1–14 units, median 2 ± 2.5. In other patients, no significant changes were observed in the routinely determined complete blood count, clotting parameters and concentration of electrolytes. The risk of PRBC transfusion was also assessed, depending on the histopathological type of cancer. This type of treatment required 7 (54%) patients with cancer, 7 (39%) with sarcoma, 1 (12.5%) with GEP-NET, 5 (83%) with melanoma and 2 (67%) with lymphoma.

Treatment

Out of 54 surgeries, 16 (30%) were performed on emergency basis, of which 10 patients (18%) were bleeding to the gastrointestinal tract. This symptom occurred in two (4%) patients with SIC, three (5.5%) patients with GIST, one (2%) patient with angioma, one (2%) patient with Brunner's gland hamartoma and three (5.5%) patients with melanoma metastasis. In 3 (5.5%) cases, the urgent indication for surgery were the symptoms of obstruction, which were caused by SIC, GEP-NET and GIST, respectively. In one (2%) patient bleeding and obstruction occurred at the same time and was caused by poorly differentiated SIC. In the remaining 2 (4%) patients the indication for urgent surgical treatment was acute abdominal pain, and in one (2%) patient with GIST there was a perforation of the gastrointestinal tract. Scheduled operations were performed in 38 (70%) patients, after discussion of indications at multidisciplinary team meetings.

The dominant type of SIT surgeries was small intestine partial resection (SIPR). In the discussed group of patients, it was performed in 39 (72%) patients. In four cases the scope of the surgery was extended by left hemicolectomy due to

Table III. Diagnostics of small intestine tumors

Test name	Number of tests carried out			
	Malignant tumors n = 48 (%)	Benign tumors n = 6 (%)	Total n = 54 (%)	Critical test*
Computed tomography	45 (94%)	5 (83%)	50 (93%)	26 (48%)
Gastroscopy	38 (79%)	6 (100%)	44 (81%)	5 (9%)
Colonoscopy	31 (64%)	6 (100%)	37 (68%)	1 (2%)
Ultrasonography	22 (45%)	5 (83%)	27 (50%)	2 (4%)
EUS	8 (17%)	–	8 (15%)	3 (5%)
Capsule endoscopy	9 (19%)	4 (67%)	13 (24%)	8 (15%)
DBE	7 (15%)	4 (67%)	11 (20%)	5 (9%)
GP	12 (25%)	2 (33%)	14 (26%)	1 (2%)
Scintigraphy	6 (12.5%)	2 (33%)	8 (15%)	1 (2%)
Diagnostic laparotomy	1 (2%)	1 (17%)	2 (4%)	2 (4%)
Fecal occult blood	12 (25%)	2 (33%)	14 (5 positive)	–

* Critical test — the investigation that resulted in the diagnosis

EUS — endoscopic ultrasound; DBE — double-balloon enteroscopy; GB — gastrointestinal passage

cancer infiltrating the transverse mesentery in the area of the spleen fold, partial resection of the colon due to cancer infiltrating the transverse wall, scheduled extirpation of uterus myomatosus during primary surgery due to GIST of the ileum and adnexectomy due to GEP-NET with intraoperative suspicion of metastases to adnexa. In 4 (7%) patients pancreaticoduodenectomy using Whipple's procedure (PD) was performed. In 5 (9%) patients the surgery was limited to local excision and one (2%) to right-hand hemicolectomy (HCD). In 4 (7%) cases tumors were considered as primarily non-resectional, which was associated with the use of palliative management in the form of bypass anastomoses. In 2 cases (4%) these lesions were located in the mesentery of the small intestine, while in 2 other patients they included successively the duodenum and the jejunum as well as the duodenum alone. One patient with jejunum angioma was qualified for diagnostic laparotomy, which was combined with intraoperative endoscopic examination (Tab. IV)

Postoperative complications were observed in 7 (13%) patients, of which 3 (5.5%) had anastomotic leaks. Other cases of complications included damage to the ureter, infection of the biliary tract, postoperative bleeding, biliary leak from the neck of the gall bladder after cholecystectomy. The duration of hospitalization ranged from 7 to 35 days, the median was 12 ± 5.37 days. Of the 54 procedures carried out, 43 (80%) were considered radical and 10 (18%) — palliative. One surgery was of a diagnostic nature. 16 (30%) patients were qualified for complementary treatment. In 8 (15%) patients with SIC FOLFOX and Mayo schemes based on fluorouracyl were applied, imatinib in 2 (4%) patients with GIST, CHOP in 2 patients with lymphoma, and CVD in 1 patient with melanoma. Somatostatin analogues were used in 2 patients with GEP-NET, and in one etoposide and fluorouracyl.

Survival

So far, 17 (31%) deaths have been reported in this group of patients. 5-year survival was 93.8% for sarcomas, 53.9% for SIC, 66.7% for GEP-NET, (Fig. 1).

Depending on the location of the tumor, the worst prognosis is for the duodenum tumors, where 5-year survival was 52.4%. These values are more favorable for the ileum and jejunum, which amounted to 83.3% and 91.7% respectively.

Figure 1. Survival analysis for the most commonly diagnosed neoplasms

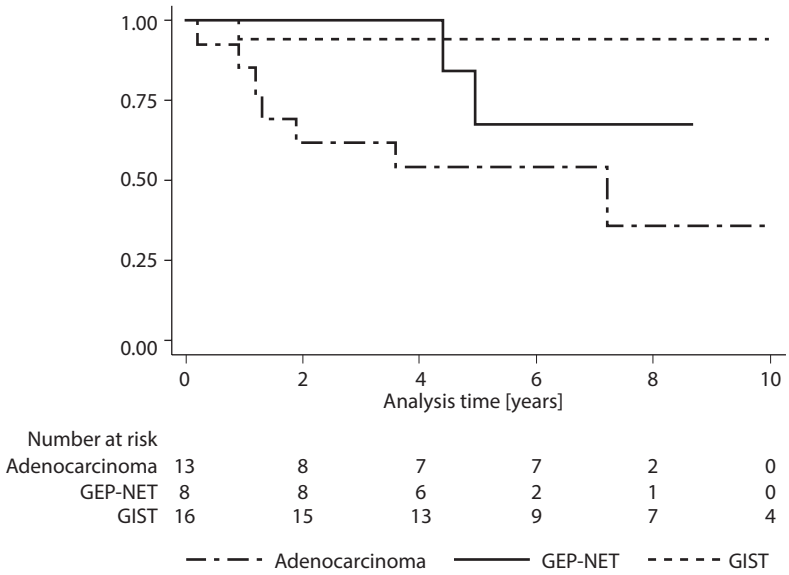

Table IV. Types of performed surgeries

Surgery type	Number of tests carried out			
	Malignant tumors n = 48	Benign tumors n = 6	Total n = 54	Complications
SIPR	36 (75%)	3 (50%)	39 (72%)	1 (2%)
PD	4 (8.5%)	–	4 (7.5%)	4 (100%)
HCD	1 (2%)	–	1 (2%)	
Local excision	3 (6%)	2 (33%)	5 (9%)	2 (40%)
Bypass anastomosis	4 (8.5%)	–	4 (7.5%)	
Diagnostic laparotomy	–	1 (17%)	1 (2%)	

SIPR — small intestine partial resection; PD — pancreaticoduodenectomy; HCD — right hemicolectomy

Discussion

In the evaluated group the highest percentage of patients were GIST patients, followed by patients with adenocarcinoma and GEP-NET. Similar data were presented after the analysis of a group of 57 Romanian patients [3], recording 42.1% patients with GIST, 33.3% with cancer, 14% with lymphoma and 3.5% with GEP-NET. Other authors report the most cases of SIC, less frequently GIST and GEP-NET [4–8]. Researchers from China analyzed a group of 141 patients with median age 53.5, SIC occurred in 43.3% of cases, GIST in 19.8%, NET in 12.1%. Another analysis of 666 patients from China describes an even higher prevalence of SIC, i.e. 87.5%. In this study only 8% of patients with GIST and 2.7% with GEP-NET were reported [9]. European publications based on a small number of patients confirm Asian data. In a Portuguese study from 2015, 28 patients were analyzed and the recorded data were: 39% — SIC, 21% — sarcomas, 21% — lymphomas and 11% —GEP-NET [4]. In our opinion, this difference may be explained by the fact that the MSCI has no A&E department. Some authors suggest that SIC is much more likely to cause sudden, acute symptoms qualifying patients for hospital treatment [5]. In this case, the vast majority of patients are admitted to regional hospitals, where they are operated on an ad hoc basis. According to the quoted authors, the main location of the SIT is the duodenum (range 25–94%). There are slight statistical differences between the jejunum and ileum (range 4.2–30.5% and 2.1–45%, respectively) [4–6, 9]. In our observations, SITs were most often located in the duodenum (36%), jejunum (33%) and ileum (32%), which corresponds to the data from the literature. The assessment of the tumor location depending on the histopathological type also coincides with the global data. In the study describing the American database of 67 843 patients diagnosed and treated in 1985–2005, the main localization of cancer was duodenum (56%), while it was jejunum for sarcomas (25%), and ileum for GEP-NET and lymphomas (45% and 21%, respectively) [10]. In our material there were no significant differences in the location of cancers.

The most frequent symptoms of SITs observed in literature were pain (14–67%), gastrointestinal obstruction (3.9–50%), gastrointestinal bleeding (3.9–39%) [4–6, 9, 11, 12]. Jaundice, fever, perforation, flatulence and diarrhea were described less frequently. The most frequent symptom in this study was bleeding (50%). The remaining results corresponded with the cited works. In 7% patients the disease remained asymptomatic. These ailments are non-specific and occur late, which postpones the onset of diagnosis and treatment [4–6, 9, 11, 12]. Some authors draw attention to the fact that the first ailment causing the beginning of diagnostics were obstruction and bleeding requiring urgent surgical intervention on emergency basis. The frequency of such a course may reach 40% [11].

SIT imaging in endoscopic examination is difficult and possible mainly in large centers with extensive diagnostic facilities. Within the range of classical gastroscopy and colonoscopy there are only tumors of the duodenum and a fragment of the ileum directly before the caecum. The other SITs can rarely be located in this way. Only the use of CE and DBE allowed to show the lesions beyond the range of classic imaging equipment [13–17]. DBE, introduced in 2001, was particularly helpful; it was the first to show the entire digestive tract in real time and to collect material for histopathological examination. Korean and Japanese studies emphasize the advantages of CE and DBE especially in comparison to CT [13–17]. Especially CE, additionally in combination with MRI or CT, is presented as the best diagnostic method due to the accuracy, high sensitivity and good tolerance by the patient [13–16]. In addition, the DBE allows the use of a tattoo to mark the location of the tumor, which may be of great importance during resection surgery, as well as the possibility to stop bleeding temporarily or final treatment of small SITs [13–17]. In the conclusions of the meta-analysis of 5 studies (1154 patients in total), both CE in combination with MRI or CT as well as DBE, the comparable sensitivity of the study and the percentage of undetected lesions were determined [13–17]. CT is still a good method of depicting SITs of a diameter larger than 10 mm, however, it does not allow for their precise location. Many authors place CT as the main diagnostic test due to its easy availability and relatively high sensitivity. It seems that the best choice for the most accurate diagnosis and imaging of SIT is to use a combination of CT and endoscopic methods [13–17]. In Poland, the limited availability of CE and DBE means that CT remains the key test.

A vast majority of authors point out that radical surgical treatment remains the only right course of action in the case of SIT. The most frequent operation is SIPR (53–68%) [4–8]. In this study 20–76% of patients were qualified for complementary treatment. The group most often qualified for chemotherapy were patients with SIC [9, 11, 18]. Recent data from the National Cancer Register indicate that the 1-year survival rate is 65.3% in men and 62.7% in women, and 5-yearly survival rates are 45.1% in men and 49.3% in women respectively [2]. Mortality due to SIT in Poland in 2010 was 0.4 and is identical to the data from the U.S. National Cancer Institute [1].

Summary

The most common clinical symptom of SIT is gastrointestinal bleeding requiring transfusion of many blood units. CT is the most common examination deciding about the diagnosis.

Surgical treatment remains the only effective way to cure patients. The most common procedure is SIPR. After 5 years of surgery, 37 (68.5%) patients remain in follow-up.

SITs remain a difficult oncological problem. Late, non-specific symptoms, slow tumor growth, occurrence in old age, the need to use difficult diagnostic techniques, results in a long time of diagnosis and appropriate treatment. The care of SIT patients should take place in centers of higher reference, with advanced diagnostic capabilities and experienced specialist staff.

Abbreviations

SIT — small intestine tumors
SIC — small intestine cancer
GIST — gastrointestinal stromal tumors
GEP-NET — gastroenteropancreatic neuroendocrine tumors
CT — computed tomography
DBE — double-balloon enteroscopy
CE — capsule enteroscopy
EUS — endoscopic ultrasound
USG — ultrasound
PET CT — positron emission tomography
PRBC — packed red blood cells
SIPR — small intestine partial resection
PD — pancreaticoduodenectomy
HCD — right hemicolectomy
MSCI — Maria Skłodowska-Curie Institute — Oncology Center in Warsaw
FOLFOX — oxaliplatin, leukovorin, fluorouracil
MAYO — fluorouracil, leukovorin
CHOP — cyclophosphamide, doxorubicin, vincristine, prednisolone
CVD — cisplatin, vinblastine, dacarbazine
MRI — magnetic resonance

Conflict of interest: none declared

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