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CASE REPORT

Gastrointestinal stromal tumors

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Abstract: In the last 3 years 9 patients with gastrointestinal stromal tumors (GIST) underwent surgery at our department. All cases were with very atypical process. From these patients 3 interesting cases are described in more details. A 75-years-old woman with gastroscopically verified endoluminal tumour in the proximal third of stomach, 6x7 cm , 76-years-old man with a large endoluminal tumour in D2–D3 part of the duodenum, 4x4 cm, and 62-years-old man with verified extraluminal tumour by CT examination in the middle part of stomach. In all cases, gastrointestinal stromal tumour was histologically confirmed. Work is well photo-documented pre-surgically with endoscopic and CT-findings and during surgery: individual steps during the removal of these tumours.
In assessment of the size and number of mitoses, tumours belonged to a group with highly malignant potential. Patients are regularly checked in 3-months intervals and also examination by positron emission tomography was performed – it seems to have the best demonstrability of possible relapse. All three patients live and are subjectively and objectively without significant problems *(Tab. 5, Fig. 5, Ref. 7)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: gastrointestinal stromal tumors, leiomyoma.

GIST is an acronym for Gastrointestinal Stromal Tumors – relatively heterogenous group of mesenchymal tumors, with specific histological characteristics (7). The term is used since 1999 and it replaced the term – leiomyoma and leiomyosarcoma (used in the past), because the smooth muscle was considered to be their base for a long time period. Immunohistochemical and ultrastructural studies are showing much more complex view This tumors are appearing primary in the gastrointestinal tract and abdominal cavity. Their sharp incidence is unknown, but for example in the USA their incidence increased from 300–500 cases yearly to 5000–6000 cases yearly (1). Based upon literature – their incidence is the same in all geographical and ethnic groups, incidence in males and females is identical and it appeares mostly in the 5th–7th. decade of life. GIST represents 1 % of all primary tumors of gastrointestinal tract, it means they are detected rarely.

We are able to divide the evolution into 3 stages from the historical point of view:

1) From the 40's to 60's years of 20th century – period connected with dividing these tumors in groups named leiomyomas, leiomyosarcomas, leiomyoblastomas and bizarre leiomyomas.

2) During the 60's and early 70's of the 20th century electrone microscope is used in the scientific research of human tumors. But now the situation has changed. They found out that only a part of this tumors is showing the ultrastructure of smooth muscle fibre.

3) The 1980's are connected with application of immunohistochemical methods:

1983 – Mazur and Clark – term of "stromal tumor" (4),

1984 – Herrera (5) described the ultrastructure of autonomous nervous differentiation in a part of these tumors and named the group as GANTs: Gastrointestinal autonomous nervous tumors, today this group belongs under the GIST,

1998 – Hirota (6), et al. finally discovered the common marker, which is finally connecting them – KIT expression.

Division of GISTs, shown in the Table 1 is the most used in the meaning of ultrastructure of its different kinds (Fig. 1, Tab. 1).

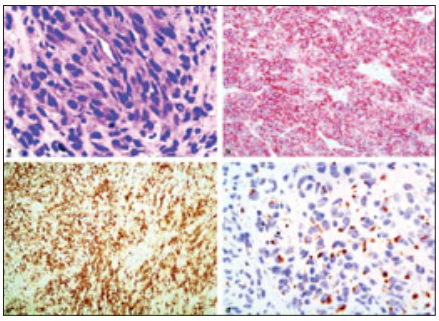

Fig. 1. Histopathological pictures/views in different colouring (2). A) Right upper – hematoxylin-eosin colouring – shows spindle cells with pleomorfism, B) right lower – immunohistochemical profile with diffuse expression of polychromal CD 117, C) left upper –expression CD 34, D) left lower – cytokeratine Cam 52 existing intracellulary not very rarely.

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Tab. 1. Classification of GISTs.

1. Tumors differentiated to the smooth muscle
2. Tumors differentiated in the direction to the nervous cells
3. Tumors showing the dual differentiation
4. Tumors with no differentiation

Tab. 2. Areas of the most common incidence of GISTs.

Oesophagus	5 %
Stomach	50 – 60 %
Small Intestine	20 – 30 %
Large Intestine	10 %
Rectum	5 %
Extra GIT localities – Mesenterium, Omentum, Retroperitoneum	5 %

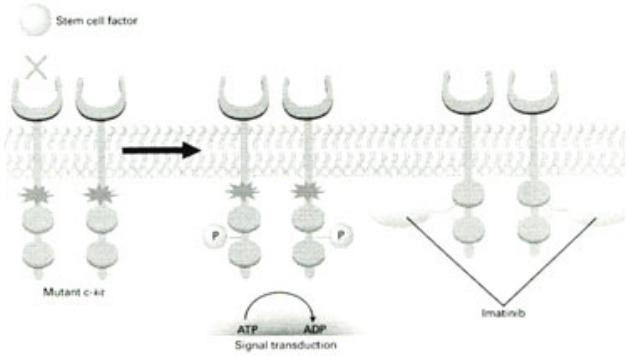

Fig. 2. The impact of immunostatine Glivec.

GIST tumor could appear in the whole gastrointestinal tract – as was already mentioned, but they appear predominantly in stomach: extraluminaly (see patient 1), and endoluminaly – (see patient 2). The gallbladder and urinebladder area are described in the literature as rare localities (Tab. 2).

Diagnostics of GIST is based on the histological examination – mesenchymal tumor mostly from spindle cells which looks like the smooth muscle. Immunohistochemicaly it is necessarry to specify expression of CD 34 and KIT (it means CD 117). From Table 3 it is clear that the positivity of CD 117 helps in the diagnostics of GIST.

Tab. 3. Immunohistochemical figure for diagnostics of GIST (2.)

Immunohistochemical scheme for the differencial diagnosis Of spindle cells tumors of gastrointestinal tract

	CD 34	SMA	DES	S-100	KIT(CD117)
GIST	+	+	rarely	5 %	+
Tumors from the smooth muscle	+	+	+	rarely	–
Schwannoma	+	–	–	+	–
Fibromatosis	rarely	+	rarely	–	discutable

Tab. 4. Case 1 – personal summary of patient (1943).

Sex, Age	Male, 61 years
Localization	Stomach, Extraluminaly
Clinical signs	Collapse
Diagnose	Ultrasound, CT
Therapy	Surgical
Histology	GIST, 1.type (from the smooth muscle)
Size of tumor	More than 10 cm
Number of mitoses	4/50 HPF
Present status	Follow up, possible relaps even after 20 years

Methods and patients

Surgical treatment was the only therapy until the year 2000, but reasoned by a high possibility of relaps (from seven months to two years), when surgical treatment failed, some solution were found – namely the immunostatine Glivec. Thyrosine-kinase has a KIT receptor and the activation of these receptors were the central compositum of pathogenesis of GIST tumors. The result of its activation is the production of mutated C-KIT genes. Glivec – by its chemical consistance *imatinib mesylate* (company Novartis), is an immunostatine that blocks the production of mutagene oncogenes (Fig. 2). It is used mostly in cases of relapses of these diseases, which are not rare. There are studies investigating a possibility of chemotherapy too, especialy the combinations of Iphosamide with Antracycline, but their effectivity is still low, around 10 %. There are radiotherapy trials as well, but the efficacy is too low, because of relative radioresistency of the tumor and its communication with surrounding tissues.

Patients

In the period of last 3 years (2005 – February 2007) we have treated 9 patients surgically, who were admitted with very atypical process. No one of these patients died till today, and no one had serious postoperative complications. We are describing three case reports with different localisation in the upper GIT in more detail.

Case 1

Haemoperitoneum reasoned by GIST localised in the stomach – growing extraluminally.

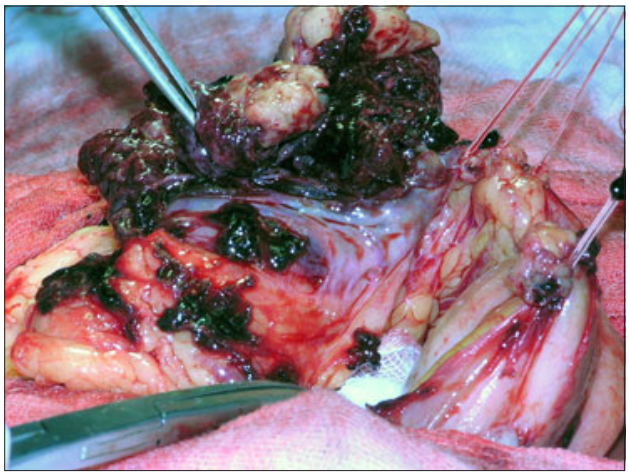

Fig. 3. Case 1 – peroperative finding – patient (1943). Extraluminaly growing GIST, filled with blood coagulas. It grows from the major curvature in the lower half of stomach.

Patient 61-years-old

Three days before admitting to our Department of Surgery the patient woke up at night with a feeling of falling down, with abdominal pain in the epigastric region and then he collapsed. He had no colics. After waking up he had some repeated diarrhoic stools – first brown, then hydrous. His wife called an ambulance, they measured low blood pressure and he was transported to the Emergency department of a hospital. Laboratory tests showed out only leukocytosis of unknown origin and the patient was released back home. Next day he was examined by a general practitioner in our hospital – abdomen with no pain, no melena, feeling well. In the personal history – 1992 and 1998 TIA, arterial hypertension for couple of years, hypercholesterolaemia. Reasoned by decrease of hemoglobin level from 150 to 107 g/l an abdominal ultrasound examination was done – summary: A pancreatic tumor was supposed. Then a CT examination was indicated – summary: Haematoma close to the wall of stomach. Patient was sent to our Department of Surgery with supposition of haemoperitoneum reasoned by the decreasing levesl of hemoglobin – to provide a surgical examination. We provided the surgery. We found a tumor growing from the ventral wall of the lower half of stomach, with a fragile wall, filled with blood coagulum and in the abdominal cavity from 500 to 1000 ml of blood with coagulas. The tumor was resected, with its shank growign from the stomach wall and with safety circle of 3 cm of the stomach wall. Peroperative biopsy with no distinct summary of the tumors character, definitive histological summary: GIST, type 1 (Tab. 4).

After considering the size of the tumor and the number of mitoses – the tumor belongs to a group with highly malignant potential. A CT examination with blood tests were done 3 and 6 months from the surgery – they are filling us with a kind of optimism. Patient has no anemia. Computer tomography findings are negative in the meaning of possible relaps or metastases, his subjective feelings are great. We are planning a regular patient check periodically every 6 months, with CT examination and with positrone emisssion tomography, which is more valuable in such cases (from literature) (Fig. 3).

Case 2

Intraabdominal bleeding due to GIST localised in stomach – growing endoluminaly.

Patient 76-years-old

The patient was followed up for more than 15 years by a haematologist for an anaemia of unknown origin. Admitted through emergency due to suspected bleeding from the upper gastrointestinal tract. The patient was silly with anaemia: hemoglobin was less than 70 g/l and melena. An oesophagogastroduodenoscopical examination was done by a gastroenterologist after admission with finding of no blood endoluminaly in stomach and duodenum. A follow-up oesophagogastroduodenoscopical examination was done by a surgeon – while using the inversion method of examination by the fibroscope a spherical formation with size of a ping-pong ball in the area of fornix of the stomach was found – based upon a macroscopical shape we supposed it should be a ventricular leiomyoma. We did not indicated laparoscopical surgical procedure because of the patients polymorbidity and through a laparotomy we have manualy localized the resistency. We have done a gastrotomy in the size of a 4 cm, after removing the gastric wall and we removed the resistency extragastricaly and then we have resected the resistency of spherical shape under visual control with a safety circle of 2 cm. Definitive histological finding: GIST type 1 (from the smooth muscle). The patient is followed up regularly by gastroscopy and clinical examination (Fig. 4).

Case 3

Intraabdominal bleeding from a GIST localised in duodenum – growing endoluminaly

Patient 76-years-old

Two days before admitting he discovered melena, felt silly, had no pain, and did not visit emergency unit immediately. The day before admitting he had a feeling of falling down, he had a melena several times daily. Gastroenterologist performed a diagnostical gastroscopical examination the day of admitting and no source of bleeding was detecetd. Two days later a follow up was done, gastroscopy by a surgeon. Spherical shape formation at the lateral site of duodenum approximately 2 cm under the level of papila Vateri was detecetd. The formation was prominating in to the lumen, while excision of a sample was markedly bleeding. On its surface was a small coagulation, which, as we suppose, was the source of bleeding. The patient was informed about the localization and the size of the tumor, so we suggested surgical solution. As the toughest possibility was mentioned a duodenopancreatectomy too. Different phases of surgery (Fig. 5).

Results

A two basical factors are mentioned in the literature concerning the problem of GIST and it is the size of the tumor and

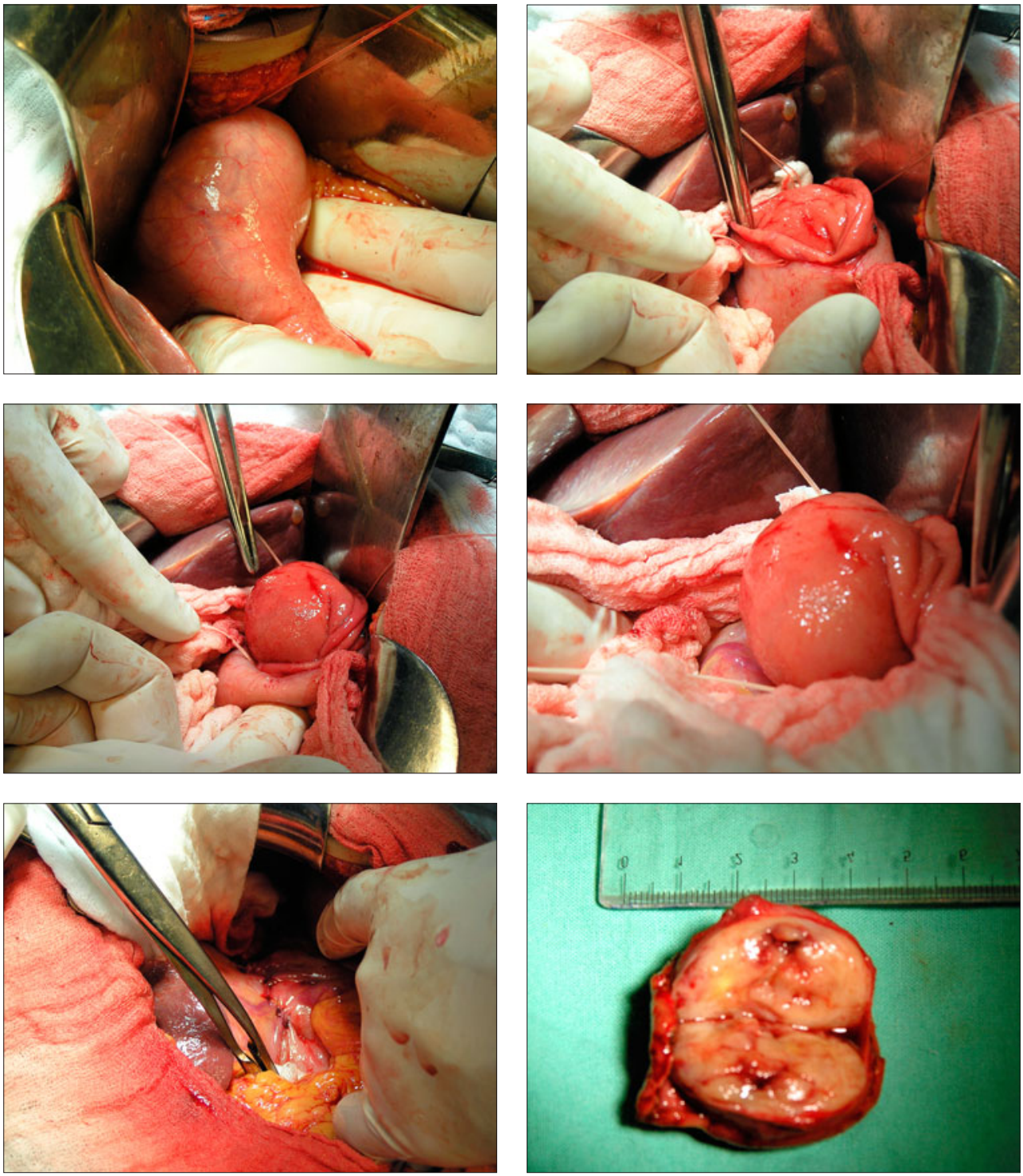

Fig. 4. Case 2 – peroperative consecutive overview. It consists of 6 pictures in three double-lines. Upper line – palpation of the tumor in the upper third of stomach from the side from curvature major and gastrotomy approximately 20 mm before the borderline of the tumor. Middle line – expression of the tumor extraluminaly. Lower line – ventricular suture after exstirpation of the tumor and the tumor size of 5 cm, definitive histological examination – GIST type 1 (olderly named – leiomyoma).

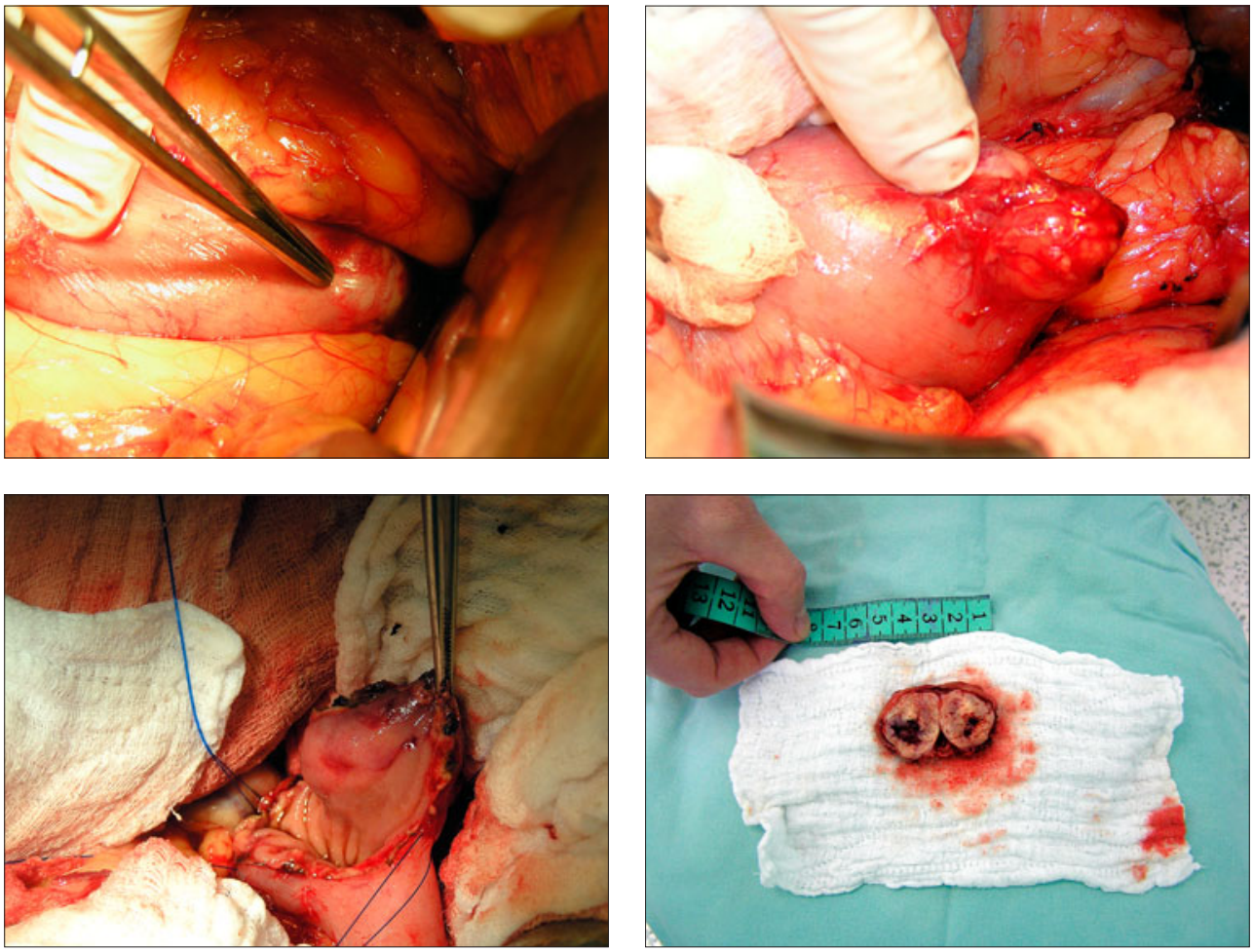

Fig. 5. Case 3 – peroperative findings. GIST type 1 – from the smooth muscle, localised in duodenal area. A) A formation signed by the tweezers, is stiff, white coloured and its majority is hidden, because it is localised endoluminaly in the duodenum. B) Palpation of the formation, we are considering a possibility of a local resection or duodenopancreatectomy. C) A wide duodenotomy, the formation growing through the duodenal wall is shown by the tweezers, we are deciding to provide a local exstirpation with a safety circle of 15 mm. D) A layer of the leiomyoma before sending it for a definitive histological examination.

the number of mitoses in 50 fields (Tab. 4). Mařatka in his book: Gastroenterology (3) is considering the stromal tumors as one third of them are benign and two thirds are malignant. In my opinion every GIST is potentially malignant with an insecure degree of malignancy (Tab. 5).

Tab. 5. The evaluation of risk of aggressive behaviour of GIST.

Risk	Tumor size (cm)	Number of mitoses
Very low	<2 cm	<5/50 HPF
Low	2–5 cm	<5/50 HPF
Middle risk	<5 cm	6–10/50 HPF
	5–10 cm	<5/50 HPF
High risk	>5 cm	>5/50 HPF
	>10 cm	high mitotic activity
	various size	>10/50 HPF

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