Duodenal Gastrointestinal Stromal Tumor Presenting with Acute Upper Gastrointestinal Bleeding Treated with Segmental Resection

Gastrointestinální stromální tumor duodena projevující se akutním krvácením do horního zažívacího traktu a léčený klínovitou resekcí

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Summary
Gastrointestinal stromal tumours (GISTs) are considered to derive from the interstitial cells of Cajal or their precursors and are defined by their expression of c-kit protein (CD117) that is positive in 95% percent of cases. These are rare mesenchymatous tumours, while they represent the most common mesenchymal tumours of the alimentary tract. The majority of GISTs develop in the stomach and small intestine and more rarely in the rectum, colon, esophagus and mesentery; only 3–5% of all GISTs are located in the duodenum. The presenting symptoms include early satiation, dysphagia, bloating, abdominal pain and gastrointestinal bleeding, either acute or chronic. Surgery remains the mainstay of treatment for localized, non-metastatic, resectable GISTs. We present a case of duodenal gastrointestinal stromal tumour of the third portion of the duodenum that presented with acute upper gastrointestinal bleeding treated with segmental duodenal resection.

Key words
angiography – bleeding – duodenum – GIST

Souhrn
Předpokládá se, že gastrointestinální stromální tumory (GIST) vznikají z Cajalových intersticiálních buněk nebo jejich prekurzorů a jsou definovány expresí c-kit proteinu (CD117), která je pozitivní v 95% případů. Jedná se o vzácné mezenchymální nádory, které však jsou nejčastějšími mezenchymálními nádory zažívacího traktu. Většinou se vyvíjejí v žaludku a tenkém střevě, vzácněji pak v rektu, tlustém střevě, jícnu a mezenteriu, přičemž pouze 3-5 % všech GIST postihuje duodenum. Mezi příznaky patří časné nasycení, dysfagie, nadýmání, bolest břicha a krvácení do zažívacího traktu, buď akutní, nebo chronické. Hlavním terapeutickým postupem u lokalizovaného, nemetastazujícího a resekovatelného GIST zůstává chirurgické řešení. Popisujeme případ pacienta s gastrointestinálním stromálním tumorem třetího oddílu duodena, který se projevoval akutním krvácením do horního zažívacího traktu a byl léčen klínovitou resekcí duodena.

Klíčová slova
angiografie – krvácení – duodenum – GIST

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Introduction

Gastrointestinal stromal tumors (GISTs) are rare mesenchymatous tumors [1] but represent however the most common mesenchymal tumors of the alimentary tract [2] and account for 0.1–3% of all gastrointestinal malignancies [3]. Their incidence is 10–20/1,000,000/year and their prevalence is estimated at 129 per million [4]. There seems to be no predilection of either gender [4,5]. GISTs usually present in patients in their sixth and seventh decades [3] with 75% of cases occurring in patients over the age of 50 [5]. They are considered to derive from the interstitial cells of Cajal or their precursors [4] and are defined by their expression of c-kit protein (CD117), which is positive in 95% percent of the cases [1]. Most cases develop in the stomach and small intestine and more rarely the rectum, colon, esophagus and mesentery while only 3–5% of all GISTs are localized in the duodenum [1,3,4,6]. GISTs are symptomatic in approximately two thirds of the patients, about one fifth is found incidentally and about one tenth is discovered at autopsy [3,4]. The presenting symptoms include early satiation, dysphagia, bloating, obstruction, abdominal pain and gastrointestinal bleeding, either acute or chronic [3–5]. We present a case of duodenal GIST of the third portion of the duodenum that presented with acute upper gastrointestinal bleeding treated by segmental duodenal resection.

Case Report

A 66 years old male presented to our hospital with acute upper gastrointestinal bleeding. The patient reported melenas for two days and a hematemesis recently. His medical history included arterial hypertension and diabetes mellitus and he received valsartan 160 mg once a day and metformin 425 mg twice a day. Also the patient had iron deficiency anemia for about a year for which he received ferrous sulfate sesquihydrate 80 mg daily.

Physical examination revealed a pale man with arterial pressure 108/52 mmHg and heart rate of 112 beats/min. Rectal examination confirmed the melena. Laboratory examination revealed anemia with a 19.1% Ht and 6.4 g/dl hemoglobin, left-shifting leukocytosis with a WBC count of 12,300 × 10^6/ml (75.7% neutrophils) and thrombocytopenia with a PLT count of 87,000/mm^3. All other blood chemistry was within the normal range. The patient was transfused with 4 units of blood. Emergency gastroduodenal endoscopy revealed a bleeding ulcer in the third part of the duodenum.

The abdominal computed tomography (CT) scan demonstrated a well demarcated tumor measuring 6 × 5.5 cm at the third part of the duodenum compressing and abutting forward the duodenum without though any intra-abdominal metastatic lesion (Fig. 1).

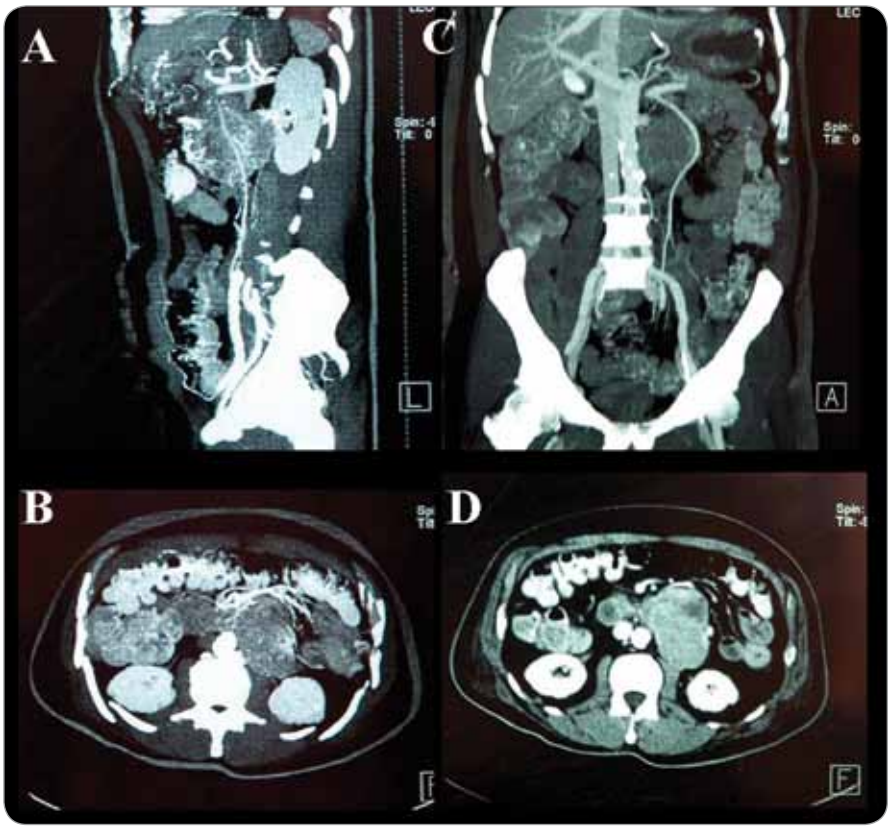

Fig. 1. The abdominal CT scan demonstrated a well demarcated tumor measuring 6 x 5.5 cm at the third part of the duodenum compressing and abutting forward the duodenum.

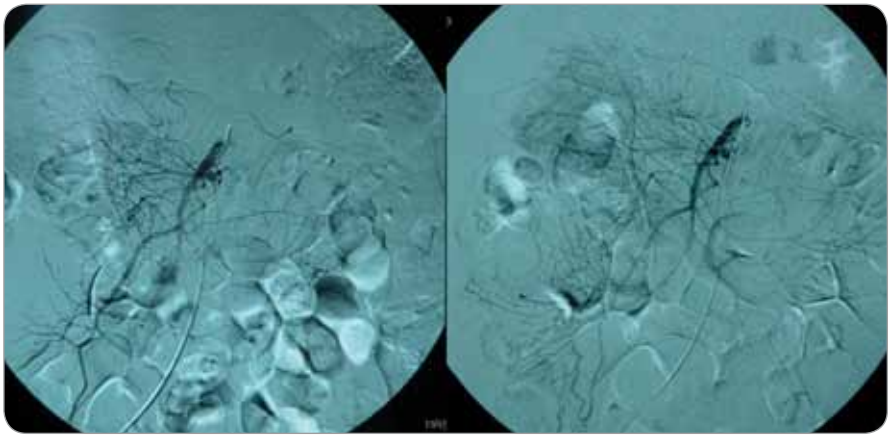

Fig. 2. The angiography revealed an abnormal leash of vessels arising from the superior mesenteric artery.

Because of persistent minor bleeding that could not be controlled by endoscopic interventional treatment an emergency angiography was performed. The angiography revealed an abnormal leash of vessels arising from the superior mesenteric artery but didn't reveal any actively hemorrhaging vessels (Fig. 2).

At laparotomy, an encapsulated mass originating from the duodenal wall at the third portion of the duodenum was recognized. No evidence of local invasion of the pancreas or distal metastasis was found and segmental resection of the third and fourth part of the duodenum was performed. The surgical margins were free of disease on frozen-section examination. Reconstruction of the gastrointestinal tract was achieved by a side to side duodenojejunostomy.

Macroscopic examination of the surgical specimen revealed a lobulated, tan, predominantly solid mass of the duodenum measuring 7 × 5 × 5 cm with clear boundary that infiltrated focally the duodenal mucosa forming an ulcer 1.2 cm in diameter (Fig. 3). The distance to the proximal resection margin was 1 cm and to the distal resection margin was 2 cm. Histopathological examination revealed a GIST consisting of spindle cells with rare mitotic figures (< 5/50 high power field – HPF). The tumor cells form bundles within a vascular stroma. Also there were areas of coagulation necrosis. Immunohistochemistry showed intense positivity for CD 117(c-KIT) and S-100, focal positivity for smooth muscle actin (SMA) but was negative for desmin and CD 34 (Fig. 4).

The postoperative course was uneventful and the patient remains alive without any evidence of recurrence or metastasis 8 months after the operation.

Discussion

Duodenal GISTs account for approximately 30% of all primary duodenal tumors [7] and present in the vast majority of patients with gastrointestinal bleeding, usually associated with melena and occasionally with massive acute bleeding as in the current case [6,7]. In the present case the patient's anemia was caused by the duodenal GIST, which however hasn't been diagnosed till the presentation of acute bleeding. Transarterial embolization is a possible alternative to control acute bleeding from duodenal GIST [6]. Duodenal GISTs most frequently involve the second portion, followed by the third, fourth and first portion [8]. GISTs are usually centered on the bowel wall and typically show a tendency to grow expansively opposite the intestinal lumen towards the abdominal cavity, having a tendency to displace, but not to invade adjacent organs [7,8] but they may also extend inward towards the mucosa [5,7,8]. Most duodenal GISTs form a gross ulceration in the mucosa or form an intramural mass with a centrally ulcerated umbilication [8]. In patients with gastrointestinal bleeding caused by GISTs endoscopy and mucosal biopsy are of a low diagnostic yield and should be used as initial screening. Endoscopic ultrasound and fine needle aspiration should be considered the gold standard as it directly visualizes the neoplasm and provides adequate cytological material for a molecular diagnosis [3]. Abdominal CT scan and MRI may also aid the diagnosis [3].

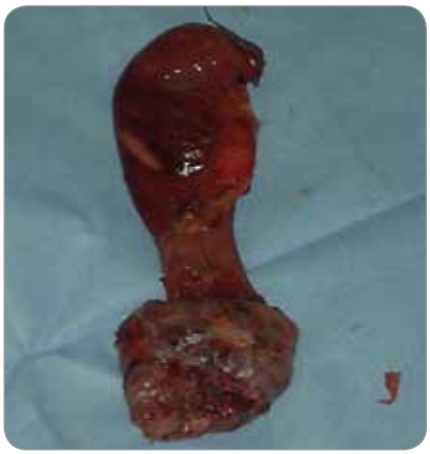

Fig. 3. The surgical specimen including the 3rd and 4th portion of the duodenum and the GIST.

Imaging studies may occasionally demonstrate incidental cases of GIST but are more commonly used for tumor localization, characterization, staging and surveillance after surgery [9]. Barium studies show the classic features of submucosal masses of the gastrointestinal tract but cannot detect extraluminal tumors [8,9]. Ultrasonography may show, in small GISTs, a homogenous hypoechoic mass in close relation with the gastrointestinal tract and, in large GISTs, a vascular mass of mixed echogenicity [9,10]. In CT scan GIST are typically well

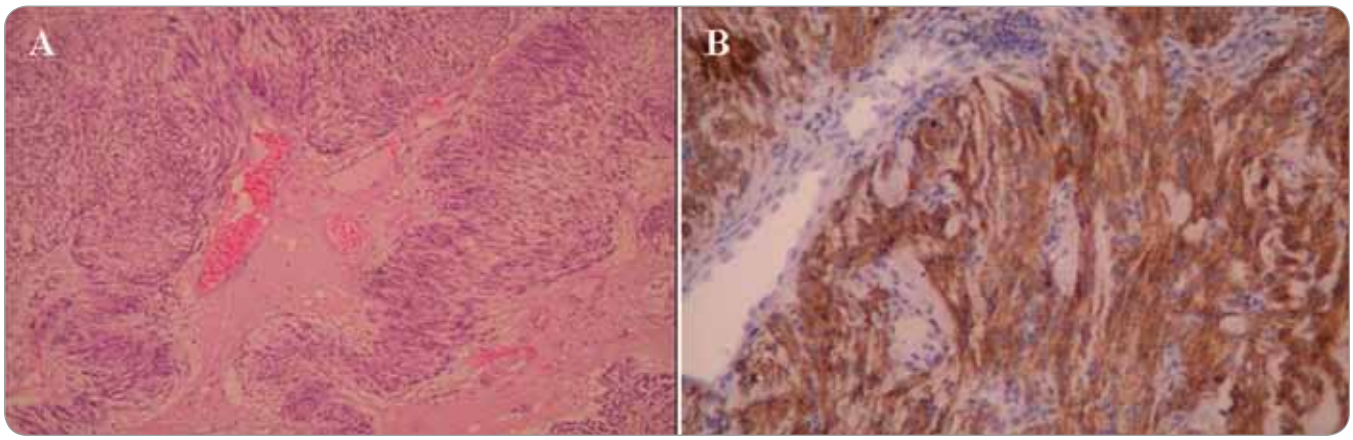

Fig. 4. A. Histologically, the duodenal tumor composed of relatively uniform spindle cells of arranged in short fascicles or whorls. B. CD117(KIT) staining in GIST show diffuse, strong, cytoplasmic positivity in the majority of tumor cells.

defined heterogeneous masses with a peripheral enhancing border of variable thickness and central low attenuation [10]. Small tumors are usually depicted as sharply marginated, smooth, homogenous masses with moderate contrast enhancement while large tumors show heterogeneous contrast enhancement and tend to have mucosal ulceration, cavitation and central necrosis [8,9]. In MRI studies the solid components of GISTs are usually low signal on T1-weighted images and high signal in T2-weighted images and enhance following gadolinium administration [9,10]. Angiography reveals a hypervascular mass with dense homogeneous capillary staining, prominent feeding arteries and enlarged draining veins [9]. Positron emission tomography (PET) is a valuable complementary tool for treatment monitoring [4,9] and provides functional information about the GIST.

Macroscopically, GISTs are often covered by a pseudocaspule and are usually fleshy and solid, grey-white in appearance but may also present hemorrhage, central cystic degeneration or necrosis [5,6,11]. Microscopically, GISTs are consisted by spindle cells (80%), epithelioid cells (20–30%), or mixed spindle and epithelioid cells (10%) [4]. Epithelioid GISTs most commonly originate in the stomach [4,5] Spindle cell GISTs are commonly arranged in fascicles, while epithelioid lesions may be arranged in nests or sheets [5]. Immunohistochemistry reveals positivity for KIT (CD117) in 95% of cases, for vimentin in nearly all GISTs, for CD34 in 60–70% and for myogenic marker smooth muscle actin (SMA) in 30–40% [4–6]. GISTs are usually negative for neurogenic marker S-100 (95%) and desmin or keratin (98–99%). Most GISTs posses activating KIT or platelet derived growth factor receptor alpha (PDGFRA) mutations [5]. GISTs can be classified in four types based on phenotypical features:

1. tumors that show differentiation toward smooth muscle cells,
2. tumors that show differentiation toward neural elements,
3. tumors that show no differentiation and
4. tumors that show dual differentiation [8].

We consider the tumor in the present case to be of dual differentiation as it expressed both myogenic and neurogenic markers (SMA and S-100 respectively).

All GISTs have a certain potential for malignancy [1] and the most important prognostic factors are their size and their mitotic count. The tumor in our case belonged to the intermediate risk group as the mitotic index was less than 5/50 HPF and the tumor size was more than 5 cm but less than 10 cm. Also, recently other clinicopathological factors have been shown to affect overall survival and disease free survival including, tumor location, male sex, R1 resection, tumor rapture and tumor grade [4,12].

Differential diagnosis of GISTs include mesenchymal neoplasms such as gastrointestinal leiomyoma, leiomyosarcoma, schwannoma, submucosal gastrointestinal lesions such as ectopic pancreas, carcinoid with a spindle cell morphology and epithelial gastrointestinal neoplasms such as adenocarcinoma. Other tumors that need to be considered in the differential diagnosis are lymphoma, local extension by a primary retroperitoneal dedifferentiated liposarcoma, intra-abdominal fibromatosis (desmoid tumors), peritoneal carcinomatosis, benign and malignant vascular tumor, inflammatory fibroid polyp and metastatic disease such as spindle cell melanoma or carcinoma [9,13].

Surgery remains the mainstay of treatment for localized, non metastatic, resectable GISTs [4,6,7]. Complete enbloc surgical resection of the tumor with negative surgical margins and avoidance of tumor rupture, which can lead to peritoneal spread should be the goal of surgery [1,4,6,7]. As GISTs metastasize extremely rare in the locoregional lymph nodes and lymph node recurrence is limited, lymphadenectomy is unnecessary. For duodenal GISTs, the commonest procedures are wedge resection, segmental resection, pancreaticoduodenectomy and pancreas sparing duodenectomy but the optimal surgical treatment of duodenal GISTs still remains unclear [2,7]. Reconstruction after segmental GISTs is very challenging and is not free of complications. Several techniques for reconstruction of the gastrointestinal tract after segmental duodenectomy have been described including end to side duodenojejunostomy with papiloplasty [14], rectocolic Roux-en-Y duodenojejunostomy [15], side to side duodenojejunostomy [16], side to end duodenojejunostomy [6] and an end to end duodenojejunostomy [17]. Wedge resection of the duodenum is generally indicated for small lesions less than 1 cm except of those lesions located within 2 cm from the ampulla of Vater. Segmental resection is indicated for large tumors, over 3 cm, on the third and fourth portion of the duodenum, while Whipple's resection is indicated for periampularry GISTs and for large tumors of the first and second portion of the duodenum [7]. In the present case we performed a segmental resection of the third and fourth portion of the duodenum. As all GISTs are virtually associated with a risk of metastasis, follow-up is essential and CT imaging is recommended every three to six months for a minimum of five years [18].

Imatinib is an ATP analogue that binds the intracellular portion of KIT and inhibits signaling [5] and is considered the first line of treatment for recurrent and metastatic GISTs [18]. Neoadjuvant and adjuvant imatinib is presently evaluated under study conditions [5,6] and is not advised for resectable non metastatic GISTs but neoadjuvant imatinib can be used when surgery would result in significant morbidity or loss of organ function [18]. Interim results of clinical trials show that adjuvant imatinib improves overall survival and delays recurrence [4].

In conclusion GISTs are considered to derive from the interstitial cells of Cajal or their precursors and are defined by their expression of c-kit protein (CD117), which is positive in 95% percent of the cases. The majority of cases (75%) occur in patients over the age of 50. They are rare mesenchymatous tumors but represent however the most common mesenchymal tumors of the alimentary tract. Most cases develop in the stomach and small intestine and more rarely the rectum, colon, esophagus and mesentery while only 3–5% of all GISTs localized in the duodenum. The presenting symptoms include early satiation, dys-

phagia, bloating obstruction, abdominal pain and gastrointestinal bleeding, either acute or chronic. Surgery remains the mainstay of treatment for localized, non metastatic, resectable GISTs. Complete enbloc surgical resection of the tumor with negative surgical margins and avoidance of tumor rupture, which can lead to peritoneal spread should be the goal of surgery.

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