Gastric Stromal Tumor: A Rare Cause of Upper Gastrointestinal Bleeding

Paula Szanto1, Anca Barbus1, Nadim Al Hajjar2, Teodor Zaharia3, Dorina Manciula4

1) 3rd Medical Clinic. 2) 3rd Surgical Clinic, University of Medicine and Pharmacy. 3) Department of Pathology, Emergency Clinical Hospital „O. Fodor”, Cluj-Napoca. 4) County Hospital Baia-Mare, Romania

Abstract
Gastrointestinal stromal tumors (GISTs) are a subset of gastrointestinal mesenchymal tumors, though relatively rare in absolute terms. They are characterized by a remarkable cellular variability and their malignant potential is sometimes difficult to predict.

We report a case of gastric stromal tumor in a 66 year old patient with a long history of anemia and intermittent upper gastrointestinal bleeding. We performed upper gastrointestinal endoscopy, biopsy of gastric mucosa and abdominal ultrasonography to establish the diagnosis. The gastric tumor was successfully resected with a postoperative favourable outcome.

Key words
Anemia - upper gastrointestinal bleeding - gastric stromal tumor

Introduction
Gastrointestinal stromal tumors (GISTs) comprise a rare group of neoplasms with unpredictable malignant potential and an annual incidence of 4 / 1 000 000 persons (1). The stomach is the most common site of involvement but GIST may occur anywhere in the gastrointestinal tract, omentum, or mesentery (2). Gastric stromal tumor is a submucosal tumor which is different from leiomyoma, leiomyosarcoma and neurogenic tumors. Immunohisto-chemical study of CD117, the c-kit proto-oncogene product, is a specific marker for GISTs. Diagnosis of this condition is sometimes difficult and treatment is often delayed because patients usually present with nonspecific abdominal symptoms. Abdominal pain, bloating, upper gastrointestinal hemorrhage or anemia may be present. Gastroscopy, endoscopic ultrasound, abdominal and pelvic imaging are helpful to diagnosis. The final diagnosis is decided by pathological and immunohistochemical examination. The operative treatment is the first choice, and complete surgical resection is the most definitive treatment.

Case report
A 66-year old man presented with a four year history of abdominal pain, bloating, anemia and two episodes of melena which resolved spontaneously. The patient had a history of cardiac disease treated with anticoagulants for many years. He was admitted in the emergency internal unit of Baia-Mare Hospital with anorexia, weakness, bloating, melena and anemia. Gastroscopy revealed an irregular gastric polyp measuring 3/2 cm, without histological signs of malignancy, and the patient was referred to our department. The physical examination showed a good nutritional status and moderate epigastric tenderness. The haemoglobin level was 9.05 g/dl. A reduced haematocrit (28.7%) and iron level suggested chronic bleeding. Upper digestive endoscopy showed a giant non-pedunculated polyp (diameter of 4 cm) with ulceration of the overlying mucosa, located in the gastric fundus in the proximity of cardia. Biopsies were nondiagnostic. Ultrasound examination described a hypoechoic, vascularized tumor of the cardia (Fig.1).

The patient was referred for surgery. Polar superior gastrectomy was performed. Macroscopically the tumor was multinodular (13/10/9 cm), adherent to the stomach, (Fig.2). Histological examination described a gastric stromal tumor with free esophageal (superior) and gastric (inferior) margins (Fig.3). Immunohistochemical markers confirmed the diagnosis of GIST (CD 117 positive, SMA negative, S 100 negative) (Fig.4). The reevaluation, performed 3 and 6 months later, showed complete recovery, without any sign of endoscopic, endosonographic or abdominal CT recurrence of the disease.

Discussion
Gastrointestinal stromal tumors (GISTs), though relatively rare in absolute terms, are the most common mesen-
chymal tumors of the gastrointestinal tract (3, 4). The common sites of location are in order the stomach, the small intestine, the rectum, the esophagus and a small percent may be located elsewhere in the abdominal cavity (<5%).

GISTs are associated with nonspecific symptoms. No physical findings specifically suggest the presence of a GIST. The main manifestation of GISTs is acute or chronic upper gastrointestinal hemorrhage (61%).

Many GISTs are discovered incidentally during operation, abdominal imaging, or endoscopy. Tumors found incidentally are usually small with a mean diameter of 1.5 cm and carry a better prognosis (6). Although extraluminal in origin, GISTs may ulcerate through the overlying mucosa (7). Tumor size alone is not a sensitive criterion of malignancy. Generally, about half of the primary localized GISTs relapse within the first 5 years of follow-up (3). The incidence of metastases at first presentation of a malignant GIST is about 50%, and liver is the most common site (8).

Gastric GISTs typically present with vague symptoms including abdominal pain, anorexia, weight loss, or GI hemorrhage, and may be discovered and biopsied during upper digestive endoscopy. Primary esophageal and gastric tumors have characteristic patterns of echogenicity, and endoscopic ultrasound may aid in the diagnosis and surgical planning. Endoscopy may occasionally help with surgical planning, but because of the infrequency of mucosal involvement, it is rarely diagnostic (9).

On the basis of their appearance on light microscopy, GISTs were first thought to be of smooth muscle origin. Most were classified as leiomyosarcomas or epitheloid leiomyosarcomas, with wide variability in malignancy (10). Hematoxilin and eosin staining usually reveals a spindle cell tumor with a fascicular pattern. The diagnosis of GIST is secured by immunohistochemical staining for the tyrosine kinase receptor KIT (CD 117), which highlights the presence of interstitial cells of Cajal (ICC). CD 117 expression also differentiates GISTs from true leiomyomas and gastric schwannomas which are consistently negative for CD 117. Approximately two thirds of GISTs also express CD 34. KIT is regarded as a key confirmatory marker in the diagnosis of this tumor. GISTs and ICCs are detected with antibodies to both CD 34 and KIT, suggesting that GISTs originate from the ICCs. Histologically, these tumors may exhibit a spindle cell pattern, an epitheloid pattern, or a mixed subtype (1, 11).

Although most gastric GISTs have a benign course, a wide spectrum of biologic behavior has been observed. A combination of prognostic factors (patient age, tumor size, histologic type, degree of necrosis, cellularity, nuclear pleomorphism, mitotic activity, and DNA analysis) have been
used to predict their behavior. Tumor size and mitotic index appear to be the most valuable (12). There is reluctance to use the term ‘benign’ to describe GISTs since this tumor may be unpredictably malignant. Patients with GISTs may be categorized into very low, low, intermediate, and high-risk on the basis of an estimation of their potential for recurrence and metastasis (10, 13).

Surgery is the mainstay of therapy for GIST when the primary lesion is deemed resectable. The surgical approach is to resect the tumor with grossly negative margins and an intact pseudocapsule. Lymphatic spread of GISTs is uncommon therefore a formal lymph node dissection is not standard surgical management. Consequently, complete surgical resection of the primary tumor is the most definitive treatment (1). The tumor must be handled with care to prevent intra-abdominal rupture and dissemination. Tumor rupture before or during resection is a predictor of poor outcome (14). Formal gastric resection is rarely required as a rule, it is indicated only for lesions in close proximity to the pylorus or the esogastric junction.

Prognosis of GIST after surgical treatment is influenced by completeness of primary resection and tumor malignant potential. A low grade GIST has an excellent prognosis after surgery alone, while a high grade GIST has a high rate of recurrence after primary resection. Adjuvant treatment should be advocated for patients with either a high grade GIST or after incomplete primary surgical treatment. Complete surgical resection offers a good chance of cure for low grade GIST, while for high grade GISTs surgery alone is not sufficient (15). The grading system could be used to identify patients who may benefit of adjuvant treatment after GIST resection.

If the tumor has metastasized or has advanced locally to the point where surgical therapy would result in excessive morbidity, the patient is treated with the tyrosine kinase inhibitor imatinib-mesylate. Imatinib is the standard of care for patients who are not surgical candidates (16). Adjuvant or neoadjuvant imatinib is not recommended for resectable nonmetastatic GISTs. Neoadjuvant imatinib may be considered when surgery would result in significant morbidity or loss of organ function (17).

The evaluation of tumor response to therapy on CT images is based mainly on the World Health Organization guidelines and the Response Evaluation Criteria in Solid Tumors (RECIST) (18). Six months after complete surgical resection our patient has a normal abdominal CT image and no adjuvant therapy is at the moment indicated.

Long-term follow-up reveals that the majority of patients with GIST tend to recur. The median time to relapse is 18 months, and most recurrences occur within 2 years of initial resection.

References