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Emergency duodenal resection for giant GIST with acute gastrointestinal bleeding. A case report

Gastrointestinal stromal tumors (GISTs) are rare tumors of the gastrointestinal tract, which cover about 1-2% of gastrointestinal neoplasms. They are more common in the stomach (40-60%) while a minor part in jejunum/ileus (25-30%), duodenum (<5%), colorectal (5-15%) and esophagus (<1%). The clinical presentation depends on the primary localization of the neoplasma and tumor size, however in 18% it is asymptomatic. Gastrointestinal bleeding is the most dangerous complication, often necessitating emergency surgery and represents a common symptom of duodenal GIST.
We present a case of a 82-year-old male presented with abdominal pain, asthenia and melena with haemodynamically stable. The patient underwent a recent coronary angioplasty and currently on double antiplatelet therapy. During observation a palpable mass was detected in the periumbilical region and right hypochondrium. A superior digestive endoscopy was performed which revealed an ab estrinseco compression of second duodenal segment and bleeding of third duodenal mucosa segment. No local haemostasis could be accomplished. An Angio-CT showed a large exophytic tumor arising from the 3th duodenal segment with approximately 13x9 cm, with apparent intratumoral bleeding. No indication for possible angioembolization. Due to gradual modification of the haemodynamic , the patient was submitted to emergency laparotomy. A segmental enterectomy was performed and the post-operative period ran without complications. The histopathologic exam showed a gastro-intestinal stromal tumor of epithelioid cell nature with low mitotic count (2 per 50HPF). The immunohistochemical analysis revealed positivity for CD117 (c-Kit) and DOG1 with Ki67<1%.

KEY WORDS: Bleeding, Duodenal GIST, Gastrointestinal, Gastrointestinal stromal tumor

Introduction

Gastrointestinal stromal tumor (GISTs) are rare tumors of the gastrointestinal tract, which cover about 1-2% of gastrointestinal neoplasms with an unadjusted incidence of around 1/100,000/year. They are also the most common non-epithelial neoplasms of the gastrointestinal tract and they are associated with a high rate of malignant transformation [1]. These tumors have been characterized by practical problems for many years due to the lack of diagnostic criteria, partly also due to the incomplete understanding of its origin and differentiation mechanisms [2]. Over the years, however, it has been discovered that their origin derives from the wall of the hollow viscera, from the esophagus to the anus [3]. In particular GISTs were supposed to arise from the interstitial cells of Cajal or their precursors, located throughout the muscular wall of the gastrointestinal tract.
They arise mostly in the stomach (60%), followed by the small intestine (35%) and rectum, esophagus, omentum, and mesentery (<5%) [4]. Duodenal GISTs account for only <5% but make up 30% of primary duodenal tumors [5]. Most cases occur sporadically, but 5% occur in the context of a familial syndrome (neurofibromatosis type 1, Carney triad) [4]. The majority of GISTs are

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benign but they can be malignant in 20-30% of cases and this percentage increases with tumor size [5].
The clinical presentation depends on the primary localization of GIST, however in 18% it is asymptomatic, and it is accidentally discovered during endoscopies, radiological examinations or surgical operations performed for other reasons, especially if it is small in size. More often, however, they are associated with non-specific symptoms such as early satiety, nausea or vomiting. A lower quota causes gastrointestinal bleeding, abdominal pain, mechanical jaundice, intestinal obstruction, massive intraperitoneal bleeding secondary to necrosis and/or ulceration of the neoformation. Gastrointestinal bleeding is the most common and the most dangerous complication, often necessitating emergency surgery. The causes of GISTs bleeding are similar to those of other primary gastrointestinal malignant tumors; however, the proportion of GISTs that bleed is greater [1,3,6].
The authors introduce a case of a giant third section duodenal GIST which presented with acute massive gastrointestinal bleeding and needed emergent surgical treatment.

Case Report

We report a 82 year old patient was admitted in the Emergency Department with symptops of abdominal pain , melena and asthenia which appeared 6 hours ago. The patient had a medical history of diabetes and currently on double antiplatelet therapy (Clopidogrel + Acetylsalicylic acid) for a recent coronary angioplasty (BMI 25 kg/m^2). The blood tests revealed a severe anemia (Hb = 6,7 g/dl) with haemodynamically stable. The examination of abdomen revealed a diffuse palpable painless mass in the right hypochondrium and periumbilical region. After the administration of red blood cell mass, a superior digestive endoscopy was performed which revealed an ab estrinseco compression of second duodenal segment and bleeding of third duodenal mucosa segment. No local haemostasis could be accomplished. An angio thoracic and abdominal computer tomography (CT) scan was requested and showed a large exophytic mass arising apparently from the third duodenal segment and pancreas approximately 13x9 cm with vascularization providen from branches of duodenal-pancreatic artery with apparent intratumoral bleeding without intraperitoneal bleeding (Figs. 1, 2). No indication for possible angioembolization.
Since endoscopical haemostasy was not be accomplished and the gradual modification of the haemodynamic with worsening of the anemia, an emergency laparotomy was performed.
The surgical exploration discovered a large mass of about 20 cm arising from the third duodenal portion that displaced the transverse mesocolon and the right colon forward. The tumor was posteriorly lying on the aortic and caval planes and cranially was related to the posterior part of pancreatic head (Fig. 3).
A segmental enterectomy was performed, resecting the third and fourth duodenal portion including the mass. A lateral-to-lateral manual duodenum -jejunum anastomosis was performed along with cholecystectomy and positioning of Kehr tube in the choledochus to protect the anastomosis.
At the opening of the surgical specimen, the tumor was filled with blood and clots (Fig. 4).
The histopathologic exam showed a duodenal GIST tumor, with low mitotic count (2 per 50HPF), with extensively necrotic. The immunohistochemical analysis revealed positivity for CD117 (c-Kit) and DOG1 with Ki67<1% and with high malignancy potential according

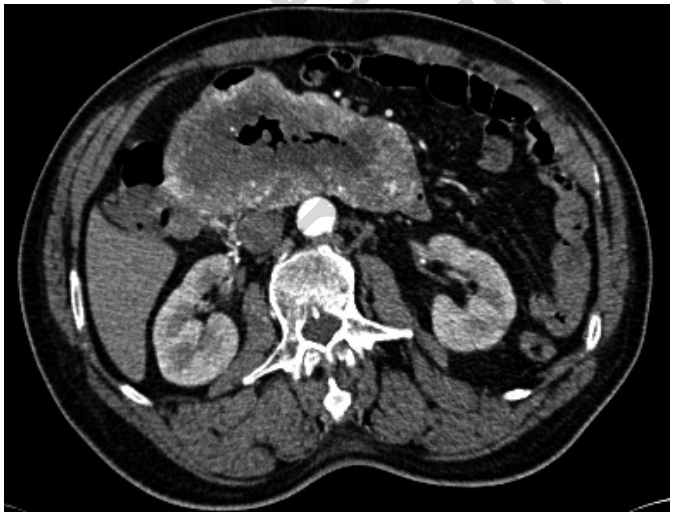

Fig. 1: Angio-CT scan in arterial phase showed a voluminous exophytic mass (approximately 13 x 9 cm) arising from the third duodenal segment with vascularization from duodenal-pancreatic artery branches and intratumoral bleeding.

Fig. 2: The mass had peripheral rim enhancement and hydro aerial level inside.

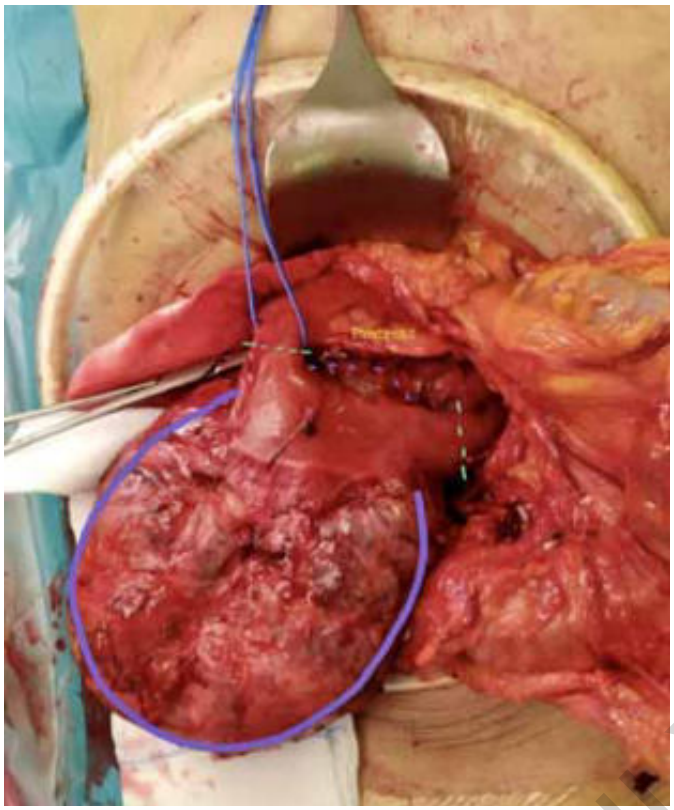

Fig. 3: GIST originates from the third duodenal portion on the antimesenteric side and therefore in the opposite position with respect to the lower edge of the pancreas. The sections of the duodenum are shown in dashed lines.

Fig. 4: The tumor was filled with blood and clots

to the Miettinen classification. No documentable neoplastic invasion and free resection margins.
The post operative period ran without complication. The patient started oral feeding at the seventh postoperative day, after performing a RX gastrointestinal oral contrast study with gastrografin and a trans kehr cholangiography that confirmed the integrity of the anastomosis. The patient was discharged after 10 days. The kehr tube was removed after 40 days.
The patient was evalueted by medical oncology and started radiological and clinical follow up. After six months follow-up neither complaints or disease recurrence were observed.

Discussion

The incidence of GISTs was estimated to be 1,5-2 cases per 100.000 inhabitants each year [1,2,7]. They usually were observed in patients in the 5th-6th decade of life. The mean age at the diagnosis is 55-63 years [2,8].
However, it is estimated, that about 20% of the tumors manifest themselves in patients below 40 years of age [9]. These tumors can be more frequently found in the stomach (40-60%), followed by the small bowel (25%) [10]. Less frequently, they can occur in the colon, rectum, appendix, oesophagus, mesentery, omentum, or retroperitoneum. Duodenal GISTs account about 5% of GISTs arising from the gastrointestinal tract [5,1].
The clinical presentation was not characteristic and depends on the localization and size of the tumor. The median size of GISTs at diagnosis is 5-7 cm, although these tumors may grow over 30 cm. [5] GISTs are usually indolent tumors. They may be discovered by symptoms, most of them nonspecific, such as abdominal pain and early satiety. The most common symptoms and signs were abdominal pain (57-74%), dysphagia, subileus or ileus (30-44%), weight loss (16-22%), palpable abdominal mass (16%), perforation with peritonitis (9-11%) [12,13]. GIST may be responsible for chronic gastrointestinal bleeding with anemia (44-70%), although, in rare cases, acute massive bleeding can occur and often necessitating emergency surgery due to hemodynamic instability of patient or the impossibility of endoscopic haemostatic control [14]. The clinical presentation of GISTs, as confirmed by Sianesi in his work [15] was influenced by two parameters: the size and the site of onset. In 30% of cases, if less than 2 cm, they are asymptomatic; self greater than 5 cm may occur not infrequently with urgency (haemorrhage, ulceration, perforation,

occlusion, pain) especially if in particular locations. The growth of these tumors tends to be exophytic and takes on peculiar characteristics in certain locations.
Characteristic is the hourglass or clapper appearance of bell on the stomach. The bleeding will be more frequently intraluminal than in cases with rupture of the tumor and haemorrhage into the abdominal cavity o in the retroperitoneum. Metastasis is mainly to the liver or intraperitoneally, while pleurae, lungs and lymph nodes are relatively fewer locations frequent (<10%) [15].
Recent studies have reported bleeding as a factor predicting poor prognosis in patients with duodenal GIST [16-17]. Endoscopic hemostasis methods, including hemoclipping, injection, and coagulation, are efficient tools for controlling upper gastrointestinal bleeding (UGIB). As bleeding is the major symptom of GIST, hemostasis is important to avoid emergency or unnecessary surgery in patients scheduled for chemotherapy in elective settings. However, studies on duodenal GISTs usually have a small sample size and studies on duodenal GIST bleeding are rare, except for case reports.
Previous studies have reported that GISTs have diferent clinicopathologic features according to the primary location and that tumor location is a key prognostic factor for GIST in addition to tumor size and mitotic index, according to modified Miettinen classification [18,19]. In this study, duodenal GISTs showed a higher incidence of tumor bleeding and a higher re-bleeding rate than gastric GISTs. Although there was no signifcant diference in the 5-year patient survival rate, the recurrence rate was signifcantly higher in the duodenal GIST group than in the gastric GIST group.
Endoscopic hemostasis for UGIB from gastric cancer has been reported in several published studies [20,21], and a few studies have evaluated hemostasis methods and the poor prognosis of gastric GISTs [20,22].
None of the studies to date have evaluated the eficacy and outcome of the endoscopic hemostasis method for duodenal GISTs. The duodenum is an organ that is difcult to reach with an endoscope because of its angulated structure and limited space for controlling the hemostasis device. However, when the bleeding focus cannot be visualized because of a large amount of hematoma or massive active bleeding as in our case, endoscopic hemostasis may fail. Obviously, the association between bleeding and hemodynamic instability of the patient remains an indication for an emergency laparotomy.
Interventional radiology includes procedures to selectively cannulate the feeding vessel of the tumor and injection of hemostatic agents and some authors use this method as an alternative or to support surgery in hemodynamically stable patients. Beddy et al. [23] used embolization in treating bleeding duodenal GIST in a surgically unfit patient and Kurihara et al. [24] used it as a bridge to surgery in achieving hemostasis and size reduction facilitating limited resection. Multiple feeders and complex anatomy will make it challenging to apply this technique in the duodenal GIST. The possible adverse effects of the procedure include pancreatitis, duodenal ischemia, and other procedure-related complication such as arterial dissection, non-target embolization, and access site hematoma [25]. However in our case there was no indication for angioembolization and urgent surgical treatment was necessary to modify the patient's hemodynamics.
In general, the three major factors associated with GISTs are tumor size, mitotic index, and tumor location. Therefore a mitotic count≥5/HPF and a large tumor diameter were signifcant factors in terms of overall survival of patients with duodenal GIST [26]. In addition, when the patients were classifed into four groups according to tumor size (<2, 2–5, 5–10, and≥10 cm), patient survival rates signifcantly decreased as the tumor size increased. Considering that the duodenum is adjacent to other organs, such as the pancreas and liver, a larger tumor size may be associated with a higher probability of metastasis or invasion than a GIST originating in other sites.
Histologically, spindle cell (70%), epithelioid (20%) or mixed type differentiation can be observed, depending on tumor site. Furthermore, the results of mutation analysis of the KIT and PDGFRA gene and comparative genomic hybridization (CGH) are employed as additional prognostic factors with impact on diagnosis and therapy [2,7]. The individualized application of tyrosine kinase inhibitors (imatimib) in patients with high-risk GISTs, certain cases of intermediate-risk GISTs, and/or incomplete surgical resection has been established during the past years and allows for adequate adjuvant or neoadjuvant treatment .
However, the role of surgical treatment remains important since only complete resection of primary GISTs is curative [1,8]. The optimal surgical technique for duodenal GISTs remains to be determined.
Concerning the operative procedure, the authors of recent european multicenter retrospective cohort study [27] preferred segmental duodenectomy to duodenopancreatectomy since this procedure has a lower operative morbidity while providing comparable oncological results. Yong Chock et al. [28] in their meta-analysis compare the clinical outcomes of patients who underwent limited resection (LR) versus pancreaticoduodenectomy (PD) for duodenal gastrointestinal stromal tumors (GISTs). In particular PD was associated with a higher postoperative morbidity rate than LR [48.3 vs. 20.7%, relative risk (RR) 2.34, 95% CI 1.61-3.42], a longer duration of operation, more intraoperative blood loss, a greater blood transfusion requirement and a longer hospital stay. LR was not associated with an increased local recurrence rate, had a better DFS [hazard ratio (HR) 2.07, 95% CI 1.07-4.01], and lower rate of distant metastasis (8.9 vs. 25.8 %, OR 0.28, 95 % CI 0.13-0.59) compared with PD. However, PD remains the procedure of choice

in cases where the tumor regard to the papilla of Vater. The discovery of Imatinib had revolutionized the treatment of GIST, increasing diseasefree survival after complete surgical resection of a primary localized GIST and extending overall survival in metastatic disease. The definition of an accurate prognostic system was critical for the therapeutic decision making process. In literature, there are three main prognostic criteria F/NIH consensus, AFIP standards and modified NIH standards. In recent years were added various risk identification methods applying mathematical calculation model, including MSKCC risk nomogram, Rossi nomogram and Joensuu high Hotline Dengjun.

Despite all these attempts, it seems that the recurrence risk probability still cannot be predicted accurately. Belfiori et al. [29] in their study compared these models with the aim of highlighting the real ability of these prognostic instruments to define if the use of the MSKCC nomogram can bring benefits in the therapeutic decision. In their statistical study they analyzed about 37 cases of GIST surgically treated in 5 years and what emerged was that MSKCC nomogram seemed to perform better than NIH, NIH modified and AFIP and could be used in clinical practice to predict the risk of recurrence, being especially helpful for the therapeutic decision making since it is at the same time simple to use and accurate and did't seem to neglect relapses. All the three risk assessement tools criteria considered were capable to predict recurrence in high-risk GISTs while they performed worse in those with lower risk. MSKCC nomogram main limit remains the not linear consideration of mitotic count.

Conclusion

Duodenl GIST is a rare neoplasma of the gastrointestinal tract and can have various clinical presentations. The majority of GISTs are benign but they can be malignant in 20-30% of cases and this percentage increases with tumor size. The chronic gastrointestinal bleeding is a common presentation, although, in rare cases, acute massive bleeding can occur in giant GIST and often necessitating emergency surgery due to hemodynamic instability of patient or the impossibility of endoscopic haemostasis controlls or angio-embolization, as in our case. Endoscopic and imaging exams are indispensable to establish the pre-operative diagnosis. The complete surgical resection is the only curative treatment for duodenal GISTs. Since both, limited and extended surgery yield comparable survival rates, tumor size and location in regard to the papilla of Vater, associated diseases and the patient's performing state should be considered when deciding between segmental duodenectomy or duodenopancreatectomy. If duodenopancreatectomy is necessary, it has no impact on overall survival and recurrence rates but has high postoperative morbidity rates.

Riassunto

I tumori stromali gastrointestinali (GIST) sono tumori rari del tratto gastrointestinale (circa l'1-2% di tutte le neoplasie gastrointestinali). Si localizzano più frequentemente nello stomaco (40-60% dei casi) mentre in minor percentuale nel digiuno/ileo (25-30%), nel duodeno (<5%), nel colon-retto (5-15%) e nell' esofago (<1%). La presentazione clinica dipende dalla localizzazione primaria della neoplasia e dalle sue dimensioni, tuttavia nel 18% dei casi la diagnosi è accidentale perché il paziente rimane asintomatico. Il sanguinamento gastrointestinale è la complicanza più pericolosa e frequente e spesso necessita di un intervento chirurgico d'urgenza. Questa complicanza rappresenta il sintomo di più comune presentazione dei GIST duodenali. La diagnosi è prevalentemente radiologica ed endoscopica. Il sanguinamento è possibile arrestarlo attraverso diverse metodiche endoscopiche, soprattutto in presenza di lesioni di piccole dimensioni e, solitamente, costituisce un trattamento transitorio ai fini dell'intervento chirurgico definitivo. Infatti, come per tutti i GIST, la terapia chirurgica rappresenta il principale elemento terapeutico e nell'ambito dei GIST duodenali, ove possibile in base alla posizione della lesione, le resezioni segmentarie sono da preferire alle duodenocefalopancreasectomia in termini di morbidità e morrtalità postoperatoria. Non sono state identificate in letteratura differenze in termini di outcome oncologico fra le due tecniche. Il trattamento chirurgico in regime d'urgenza è richiesto nei casi di sanguinamento con instabilità emodinamica del paziente o nei casi di fallimento delle procedure endoscopiche.

Presentiamo il caso di un uomo di 82 anni che accedeva presso il nostro Dipartimento di Emergenza ed Urgenza per dolore addominale, astenia e melena insorti nelle ultime 48h. Alla Valutazione primaria l'emodinamicamente risultava essere stabile e durante la visita veniva evidenziata la presenza di una massa palpabile in sede periombelicale e in ipocondrio dx. In anamnesi una recente angioplastica coronarica con assunzione di una doppia terapia antiaggregante. Dato il quado clinico il paziente veniva sottoposto ad un'esofagogastroduodenoscopia che rivelava una compressione ab estrinseco del secondo segmento duodenale con un sanguinamento attivo dalla mucosa del terzo segmento con impossibilità ad eseguire un'accurata emostasi locale. Il paziente, pertanto, veniva sottoposto ad un'angio-TC dell'addome che mostrava un grossa neoformazione esofitica originata dal 3° segmento duodenale di circa 13x9 cm, con apparente sanguinamento intratumorale. Nessuna indicazione veniva posta dai colleghi della radiologia interventistica per un eventuale angioembolizzazione. A causa della graduale modifica dell'emodinamica, il paziente veniva sottoposta ad una laparotomia d'emergenza con resezione segmentaria del duodeno e asportazione en-blocc della voluminosa massa e confezionamento di un'anastomosi duodeno-digiunale manuale in doppio strato. Veniva

inoltre eseguita la colecistectomia e posizionamento di tubo di Kehr nel coledoco a protezione dell'anastomosi. Il decorso periodo post-operatorio è stato regolare e senza complicanze. L'esame istopatologico ha evidenziato la presenza di un tumore stromale gastro-intestinale a cellule epitelioidi duodenale con bassa conta mitotica (2 per 50HPF) e quindi non richiedente alcun trattamento oncologico adiuvante.

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