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THE IMPORTANCE OF RIGHT DIAGNOSIS AND TREATMENT OF GASTROINTESTINAL STROMAL TUMORS (GISTs)

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ABSTRACT. Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal-derived tumors of the alimentary tract , covering over 1% of gastrointestinal neoplasms. G.I.S.T. are originating from the interstitial cells of Cajal , given the expression of protein CD117, which is the tyrosine kinase receptor known as KIT. **Material and method.** We studied 11 patients with GIST along last 10 years. **Results and discussions**. Malignancy is directly proportional to tumor size and mitotic count. The findings on CT frequently include tumors with smooth borders or rounded appearance or an exophytic lobulated lesion. The positive diagnosis is made on immunohistochemical staining. Complete surgical resection remains the mainstay of treatment. Neoadjuvant as well as adjuvant therapy is based on imatinib, which is an oral medication that binds to the thyrosine kinase receptor . **Conclusions.** GISTs are rare tumors , with difficult diagnosis based on CT, endoscopy and biopsy , very important being the immunohistochemical staining. Excision of these tumors is mandatory.

KEYWORDS: Gastrointestinal stromal tumors (GISTs), immunohistochemical staining, excision, imatinib, CD117.

INTRODUCTION

GISTs, gastrointestinal stromal tumors are the most common neoplasms arising from connective tissue in the digestive tract, covering over 1% of gastrointestinal tumors. This tumors are rare, primary mesenchymal, non-epithelial, located in the wall of the digestive tract from the esophagus to the anus, mesentery, mesocolon, omentum, with high malignant potential. GISTs have been considered for a long time smooth muscle tumors or with origin in nervous cells, but the development of immunohistochemistry techniques has changed these concepts demonstrating that GISTs are mesenchymal tumors expressed through a common marker CD117.GISTs not fully show the characteristics of smooth muscle differentiation or differentiation of neural cell. Gastrointestinal stromal tumors (GISTs) have been recognized as a biologically distinctive tumor type, different from smooth muscle and neural tumors of the gastrointestinal tract (GIT).

Histological origin is controversial.There are two hypotheses. The first one and the most supported hypothesis attributes the origin in the intestitial myenteric plexus Cajal. The starting point is considered the interstitial Cajal cell, ICC, interstitial cell disposed like peacemaker between intramural neurons and smooth muscle cells of the digestive tract.

The cell is named after Cayala Ramon Santiago, Spanish doctor and histologist, considered the father of modern neuroscience , who won the Nobel Prize for medicine in 1906. The second hypothesis considers GISTs having the origin in a pluripotent stem cell, based on common origin of Cajal cells and smooth muscle cells. The general incidence of GISTs is considered 15 cases/million/year. (Elisabetta de Lutio ,2011).The diagnosis of these tumors relies in the first place on morphological and immunohistochemical features, most of the tumors 86% showing KIT(CD 117) or DOG1 positive cells ,also important aspect in the treatment .(Y. Kitamura et al ,2005)

MATERIALS AND METHOD

In this study we analysed 11 patients suffering of gastrointestinal tumors ,in the last 10 years ,admitted and treated to the General Surgery II Department of Emergency Clinical County Hospital Arad. This patients underwent operations for gastric and small intestine tumors, having postoperative positive diagnosis of GIST after the immunohistochemical exam of the resection piece. We

followed aspects concerning symtomps, clinical, imagistic explorations, localization,growth point,type of operation, postoperative treatment.

RESULTS

In the studied group we have 7 males and 4 males, with ages between 50 and 74 years old ,8 patients having the age between 50 and 60. 8 patients had gastric GIST,7 males and 1 female;3 patients had small intestine GIST (jejunum) ,1 male and 2 females.

The patients with gastric GIST presented abdominal pain, nausea, vomiting, loss of appetite, fatigue, weight loss in 6 cases, the tumor being 5-6 cm in diameter, growing out of the lumen of stomach compressing the neighboring organs. In one case the tumor was 9-10 cm in diameter, palpable through the anterior abdominal wall, in the epigastric region. In one case at the only women with gastric GIST from our study, the patient presented upper digestive bleeding, from an ulcerated tumor on the lesser curvature of stomach ;the tumor was growing in the gastric wall, having 5 cm in diameter, with ulceration on the part situated in the gastric lumen.(Figure1-2) The three small intestine GISTs were localized on the jejunum, without signs of occlusion ,one growing on the mesentery and one on the serous of small intestine, having between 7-9 cm in diameter ,being palpable. All the patients after the clinical signs presented at the initial consultation followed CT-scan tests and traditional surgery intervention. The patients with small intestine GISTs suffered segmental enterectomy, with end to end anastomosis. The patients with gastric GISTs suffered total gastrectomy with esojejunostomy and Roux-en- Y Reconstruction (6 patients) and two patients suffered gastric resection, Pean- Bilroth II type(Figure 3). The postoperative treatment contained imatinib. We don' t have all the informations about the surviving period, but we succeed to find out that 4patients have 4 years from the diagnosis, 2 have 2 years and 1 an year.

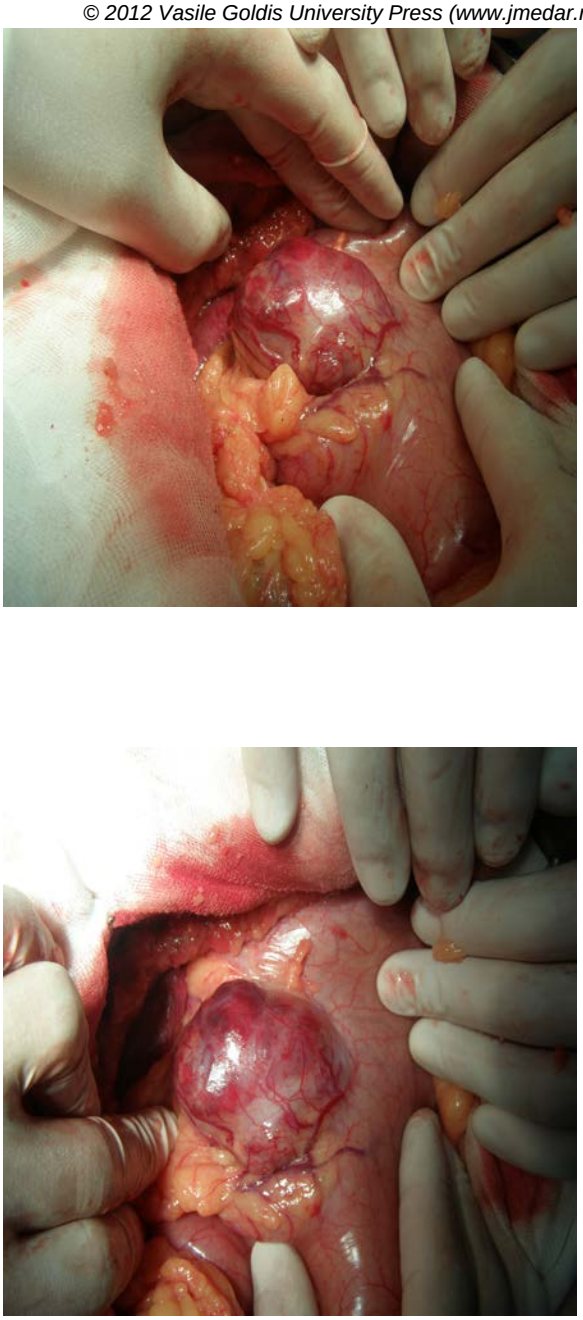

Figure 1-2 Intraoperative picture of gastric GIST on the lesser curvature of stomach. The internal ulcerated surface of tumor was the source of an upper digestive bleeding

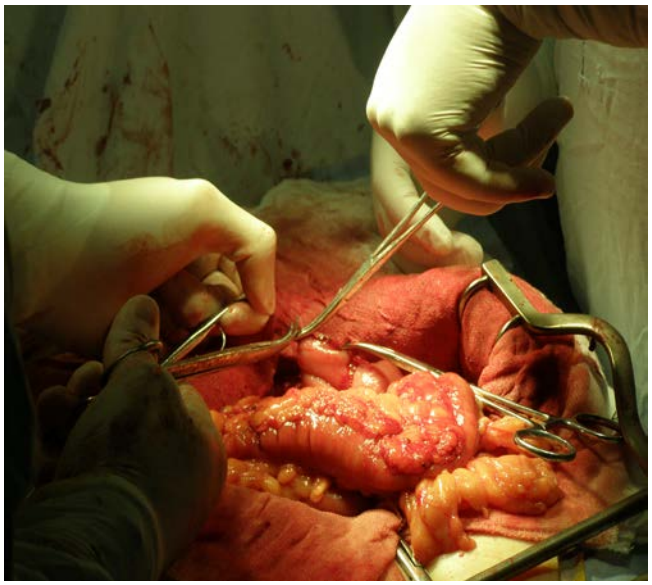

Figure 3 Pean- Bilroth II gastric resection performed at the same patient

DISCUSSIONS

Age affected is between 55-60 years, males repesenting 60-70% and 30-40% females.Symptoms of GISTs are in relation with location and size of the tumor, most often lacking, tumors were discovered accidentally in investigations for other conditions or at necropsy. GIST patients may present abdominal pain, dysphagia, satiety, fatigue, nausea, vomiting, loss of appetite, loss of weight, signs of compressing neighboring organs. In some cases ,rarely,patients may present GI bleedings ,which may be acute (melena or hematemesis) caused by tumor rupture,or chronic resulting in anemia.(AuroraD.et al,2010).Also the GISTs can produce GI obstruction ,the patient coming in emergency to the hospital ,needing urgent surgical intervention.

Paraclinical examinations help to find the tumor, in evaluation of its location, size, resecability, the existence of possible metastases.

The treatment of choice is the surgical excision of the tumor in healthy tissue according with his location, without lymphadenectomy because lymph nodes are rarely interested. The metastatic spread is predominantly made through the bloodstream.

Morphopathology of GIST reveals, a macroscopic tumor with size between 2-25 cm(40 cm) with an average of 5 cm, growing in lumen, intramural or outside of the organ, with fatty layout, gray, rodent, yellow sectors, with low consistency with areas of hemorrhage and cystic transformation. Most common localization is in the stomach, followed by the small intestine .The most common localization in the stomach is the gastric body. Microscopically are mesenchymal spindle cell, epithelioid or mixed tumors, expressing KIT protein highlighted by CD117 antibody. Are positive for c-kit immunohistochemistry is essential for positive and differential diagnosis. Malignancy is directly proportional to tumor size and mitotic index, the diameter over 5 cm or more than 5 mitoses / 50 fields ix 40 meaning high malignant potential. GIST tumors are considered to be the expression of c-kit protein, discovered in 1998, highlighted in CD117 antibodies, used to differentiate them from smooth muscle tumors or other tumors. (Charles J. Yeo MD et al.,2012).

Postoperative treatment has a major importance after the positive diagnosis of GIST, consisting of administration of Glivec (imatinib-mesylate) , an inhibitor for protein tyrosine kinase, which is a targeted treatment of KIT (CD117). Imatinib acts at the site of attachment of ATP-phosphate fixation on protein substrate of intracellular signaling pathways by activating c-kit. It was originally used in myeloid leukemia for inhibiting tyrosine kinase and subsequently to inhibit tyrosine kinase and KIT in unresecable or metastatic GIST tumors when classic chemotherapy has failed.

This dates are highlighting the importance to develop the knowledge about GIST tumors for the identification, diagnosis and appropriate treatment of this pathology. It is possible that a large part of surgeons to meet at least once in their careers such tumors.

CONCLUSIONS.

GISTs are rare tumors, affecting most often males, between 50-60 years old;most often organ affected is the stomach , followed by the small intestine.Symptoms of GISTs are in relation with location and size of the tumor, most often lacking, tumors were discovered accidentally in investigations for other conditions or at necropsy. Paraclinical examinations are very important to help to find the tumor, in evaluation of its location, size, resecability, the existence of possible metastases. Immunohistochemistry is essential for positive diagnosis and differential diagnosis of GIST. The surgical treatment is mandatory, consisting in large excision of tumor, in healthy tissue without lymph nodes dissection. Postoperative treatment has a major importance after the positive diagnosis of GIST, consisting of administration of Glivec (imatinib-mesylate) , an inhibitor for protein tyrosine kinase, which is a targeted treatment of KIT (CD117).

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