GASTROINTESTINAL STROMAL TUMOR: A CASE REPORT AND REVIEW OF THE LITERATURE

Le Trong Binh, Hoang Minh Loi, Le Trong Khoan
Nguyen Van Mao, Tran Van Huy
Hue University of Medicine and Pharmacy, Vietnam

Abstract
Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract. Stomach is the most affected site. Clinical manifestation is erratic depending on the locations, size, histological type and stage. Confirmed diagnosis of GISTs bases on immunohistochemical study. Most of GISTs are histopositive for the tyrosine kinase KIT receptor (also known as CD 117). CT scan is the imaging modality of choice in the detection of tumors, evaluation of tumor expansion or seeding, treatment planning and surveillance of recurrence. Complete surgical resection of the tumor remains the first line treatment. Imatinib mesylate, an oral tyrosine kinase inhibitor, has dramatically changed GIST therapy.
Key words: *Gastrointestinal stromal tumor, KIT, immunohistochemical, computed tomography, surgical resection, Imatinib.*

1. BACKGROUND

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gastrointestinal tract (80%). The incidence of GIST globally is 10-20 million people per year with malignant potential of 20-30% [1]. It accounts for less than 1% of all gastrointestinal tumors and about 5% all sarcomas. It represents a wide clinical spectrum of tumors with different clinical presentations, locations, histology and prognosis [2].

2. CASE PRESENTATION

We report a case of GIST which was diagnosed and treated at Hue University Hospital. A fifty-seven year-old woman presented to our institution complaining of a long lasting epigastric pain. The pain was irregular, vague without spreading or progression or correlation to alimentary habit. She had no nausea or vomiting, neither hematemesis nor hematochezia. She did not report any change in her bowel habit and had not experienced any recent fevers. She denied any history of alcohol consumption, cigarette smoking, non-steroid anti-inflammatory medications intake and weight loss. Her past medical history and previous routine abdominal ultrasound check were unremarkable. On physical examination, her heart rate, blood pressure, respiratory rate and body temperature were normal. The cardiovascular and respiratory findings are unremarkable. There is little to no tenderness to palpation in the upper abdomen. Neither bowel distension nor abnormal motility was noticed. Auscultation of bowel sound revealed normal. General blood and urine tests were in normal range. She was primarily diagnosed with intramural gastric tumor (which is very suggestive of GIST). A subtotal gastrectomy was performed and the diagnosis of low-grade GIST was confirmed (CD117 +, CD34+, Desmin -). The patient is currently undergoing surveillance.

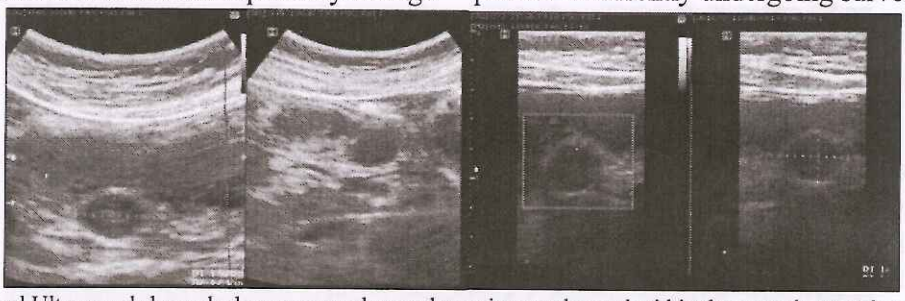

Fig 1. Abdominal Ultrasound showed a homogenous hypoechogenic mass located within the posterior gastric wall, protruding into the inner lumen. The mass was oval in shape, had regular and distinct margin without infiltration. There was no gastric wall thickening and the layers remained intact. No evidence of hypervascularity on Color Doppler ultrasound of the mass.

- *Corresponding author: Le Trong Binh, email: binhr_vn@yahoo.com.vn*
DOI: 10.34071/jmp.2013.2e.6
- *Received: 7/11/2013 * Revised: 15/12/2013 * Accepted: 27/12/2013*

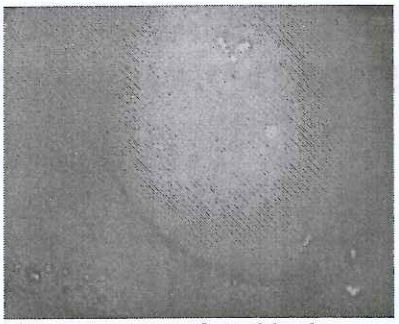

Fig 2. Gastric endoscopy: lesion was found in the antrum, oval and smooth, the mucosa was nearly normal and relatively firm on compression.

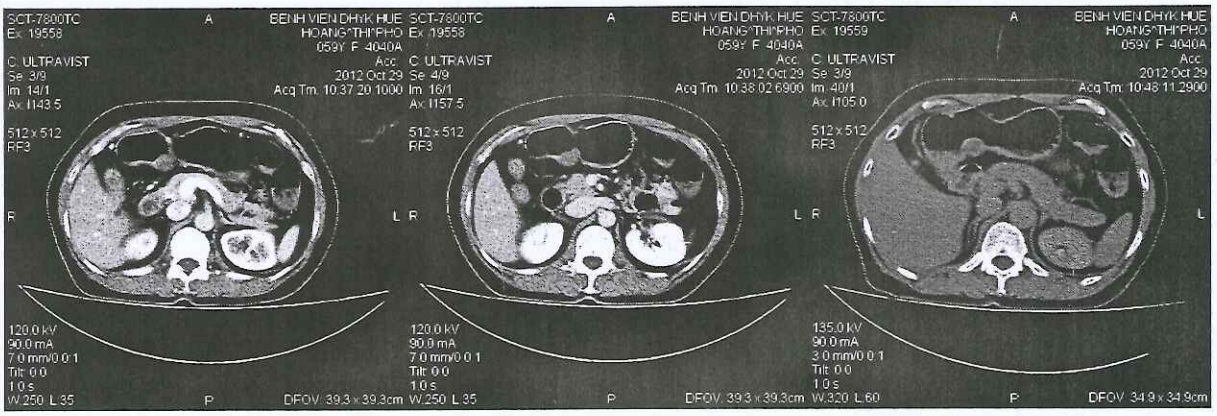

Fig 3. Axial contrast-enhanced computed tomography (CECT) showed a well-defined, ovoid, homogeneous, intramural mass arising from the gastric antrum with slightly enhancement. The mass was measured 2 cm in diameter. There was no evidence of adjacent tissue infiltration or lymphadenopathy or ascites. CT scan findings were suggestive of a gastric GIST.

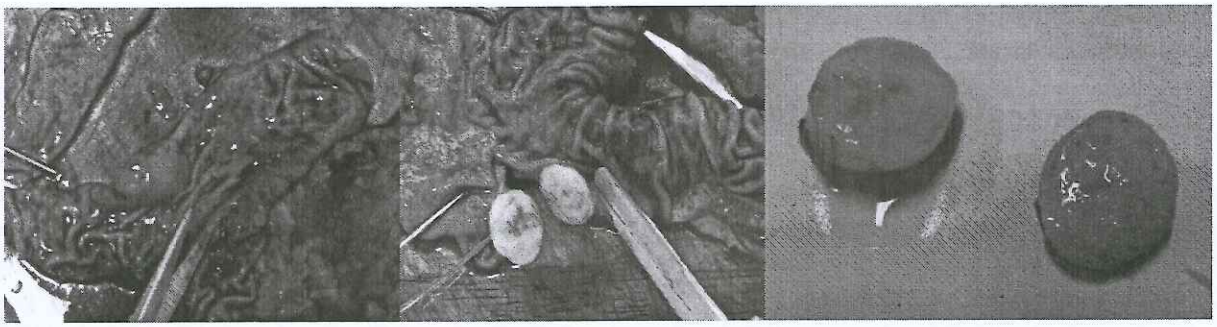

Fig 4. Gross section showed a submucosa tumor located in the pyloric antrum which is firm and fleshy in nature. The mucosa surface remained normal.

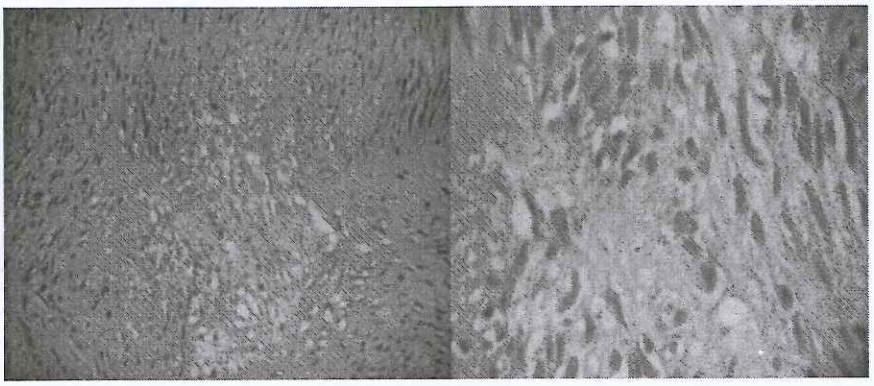

Fig 5. Histopathology HE staining x 400. Tumor cells are fusiform in shape, with vacuolated cytoplasm and arrayed palisade.

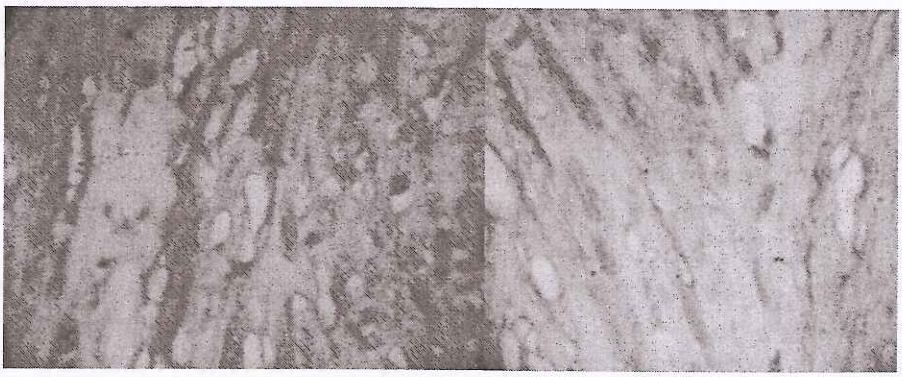

Fig 6. Immunohistochemical staining x 400. CD117+, brown-yellow membrane staining.

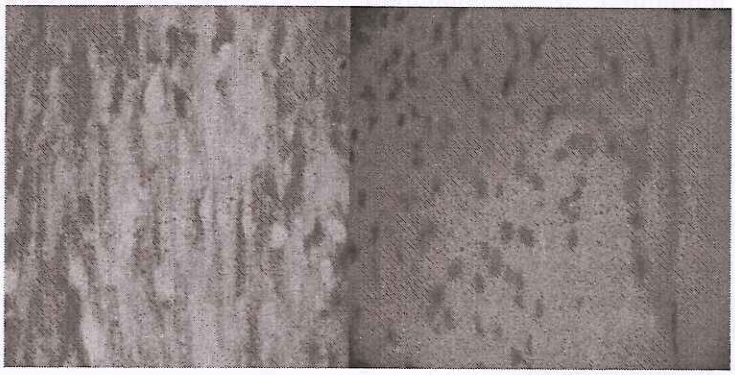

Fig 7. CD34+

Fig 8. Desmin -

3. DISCUSSION

Gastrointestinal stromal tumors (GISTs) are currently the most common mesenchymal tumors of the gastrointestinal tract, with an estimated 4500-6000 new cases reported each year in the United States. The incidence of GIST is estimated to be approximately 10-20 cases/million/year. Malignant possibility is 20-30%. A few estimates and studies indicate the incidences of approximately 14.5 cases/million/ year in Sweden, 14.2 in Northern Italy, 13.7 in Taiwan, 12.7 in Holland, 11 in Iceland and 6.5 in Norway. Recent report shows an incidence of 6.8/million from 1992-2000 in the United States [2]. However, the precise incidence of GISTs is still unknown because of the incomplete definition and classification. Over 90% of GISTs occur in adults over 40 years old, in a median age of 63, though GISTs have been reported in all ages, including children. No difference in prevalence between sexes. There are no elements that indicate any association with geographic location, ethnicity, race or occupation [3].

The term of stromal tumor was first described as a separate entity by Mazur and Clark in 1983 and Schandelbrand and Appleman in 1984 [2]. GIST are now thought to derive from a precursor of the interstitial cells of Cajal (ICC), normally present in the mysenteric plexus, and are clearly distinct from other mesenchymal tumors, such as leiomyoblastoma, leiomyomas or leiomyosarcomas [4]. In 1998, Hirota and colleagues published a discovery of KIT mutations in GISTs and 95% GISTs are immunohistochemically positive for the receptor tyrosine kinase KIT (also known as CD 117). CD 117 then becomes a crucial diagnostic marker for GIST, and mutant KIT provides an important therapeutic target clinically in GIST treatment [2]. The basic pathology is an activating mutation of chromosome 4 which codes for c-KIT resulting in uncontrolled proliferation of stem cell that differentiate towards ICC [1]. Many GISTs have an activating mutation in either KIT or PDGFRα (Platelet-derived Growth Factor Receptor Alpha), accounting for < 1% of all GISTs [3].

The most common location of GIST is stomach (50- 60%), small intestine (30-40%), colon and rectum (5-10%), esophagus (5%). Other less common locations are those outside the GI tract (known as extra-gastrointestinal stromal tumors), such as mesentery, omentum or retroperitoneum [3]. GISTs smaller than 2 cm are generally considered benign with a very low risk of recurrence. Macroscopically, small GISTs locate in the submucosa layer with the surface smooth or sometimes a small ulcerous hole, form solid subserosal, intramural, or less commonly polypoid intraluminal masses. A majority of larger GISTs form external, sometimes pedunculated masses attached to outer aspect of gut involving the muscular layers. Many larger tumors are centrally cystic, and some develop a diverticulum-like appearance with the external tumor communicating with the lumen by a fistula tract. Some GISTs have an asymmetric hourglasslike pattern with a smaller internal and a larger external component. Histologically, GISTs manifest in one of three patterns: predominantly spindle cells (most common), epithelioid cells or mixture. Identifying KIT (CD 117), a tyrosine kinase receptor in the ICC is the key to make a diagnosis of GIST in 95% of patients [4]. Prognosis on the basis of morphologic features according to NIH 2001 that the Risk of Aggressive

• leiomyoma leiomyosarcoma (LMS)
• Schwannoma malignant peripheral nerve sheath tumor (MPNST) neurofibroma
• neuroendocrine tumor carcinoid carcinosarcoma
• fibromatosis or desmoid tumor solitary fibrous tumor inflammatory fibroid polyp
• angiosarcoma clear cell sarcoma liposarcoma synovial sarcoma
• malignant mesothelioma
• dedifferentiated carcinoma sarcomatoid carcinoma
• metastatic melanoma

Fig 9. Tumor type in differential diagnosis with GISTs [3]

Behavior as 4 levels basing on the tumor size and the mitosis index per 50 HPFs: high, intermediate, low and very low risk.

Clinical manifestation of GIST is erratic. Seventy percent are symptomatic at presentation, 20% are asymptomatic and 10% are detected at autopsy. Common presentations include vague abdominal pain, palpable mass, gastrointestinal bleeding, fever, anorexia, weight loss and anemia [1].

Ultrasound may identify GISTs fortuitously, especially if they are large, so that other imaging tests can be performed to confirm the diagnosis. Echoendoscopy can be used to study the esophagus, gastric or rectal tumors to determine local extension. During this procedure, cytopuncture or biopsy can be performed [5]. Computed tomography (CT) is frequently the imaging technique used in the first intention in case of suspected GISTs and CT is also the standard imaging method in patients with GISTs. CT has a high reliability in tumor detection and staging and has been established as the standard method for assessing therapy response. Indeed, CT is considered to be the

reference examination for the local study of these tumors and for tumors extension. GISTs usually present as well circumscribed exoluminal masses of different size. Primary GISTs are typically large, hypervascular, enhancing masses on CECT scans and are often heterogeneous because of necrosis, hemorrhage, or cystic degeneration at the time of presentation. Calcified are rare before treatment. GISTs may also contain gas bubbles or contrast media from the GI tract in case of fistula. Enhancement is often heterogeneous. According to Ghanem et al, GISTs smaller than 5 cm are usually homogeneous with smooth edges and intraluminal development. Larger size GISTs are usually exoluminal, heterogeneous appearance and may invade adjacent structures. Nearly 50% of patients with GISTs present with metastasis. Most metastases of GISTs involve the liver and peritoneum by hematogenous spread and peritoneal seeding, respectively. Less common, metastases are found in the soft tissues, lungs and pleura. Unlike gastrointestinal adenocarcinomas, metastases to the lymph node are extremely rare [4], [5], [7]. MRI should be applied in cases of potential resection of liver metastases due to the higher sensitivity in detection small liver lesions. Moreover, MRI is an alternative method to CT if contraindications to CT exist (allergy to iodine contrast agents) [7]. Angiography plays a very limited role in the management of GISTs, and has no diagnostic value. On the other hand, in case of gastrointestinal or intraperitoneal hemorrhage with heavy bleeding or hemodynamic instability, angiography and endovascular intervention could be considered to ovoid emergency surgery with high morbidity [5].

Although surgical resection is the treatment of choice for the primary GISTs, recurrence occurs in most patients, even after a complete resection with tumor-free margin. The median time to recurrence after operation is approximately 2 years. The main goal of imaging is surveillance to detect recurrence of progression as early as possible. Recurrences typically occur first in the liver of peritoneum. Traditional criteria for progression include tumor size increase, development of new lesions and metastasis [4]. Imatinib and sunitinib were found to be able to potently inhibit the tyrosine kynase activity of KIT [8]. The specific identification of GIST has become more important after the availability of Kit-selective tyrosine kinase inhibitor Glivec, especially in the treatment of high risk, unresectable and metastatic tumors.

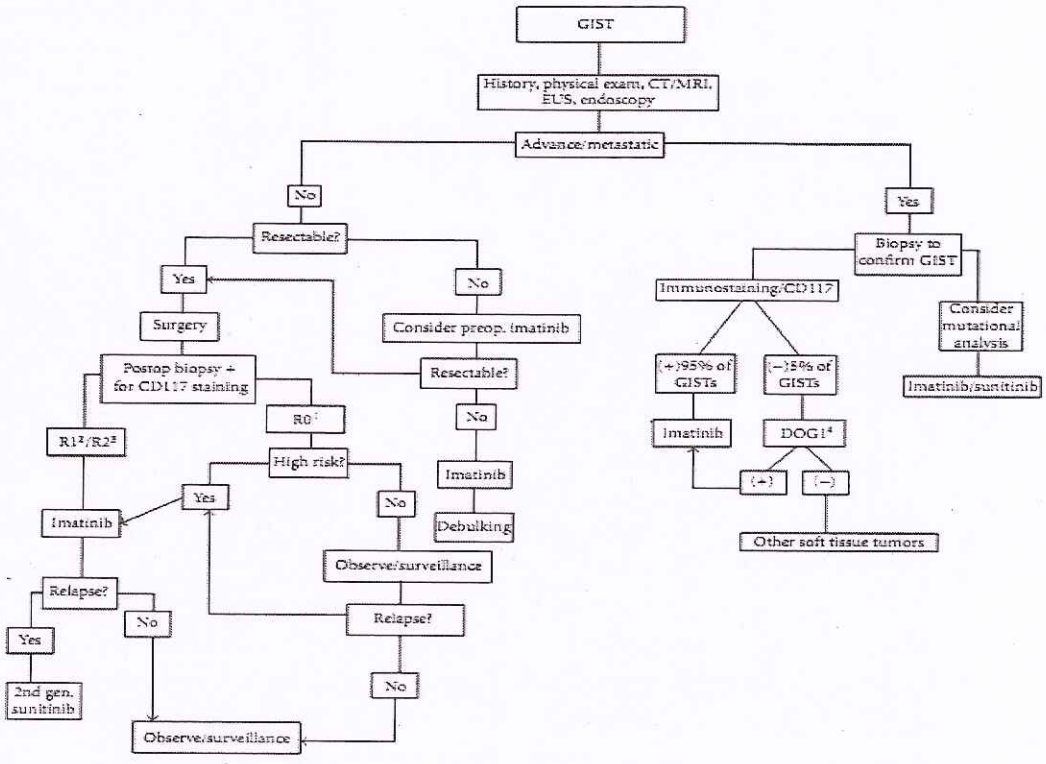

Fig 10. Schematic diagram on the stepwise approach to the patients with GIST [6].

REFERENCE

1. Roy et al. Spontaneous perforation of jejuna Gastrointestinal Stromal Tumour (GIST). Case report and review of literature, *World Journal of Emergency Surgery* 2012, 7:37.
2. Xiaohui Zhao, Changjun Yue. Gastrointestinal Stromal Tumor, *J GastroIntest Oncol* 2012; 3 (3): 189-208.
3. Stamatakos et al. Gastrointestinal Stromal Tumour: review. World Journal of Surgical Oncology 2009, 7:61.
4. Xie Hong, Haesun Choi, Evelyne M. Loyer, Robert S. Benjamin, Johnathan C. Trent, Chusilp Charnsangavej. Gastrointestinal stromal tumor: role of CT in diagnosis and in response evaluation and surveillance after treatment with Imatinib, *Radiographics* 2006, 26 (2): 481-495.
5. Bensimhon D. et al. Imaging of Gastrointestinal Stromal Tumors. *J Radiol 2009*; 90: 469-480, Elsevier Masson.
6. Christopher B. Tan et al. Gastrointestinal Stromal Tumors: a review of case reports, diagnosis, treatment, and future directions. *ISRN Gastroenterology* 2012.
7. Stattaus J. Consensus report on the radiological management of patients with Gastrointestinal Stromal Tumors: recommendation of the German GIST imaging work up. *Cancer Imaging* 2012 (12), 126-135.
8. Lamba et al. Recent advances and novel agents for Gastrointestinal Stromal Tumors. *Journal of Hematology and Oncology* 2012, 5:21.