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Case Report

Gastro Intestinal Stromal Tumor: Cases Series Report

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Abstract: Gastrointestinal stromal tumors (GISTs) are rare mesenchymal tumors of the alimentary tract. Now a day GISTs represents 0.1-3% of all gastrointestinal malignancies, making it a diagnostic challenge. Lesions are frequently located in stomach and proximal small intestine but rarely elsewhere in the abdomen. They are believed to result from mutations of protooncogenes c-Kit or platelet-derived growth factor receptor alpha polypeptide, this increase tyrosine kinase receptor activity, leading to uncontrolled proliferation of stem cells that differentiate into cells of Cajal. They can occur at any age but predominantly in middle-aged people and in elderly. We reported the cases presented to our hospital with progressively distension of the abdomen, finding in diagnostic image suggested GIST without evidence of metastasis disease, total excision was done, Cytologic and immunohistochemistry analysis confirm diagnosis of GISTs.

Keywords: Gastro Intestinal Stromal Tumor, immunohistochemistry, polypeptide.

INTRODUCTION

Stromal or mesenchymal tumors that affect the gastrointestinal tract typically appear as subepithelial neoplasms and they are classified in two groups. The most common is Gastrointestinal Stromal Tumors Group (GIST), which arise from mesenchymal stem cells programmed to differentiate into interstitial cells of Cajal in the myenteric plexus. The cells of Cajal form a complex cell network within the gastrointestinal tract wall where they function as a pacemaker system.

The GIST can arise from anywhere into the gastrointestinal tract and are frequently located in stomach (66%) and small intestine (30%) particularly in duodenum, as well as in esophagus, colon, anus and rectum (particularly in duodenum, as well as in esophagus, colon, anus and rectum.

CASE PRESENTATION

Case 1

A 63 yrs female presented to our surgical outpatient clinic department with abdominal pain for 9monthy with was on and off more marked at epigastric associated with early satiety, general body malaise with no significant loss of weight but no history of dysphagia, constipation or yellowish colour of eye. Patient was treated in lower level hospital without improving.

General Exanimation. Pale with hemogrobin lever of 7.9g/dl. Abdominal Examination. Asymmetrical abdomen, with slight distended abdomen at epigastric, with palpable mass at epigastric with slight tender, mass was mobile about 7cm to 10cm approximately. Normal finding on digital rectal examination. Blood work up was done was normal except hemoglobin level which was 7.9g/dl. Upper endoscopic was done mass was seen with was not bleeding, tissue was histology was taken.

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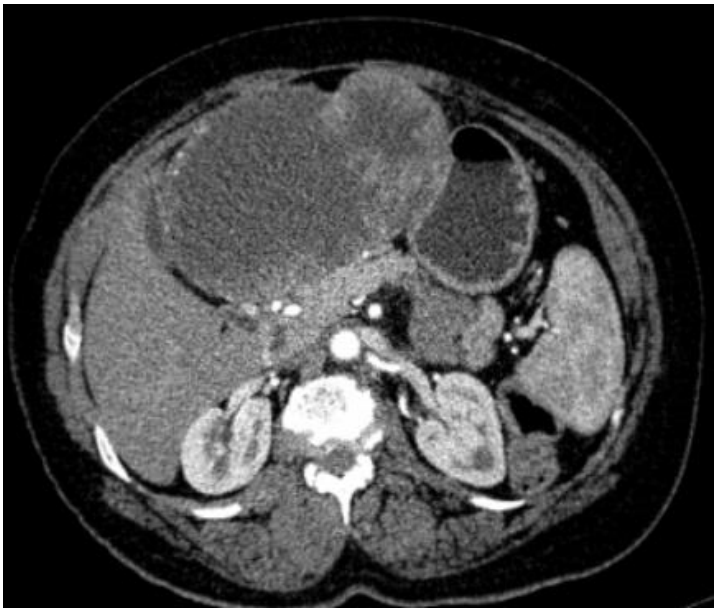


Figure 1: axial

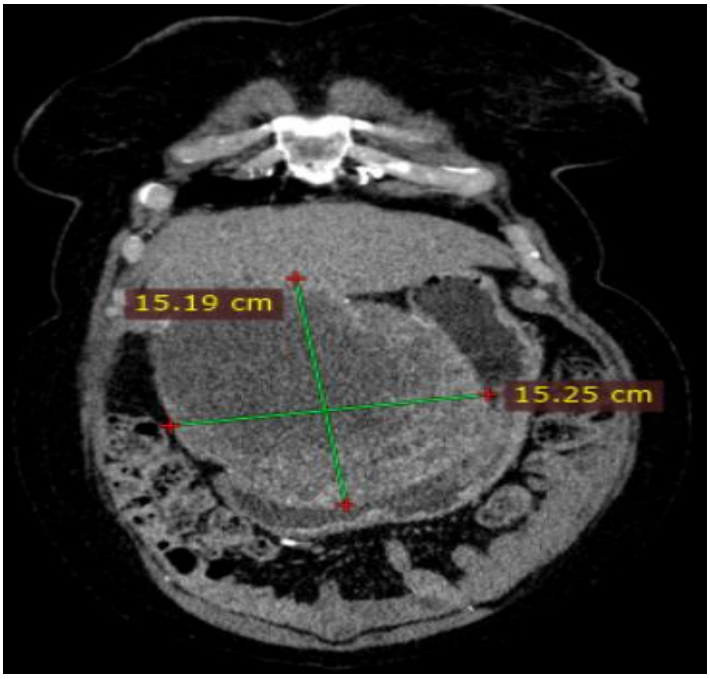


Figure 2: coronal

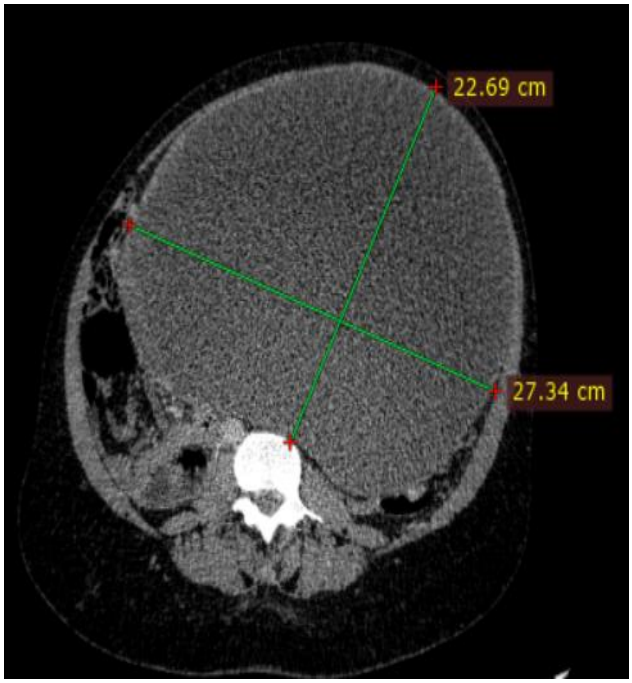
Figure 1 [axial] and figure 2 [coronal] shows a well-defined large heterogeneous, mostly cystic mass with peripheral solid component measuring 15.3x15.2cm is visualized between the left lobe of the liver and lesser curvature of the stomach. The mass is inseparably from the lesser curvature of the stomach. No surrounding fat stranding, signs of local invasion to adjacent structures or regional lymphadenopathy.

Case 2

A 61-year-old male patient, presented to our hospital with progressively abdominal distension for about 3 monthly, which was associated with abdominal pain more on epigastric area, loss of appetite and weight, but no nausea, no vomiting, no hematemesis, neither fever. His medical history was unremarkable and he has not recently used non-steroidal anti-inflammatory or steroid drugs. He does not have family history of note but was on regular medication metformin for diabetic mellitus.

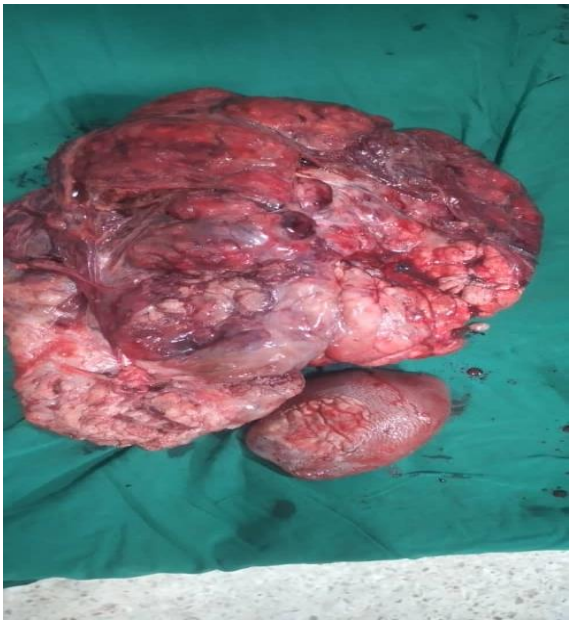
On examination patient no pale no jaundice no lower limb edema with normal blood pressure of 130/79mmhg, with pulse rate of 77bperm, with body temperature of 37.

Per abdomen examination, symmetrical abdomen distension, with traditional mark noted, abdomen move with respiration, palpable mass which is firm, mobile, non-tender with regular margin. Dull percussion note was heard and bowel sound was no appreciated.



Patient was prepared for surgery intraoperative mass measure about 34cm to 25cm in long and short diameter, and it weight about 8kg.

Mass was originated to omentum invading the part of the posterior wall of the stomach, where excision of part involved was done also mass extended to spleen where splenectomy also was done plus excision of the whole mass together with omentectomy.



In histopathology we receive a disoriented tissue biopsy specimen total measured (34x25x10) cm in greatest dimension, homogeneous greyish in color and on c/s area of hemorrhage and necrotic tissue seen. Multiple samples were taken for microscopic examination diagnosis of the lesion confirmed to be Malignant Gastrointestinal Tumor (Spindle cell type). The microscopic features showing the spindle cell tumor of variable pattern with fascicles of interlacing bundles in haphazard arrangement, area of peripheral nuclear palisading (see Figure A and B). Multiple mitosis also seen. Immunohistochemical stain CD-117 stain positive about 40% of the tumour lesion (see Figure C) and ki-67 stain more than 30% of the neoplastic cells with mitotic index (see Figure D).

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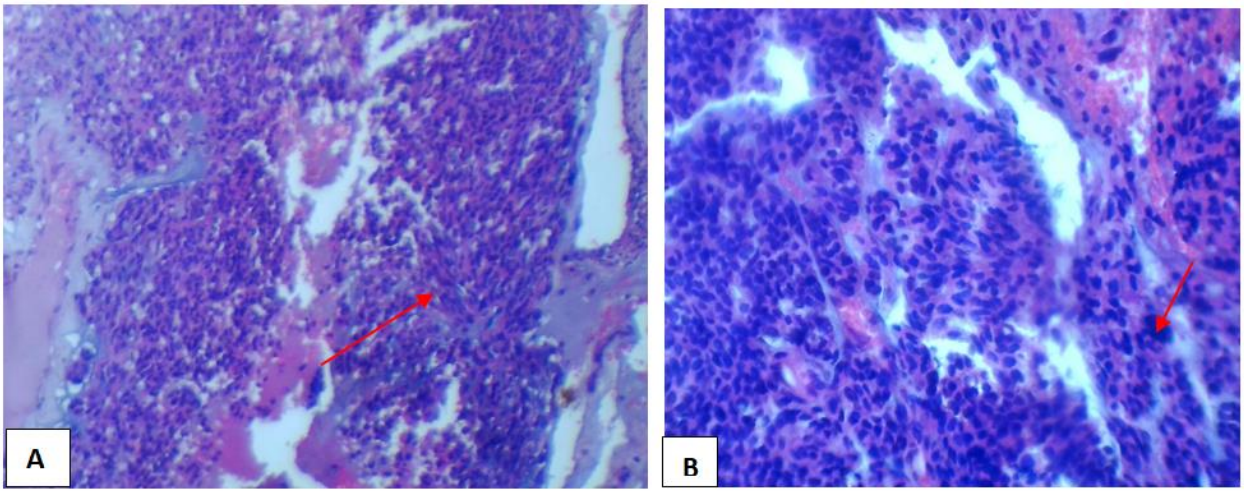

Figure A showing hypercellular hyperchromatic area of spindle cell tumor arranged in haphazard arrangement (x10 hpf). Figure B showing the spindle cell tumour with mitosis pointed by red arrow (x40 hpf) in H&E stain

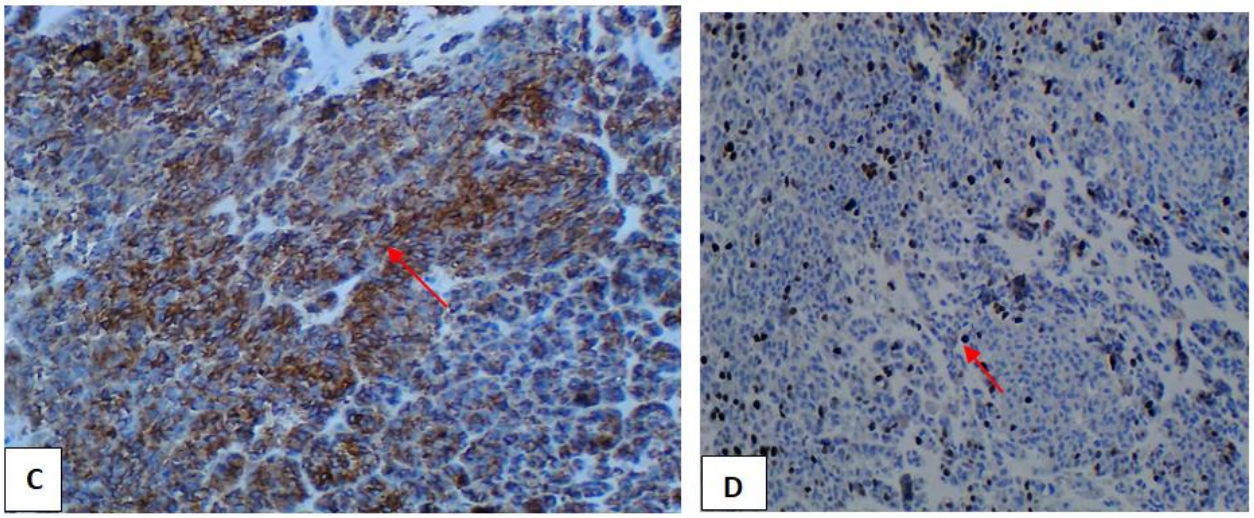

Figure C showing neoplastic spindle cell stain positive cytoplasm of CD-117 immunohistochemical stain more than 70% of malignant lesion. (x4 hpf). Figure D showing immunohistochemical stain of Ki-67 stain mitotic index of neoplastic spindle of more than 40% of malignant lesion. (x4 hpf)

DISCUSSION

Gastrointestinal stromal tumors are neoplasms with a genetic origin. They are very similar to other family oncologic syndromes like NEM 1 and 2, VHL, and Carney complex (e.g. gastric leiomyosarcoma, pulmonary, and functioning extra adrenal paraganglioma). Consequently, GIST pathophysiology follows a common pathway with other mesenchymal neoplasms of the gastrointestinal tract and so, this may lead to obscure the diagnosis or to being confused with leiomyoma or leiomyosarcoma. Immunohistochemical resources (i.e. KIT, CD117, CD34, S-100 protein, Actin, Desmin, etc.), and imaging studies are crucial for getting a right diagnosis [1]. Despite that the GIST are the most common benign not epithelial neoplasm of the gastrointestinal tract, it just represents 1% of all gastrointestinal primary tumors [2]. Worldwide incidence of 11-19.6 per million populations; we do not know incidence and prevalence in Mexico. However, in USA, recent studies estimate an annual incidence of 4000 to 6000 new cases (7-20/1,000,000 per year). Typically, GIST affects the population over 50-years old, rarely those under 40s, and the average age of diagnosis is around 63 yearold [4-6]. GISTS are characterized by staining positive by KIT and some of them by PDGFR-alpha. In 1998, Hirota et al. showed the existence of

mutations in these kind of tumors, by proving that the KIT mutation stains positive on 60---80% of GISTs cases [2, 7]. The activity of KIT tyrosine kinase receptor is regulated by ligand dependent activation. On the other hand, on GIST a gain of function mutation in the exon 11 in the juxta membrane domain of the c-Kit gene leads to the consecutive ligand-independent activation of KIT receptor kinase, which may cause tumorigenesis [2, 9].

Imatinib mesylate is a potent and selective inhibitor of tyrosine kinase (including KIT, BCR-AL, and PDGFR-alpha). By considering that GIST are not sensitive to radio or chemotherapy, the patients in whom the surgical resection was not enough have increased their survival rate since Imatinib FDA approval. Staining positive for CD117 confirms diagnosis of GIST. The absence of intense and diffuse activity for S-100 rejects melanoma, which is important because this entity commonly promotes metastatic activity in gastrointestinal tract. Tumor size by itself does not predict its biologic behavior [2].

Nowadays, imaging studies methods like endoscopy, endoscopic ultrasound, computed tomography scan, and magnetic resonance tomography. These studies have become crucial for the diagnosis of subepithelial neoplasms, such as the case of GIST [10-13]. When the imaging studies reveal suggestive features of GIST, and the tumor is considered resectable by size, localization or any other parameter, biopsy should not be performed due to the imminent risk of rupture and intraabdominal spread. Tumor size >4 cm, irregular borders, echogenicity foci and presence of cysts are suggestive features of malignancy [14, 15].

In absence of metastatic disease, the GIST curative treatment is the complete surgical resection [2, 3, 8]. The first symptom of patient was the upper gastrointestinal bleeding. Then, the tumor was revealed by endoscopy and CT scan. Moreover, the metastatic activity was discarded and in accordance with the imaging study, the biopsy was not required. Histopathologic features were compatible with GIST and immunohistochemical analysis of the tumor stained positive for KIT (DC117) in an intense way. Furthermore, the tumor stained positive for Ki-67 at 2%, this molecule is a nuclear protein present in all active phases of cell cycle (G1, S, G2 and mitosis), but is absent in cells on latent phase and undetectable during the DNA repairing process. The activity percentage of Ki-67 point out the presence of tumor proliferation (activity ≥15% is related to malignancy) [16, 17]. Due to the physiopathologic and immunohistochemical tumor features, the patient was diagnosed with gastric GIST, in accordance with the National Comprehensive Cancer Network. Surgical resection was the best treatment option for him and could be considered curative for this particular case, by having a very low risk for progressive disease (i.e. 1.9%). The patient remains well after six months following surgery. Imatinib mesylate was not indicated as neoadjuvant treatment in the case under study. This work reveals the necessity of early recognition and appropriate investigation of gastrointestinal symptoms at all age groups for excluding potential malignant causes.

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