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CASE REPORT

Gastrointestinal Stromal Tumour of the Lower end of Esophagus involving gastroesophageal Junction, a case report.

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Abstract

Gastrointestinal Stromal Tumours (GIST) are rare mesenchymal tumours of the Alimentary tract which represent 0.1 – 3% of all GIT malignancies. Lesions are frequently located in the stomach (60%) and only 1-2% in the esophagus. They are believed to result from mutation of protooncogenes c Kit or Platelet derived growth factor receptor alpha polypeptide which increases 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 & in the elderly. We are going to present a case of 30 years old male patient, admitted in our hospital with dysphagia, anorexia, regurgitation. Diagnostic studies suggested a GIST involving lower end of esophagus and cardioesophageal junction of the stomach.

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Introduction:

Gastrointestinal stromal tumors (GIST) are the mesenchymal tumors of the digestive tract, with an incidencxe of 1-3% of malignancies with this location.[1] The most frequent location is the stomach (60 -70%), followed by the small intestine (20-25%), and colon (5%) and esophagus (about 1%).[2,3] It usually occurs in patients aged 50-60 years. The size ranges from small tumours less than 1 cm, typically discovered incidentally during investigations of other diseases, up to large tumors of 35 cm (mean diameter 5 cm), with various and nonspecific symptomatology.[4-6] Regardless of size, GIST have in common histological and immunohistochemical characterstics: positive tyrosine-kinase receptor (KIT, CD117) and containing a single mutation in the KIT gene (80-85%) or platelet derived growth factor alpha PDGFRA gene (5-7%).[7] Although the majority of GIST occurs by KIT or PDGFRA activating mutations, a small subset is associated with other mutations- wild type, their production mechanism involving other intracellular signaling pathways.[8] Surgery is the main treatment, complemented by

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targeted therapy with tyrosin-kinase inhibitors like imatinib mesylate, in adjuvant or neoadjuvant therapy, when biopsy specimen is accessible.[9]

In our report we will present a case of giant esophageal GIST, significant due to clinical and laboratory investigations, to perioperative anesthetic-surgical issue and to the surgical treatment. The histopathological and immuno-histochemical tests that indicated for the diagnosis, and complementary treatment and follow-up program initiated for this patient are also presented.

Case report:

Mr. Shakil, 30 years old male patient from Rowjan, Chittagong has got admitted into our Hospital with dysphagia, anorexia, regurgitation. Gradually he became intolerant to solid & liquid food and he had been losing body weight day by day. He had no significant family history of sufferings from such type of disease. He had no history of corrosive ingestion but he had history of Endoscopy of UGIT 4 years back with completely normal findings. He is non smoker, no betel nut history. No history of alcohol or drug abuse.

On general physical examination he was found mildly dehydrated and mildly anemic. Systemic examinations were normal in all the systems.

Regarding investigations:

Endoscopy of Upper GIT – Gastric Submucosal lesion.

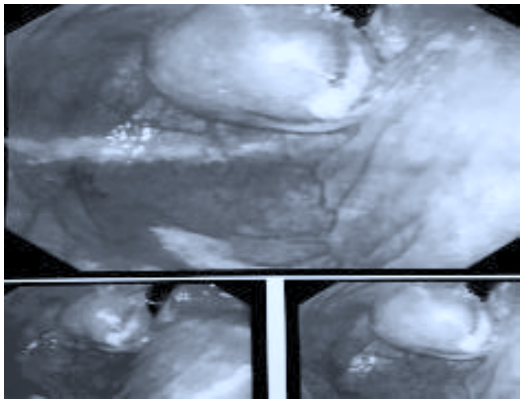

Fig.-1: *Endoscpic View of GIST*

Barium Esophagogram: Dye passed beyond the lesion. USG of whole abdomen - Oval shaped well demarcated hypoechoic soft tissue mass at cardiac end of stomach.

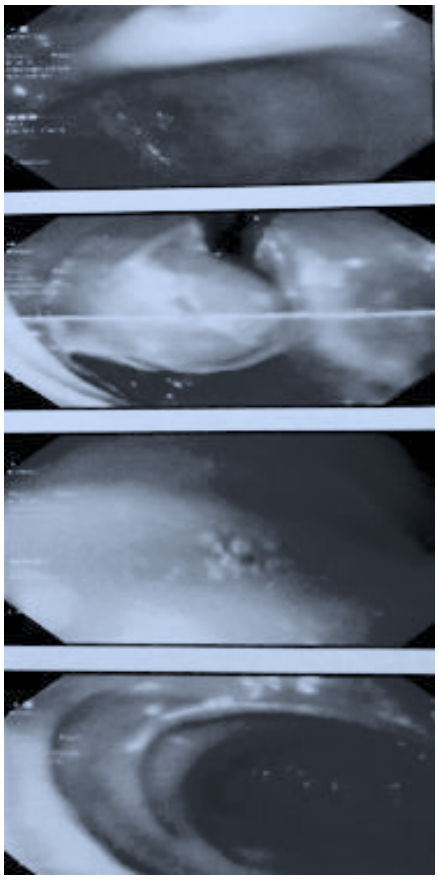

Fig.-2: *Endoscpic View of GIST*

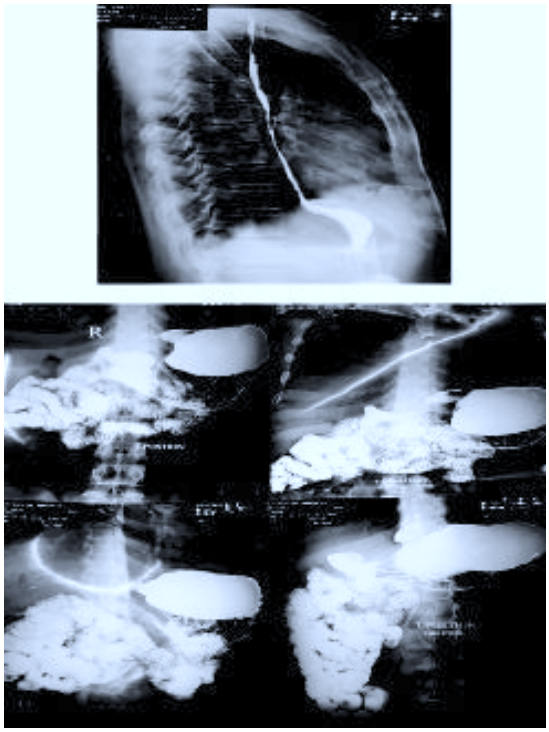

Fig.-3: *Barium esophagogram*

FNAC from GE submucosal lesion- No malignancy

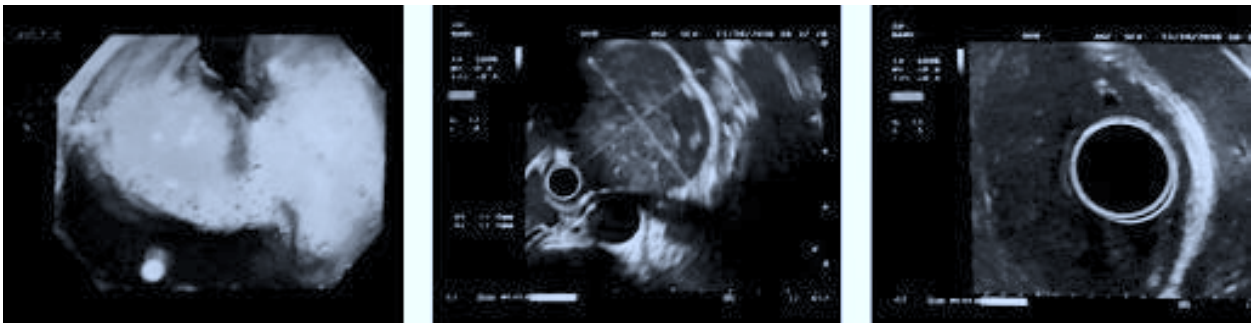

Fig.-4: *Endoscopic Ultrasonic view of GIST*

was seen, Possibility of GIST could not be ruled out. CECT Abdomen- Large hypodense poorly enhancing lesion seen at the GE junction, may be GIST. EUS – Large GIST involving GE junction.

Endosonogram – Submucosal Lesion of Stomach (GIST?).

Our clinical diagnosis was GIST at the lower end of esophagus involving Gastroesophageal junction. We formed a multidisciplinary team composed of general and thoracic surgeons, anaesthesiologists, pathologists, radiologists and oncologists.

Our Planning was Thoracotomy and access to the peritoneal cavity via phrenotomy through left sided thoracoabdominal route under GA with OLV. Anaesthesia was marked by the existance of high risk of potentially fatal accidents such as complete obstruction of the airways, cardiovascular collapse- these complications can occur in transition to the supine position, during induction of the general anaesthesia, placement of the endobronchial tubes, during positioning of the patient into right lateral decubitus position, manipulation and extraction of the tumour, and extubation. In literature, incidence of these complications in the perioperative period is between 7-20%.[10]

During surgery, the team assured jugular central venous catheter, non invasive blood pressure monitoring, selective right bronchus intubation, positive pressure ventilation, muscle relaxant along with thoracotomy. Intraoperatively the mechanical one lung ventilation was difficult but it was meticulously maintained by our anaesthesiologists' team.

Sugery was performed by left thoracoabdominal approach. After opening the thorax, phrenotomy was done and we have found a firm to almost solid globular mass in the lower end of esophagus extending up to the fundus of the stomach measuring about 10 cm x 8 cm. Macroscopically the appearance of the tumor was encapsulated

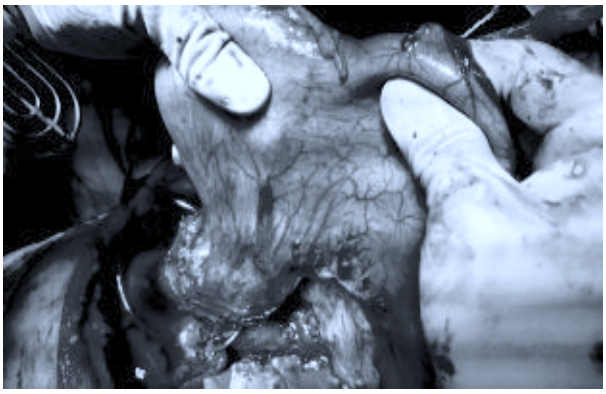

Fig.-5: *GIST after Thoracotomy*

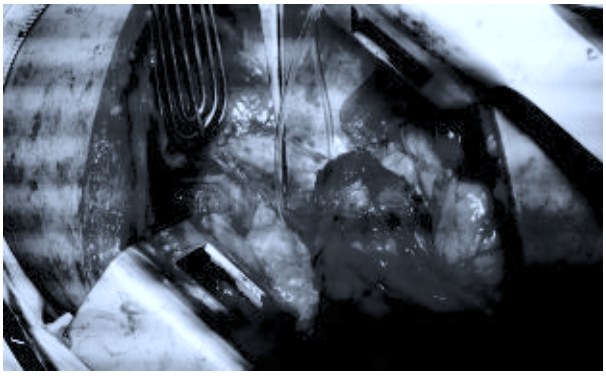

Fig.-6: GIST after Thoracotomy

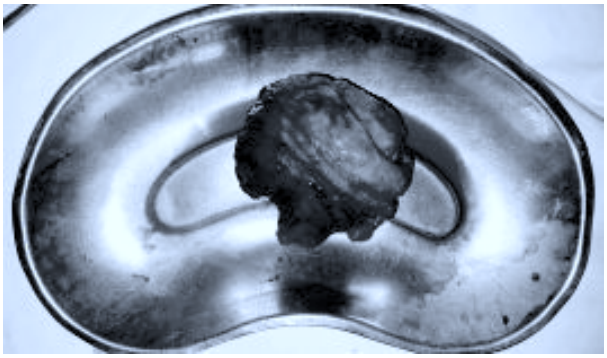

Fig.-7: *Resected GIST*

tumor of a heterogenous consistency, with the alternating areas of necrosis amd fibrous srictures. We have done esophagogastrectomy followed by esophagogastrostomy using circular stapler in the left thoracic cavity. A feeding jejunostomy was also done. After proper hemostasis diaphragm was repaired and wound was closed in layers keeping one abdominal drain and one ICT in situ.

Immediate post operative period was uneventful. Liquid diet like plain water, ORS were started from 3rd POD onward through Feeding jejunostomy Tube. On 7th POD, test meal was given orally, no anastomotic leakage was found and ICT was removed after having contrast CXR. Progressive oral food intake was started and patient didn't have any complications. Patient was discharged on 10th POD with some special advices. He was advised for not taking any solid food, bolus of food, fiber containing food and should take frequent low volume less residual food.

Resected specimen was sent for histopathological examination which revealed GIST and CD117 was positive on immunohistochemistry.

In the 1st post operative month a barium esophagogram was done which revealed passage of dye without any filling defect. There were no signs of local recurrence or metastasis at CT scans made at 6th post operative month.

About one month later, feeding jejunostomy tube was removed and he was referred to the professor of radiation oncology. Now Patient is on imatinib and is running a reasonable good food habit and his general condition is better than previous status.

Patient was advised for regular follow up with CT scans at 3 months in 1st year, at 6 months for 3 years, and annually in the next five years. Clinical and imagery follow up is very important especially in the first month from the beginning of treatment.

The appearance of local recurrence or distant metastases means imatinibmesylate resistance and treatment will be modulated according to clinical guidelines. Genetic tests are necessary and we are supporters of systematic mutational analysis in each case. It can identify the genetic profile that might offer any resistance to imatinibmesylate and orientation to the second line treatment with sunitinib maleate.

Discussion:

GIST is a kind of KIT positive mesenchymal tumors, which usually harbours activating mutations in KIT or platelet derived growth factors receptor or tyrosine kinase genes. The biologic behaviors of GISTs are diverse, varying from a small, harmless tumour nodule to a metastasizing and life threatening sarcoma.[11] Several risk criteria have been proposed for estimating the risk of tumor progression for localized GISTs.[12]

GISTs are rare accounting for 0.1-3% of all GI neoplasm.[1] The biological potential of stomach or small intestinal GIST is related to their size and mitotic activity which may also be true for the esophageal GIST as well. Esophageal GISTs commonly present with dysphagia but bleeding, perforation, back pain, anorexia, regurgitation, weight loss have been reported.[13,14] Initial testing and cytology created a diagnostic dilemma because immunohistochemistry was not advised and diagnostic reports were inconclusive.

The current case represents an extremely peculiar example of subdiaphragmatic abdominal GIST, which presented as mass lesion involving lower end of esophagus and GE junction. And posed diagnostic pitfalls with potential therapeutic consequences. Although GIST is well known in the gastrointestinal tract, thoracic region is an uncommon anatomical location for it. GIST can simulate the other tumors in the thorax. So

identification of GIST involving the thoracic area sometimes might be very challenging, especially in small biopsy samples.

GIST tumor biology allows the development to giant sizes without altering the general condition, which is a clinical characteristic of these tumors. Heterogenous appearance with solid and necrotic areas, encapsulated tumors that also compress the surrounding digestive organs are radiological characteristics which guide the clinician to the suspicion of GIST. The development from interstitial cells of Cajal does not involve the digestive mucosa and often endoscopic mucosal biopsy is negative. Lack of lymphatic dissemination of GIST is another characteristic that can be detected by imaging as absence of lymph nodes. On one hand it makes unnecessary local and regional lymph node dissection and on the other hand it allows resections with organ preservation. The clinical and imaging data may allow the suspicion of GIST and adjustment of diagnostic algorithm according to current guidelines. Being in front of a sarcoma biopsy is to be avoided, although trucut biopsy is acceptable regarding dissemination risk in the opinion of many authors. This would allow a biopsy specimen necessary to start targeted neoadjuvant treatment with tumor down staging and organ spare resections with function preservation.

Surgery is the only curative treatment far available in this type of neoplasia.[9] Surgery of this type of tumor is delicate, performed in the extracapsular plan, in order to obtain R0 resection, avoiding trauma of tumor capsule which would place the tumour in the metastatic setting. This goal can be achieved especially for tumors up to 10 cm diameter, while for larger sizes, the esophagectomy seems to be the correct oncological intervention.[15] After obtaining the biopsy specimen diagnosis is confirmed by IHC staining using a panel of monoclonal antibodies Characterstics are CD117 and DOG1. Stratification of tumour aggressiveness using the scale AFIP (Armed Forces institute of Pathology) is most often used by large volume centyers, taking into account different malignant behavior of GIST, relying on a number of parameters such as tumor size, number of mitosis, tumor site, adding tumor capsule rupture , multiorgan involvement or incomplete resection.[16] Mutational analysis comes to finalize the diagnosis, stating mutant gene which gives a better targeted treatment, tumors with exon 9 mutated KIT gene being recognized as more aggressive than the exon 11ones and known that some GISTs are resistant to standard treatment with tyrosine kinase inhibitors.[17]

Comparing mutational analysis costs with two or three months of ineffective treatment with tyrosine kinase inhibitors it is justified the use of this genetic methods for the benefit of the patient and the healthcare system. It is absolutely necessary to address each case to a multidisciplinary team that includes different specialties working with this type of pathology.[18] This can ensure correct diagnosis and therapy of these patients, according to actual clinical guidelines, applying effective and specific treatment and consistent reporting of each case.

Ethical consideration:

Informed written consent was taken from the patient for presentation and publication of the case report with accompanying images.

Conclusion:

Esophageal GISTs presenting with dysphagia is rare. Imatinib is the 1st line of drug though treatment failure has been reported where sunitinib is used. Future trials with combined or sequential use of tyrosine kinase inhibitors with other medications and personalized therapy after tumour molecular subtyping are promising in the management of GISTs. In this article we presented the issue of diagnosis and surgical treatment of a giant GIST of GE junction. We insist that such a case should be treated in a multidisciplinary team assessing the immediate anaesthetic and surgical risk and also the risk of recurrence by complete pathological and genetic evaluation, in conjunction with adjuvant or even neoadjuvant specific therapy.

Abbreviations:

GIST- Gastrointestinal Stromal Tumour; UGIT- Upper Gastro intestinal tract; USG- Ultrasonography; FNAC- Fine needle aspiration for cytology; CECT- Contrast enhanced computed tomography; EUS- Endoscopic ultrasound, POD- Post operative day; ICT- Intercostal tube; CXR- Chest X ray. OLV- one lung ventilation; GA- General Anaesthesia.; GE- Gastroesophageal; AFIP- Armed Forces institute of Pathology

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