A Targeted Approach to a Giant Gastrointestinal Stromal Tumor of the Esophagus

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Sir,

Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, accounting for 0.1 %–3.0 % of all gastrointestinal malignancies. GISTs can arise anywhere in the gastrointestinal tract: 50–70 % in the stomach, 20–40 % in the small bowel, 5–15 % in the colon and rectum and rarely in the mesentery or retroperitoneum. Esophageal GISTs are extremely uncommon, representing approximately 5 % of GISTs with a majority occurring at the esophagogastric junction (GEJ). [1, 2] We report a case of a borderline resectable GIST of the lower esophagus, treated with neoadjuvant imatinib mesylate (IM) which ultimately resulted in a successful R0 resection.

A 50-year-old lady with no co-morbid conditions was referred to us for progressively worsening dysphagia of 6 months. An upper gastrointestinal endoscopy revealed a circumferential ulcerated growth in the lower end of the esophagus, from 30 to 36 cm, which was seen extending to the GEJ. An endoscopic biopsy was suggestive of a spindle cell neoplasm, which on immunohistochemistry correlation (CD117 and CD34 positive, Ki-67–30 %) was suggestive of a high grade GIST. Computerized tomography (CT) scan of the chest and abdomen revealed a large lobulated, hetero-dense, poor-

ly enhancing mass (10.9×7.4×16 cm) in the thoraco-abdominal region, involving the lower end of the esophagus, GEJ, posterior stomach and extending along the retroperitoneum to infiltrate the body and tail of pancreas, causing a mass effect on the left kidney. (Figures 1a and 2a)

After thorough discussion of the issues of borderline resectability/unresectability, the patient consented to attempt to downstage the tumor by neoadjuvant treatment with IM. (400 mg/day) An interim CT scan at two months revealed a regression of the tumor diameter, IM was hence continued for another 4 months. A follow-up CT at 6 months revealed a regression of the tumor diameter from 10.2 cm to 4.2 cm. (Figures 1b and 2b) Resection of the residual tumor was deemed feasible and the patient was taken up for an exploratory laprotomy. The residual tumor was found to be densely adherent to a portion of the distal body of the pancreas; a distal pancreatico-splenectomy had to be combined with an esophago-gastrectomy via a transhiatal approach to attain a R0 resection. (Figures 3 and 4) The bowel continuity was restored using a gastric tube conduit through the posterior mediastinum. Histopathological examination of the resection specimen confirmed a GIST with extensive post treatment changes and clear margins. The postoperative course was uneventful, after recovery the patient continued adjuvant therapy with IM for 6 more months, she is currently disease free.

GISTs are thought to arise from the intestinal cells of Cajal, which are intestinal pacemaker cells that regulate peristalsis. Considerable progress has been made

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Fig. 1 **a-** Axial CT scan at presentation (Maximal diameter-10.9 cm). **b-** Axial CT scan following 6 months of Imatinib Mesylate (Maximal diameter-4.2 cm)

Fig. 2 **a-** Coronal CT scan at presentation. **b-** Coronal CT scan following 6 months of Imatinib Mesylate

Fig. 3 Specimen photograph (Esophago-gastrectomy along with distal pancreatico splenectomy)

recently in our understanding of the natural history, risk stratification, and molecular biology of GIST. The vast majority of GISTs contain an activating mutation in either the KIT or platelet-derived growth factor-A gene. GIST is highly responsive to several selective tyrosine kinase inhibitors.

Despite the efficacy of targeted therapy, surgery remains the only curative primary treatment and cures >50 % of GIST patients who present with localized disease. Many authors agree that loco regionally advanced tumors or those poorly positioned which require an extended/multi-organ resection should be considered for neoadjuvant treatment with IM and should be re-evaluated for a possible curative resection. [3–5] This approach has been proven to be safe and feasible even in the management GIST of the esophagus as was also seen in our patient. In conclusion a multimodal approach with neoadjuvant administration of IM is emerging as a viable treatment strategy for borderline

Fig. 4 **a**- H&E x40- Shows tumor composed of fascicles and sheets of spindle cells with dark staining nuclei in a myxoid background. **b**- IHCx40- Tumor cells showing immunopositivity to CD-117. **c**-

IHCx40- Tumor cells showing immunopositivity to CD-34. **d**- IHCx40- 30 % of tumor cells showing strong nuclear positivity to ki-67

resectable esophageal GIST, although the dose and duration have not been clearly established. The long-term impact of this approach on survival is presently under investigation in multi-center prospective randomized trials.

Competing interests None declared.

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Ethical approval Not required.

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