Gastrointestinal Stromal Tumours: a Case Report and Recent Concepts

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Introduction
Gastrointestinal stromal tumours (GIST) comprise 1% of all the gastrointestinal tumours.1 GIST consists of several different types and the biological behavior ranges from completely innocuous to highly malignant metastasizing tumour. Gastric leiomyosarcoma is a form of malignant GIST.2 Recently, new concepts have evolved in the pathogenesis of these tumours.

Case Report
A 40 years old female was referred for upper gastrointestinal endoscopy. Her complaint was recurrent haematemesis for the last 3 months. On examination she was severely anemic; rest of her examination was unremarkable. No mass or visceromegaly was detected on examination. Endoscopy showed a hemispheric 5 cm swelling on greater curvature near the junction of body of stomach with antrum. There was a central area of ulceration (Figure 1). Endoscopic findings suggested a leiomyoma. Endoscopic biopsies were taken. Histopathological examination showed a tumor composed of round to ovoid cells arranged in diffuse sheets. No pleomorphism or mitosis was seen and diagnosis of gastrointestinal stromal tumour (GIST) of epitheloid leiomyoma type was made. Chest X-ray showed no tumour metastasis and ultrasound abdomen was unremarkable.
Patient was operated, tumour was excised and partial gastrectomy with end to end anastomosis was performed. Gross examination of the surgical specimen showed part of wall of stomach containing a hemispheric nodule measuring 5.5 x 4.5cms with central area of ulceration (Figure 2). Histopathological examination revealed a large tumour centered in the submucosa and muscularis layer. The tumour was composed of spindle to oval cells with abundant eosinophilic to clear cytoplasm. Nuclei were round to spindle shaped with moderate pleomorphism. Tumour cells were arranged in fascicles and diffuse sheets. The tumour was penetrating the muscularis propria and reaching perimuscular tissue in one area. The tumour also extended to mucosa causing ulceration. Mitotic count per 50 high power field (HPF) was 10. Taking together the size, cellularity, pattern of invasion and mitotic count, a diagnosis of a malignant GIST (leiomyosarcoma) type was made (Figures 3 and 4). Patient made uneventful recovery and was discharged home with advice for follow up.

Discussion
Gastrointestinal stromal tumours are the most frequent mesenchymal tumours of gastrointestinal tract, constituting 1% of all the G.I. tumours.1 Approximately 2/3 of all GIST occur in the stomach. The reported incidence of gastric stomal tumours is quite variable ranging from 0.18% to 46% of the total gastric tumours based on autopsy or surgical resection specimens.2 The peak incidence of this tumour is in the adulthood (fifth and sixth decade) and young people under the age of 40 are very rarely involved. There is not a clear cut gender predilection. The risk factor and etiology of GIST remain undetermined.3
GIST depict a broad spectrum of differentiation ranging from completely differentiated tumours with myoid (i.e., leiomyoma and leiomyosarcoma), neural (schwannoma) or ganglionomas to tumour with incomplete, mixed or totally lacking differentiation.3 GIST may show a range of size (from mm to over 30 cm) arising within the muscularis propria of the gastrointestinal tract.
Cytologically, the tumour cells show highly varied appearance spindle shaped, round (epitheloid), plasmacytoid, mixoid, signet ring, granular or multinucleated with other benign or malignant cytologic features. The expression of transmembrane receptor tyrosine kinase KIT, which is identified as the CD 117 antigen and is the product of cKIT proto oncogene, is a peculiar feature of GIST.
Affected patient may be totally asymptomatic. Symptoms are generally variable according to the tumour size and localization. Abdominal pain or bleeding is the most frequent symptom.
The malignant potential of these tumours is often classified into 3 categories, no malignant potential, low malignant potential and high malignant potential.4 High risk factors for malignancy include size greater than 5 cm, greater than 5 mitosis per 50 HPF, tumour necrosis, nuclear pleomorphism, dense cellularity, microscopic invasion of the lamina propria or blood vessels and an alveolar pattern in the epitheloid

variant.5 On endoscopy, gastric stromal tumours often have a central umblication or ulceration and many appear dumbbell shaped.There is consensus on the fact, that chemotherapy and radiation are lacking any efficacy in GIST treatment. Surgery is the primary modality. The finding that GIST are characterized by the expression of the transmembrane receptortyrosine kinase KIT, has recently suggested new alternative treatment approach to advanced disease. Imatinib is a tyrosine kinase inhibitor that selectively inhibits various tyrosine kinases. The role of this drug in the preclinical experiences showed rapid inhibition of KIT phosphorylation, with decrease cellular proliferation and induction of apoptosis after exposure of GIST cells.6 Clinical application of this drug in metastasized disease has been encouraging.

We tried to investigate our case for possible Carneys triad which is the association of the GIST with pulmonary chondroma and extra-adrenal paraganglioma.7 We could not identify the associated tumours. In our case endoscopic biopsy did show the tumour cells. Usually these tumours are missed on endoscopic biopsies as these biopsies take bite of mucosa only while the tumours are deep seated. However, taking second biopsy from the first biopsy side may increase the yield as in our case. Moreover, this tumour was malignant and had already invaded the mucosa. Surgical option was chosen due to recurrent haematemesis and keeping in mind the tumour size with possible malignant potential. Surgical excisional biopsy did confirm the malignancy. The patient did not have any metastatic disease but regular follow up would be mandatory.

References

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