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CASE REPORT

# Pre-Operative Diagnosis Of Gastrointestinal Stromal Tumour Of Stomach By Endoscopic Biopsy: Report Of Two Cases

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**ABSTRACT**

Gastrointestinal stromal tumor (GIST) is a rare mesenchymal tumour of the gastrointestinal tract. Submucosal GIST grows most frequently towards the lumen of the gut along with attenuated, degenerated or regenerative proliferative epithelium, with bridging folds, and may be endoscopically misdiagnosed as adenocarcinoma. Pre-operative diagnosis can be done by endoscopic ultrasound guided fine needle aspiration cytology. However, diagnosis by endoscopic biopsy is rarely reported. We report here, two cases of GIST that were diagnosed by endoscopic tissue biopsy and confirmed by examination of the resected mass

**Key words**
Endoscopic biopsy, Gastric, GIST

**Key messages –**

1. GIST can be diagnosed by endoscopic biopsy
2. Larger and deeper biopsies are helpful.
3. Mesenchymal proliferation in deeper areas of endoscopic biopsy should be evaluated properly to avoid the misdiagnosis of GIST as adenocarcinoma, due to regenerative changes of overlying mucosa, as GIST and adenocarcinoma have different management and prognosis.

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## Introduction

INTRODUCTION

Gastrointestinal stromal tumours (GIST) are rare mesenchymal tumours of the gastrointestinal tract. They constitute only 0.1-1% of all G.I. malignancies. The stomach is the most common site of localization (50%-70%), followed by small intestine (20%-30%).1 They are believed to arise from the interstitial cells of 'Cajal' (the pace maker cells of G.I. tract). They can exhibit one of the two growth patterns. In the endoenteric growth pattern, tumours tend to be submucosal or intramural. These are more likely to ulcerate and bleed, leading to an early diagnosis. Tumours with an exoenteric pattern grow more slowly, leading to a late diagnosis.2 Submucosal GIST most frequently grows towards the lumen of the gut, along with attenuated, degenerated or regenerative and proliferative epithelium with bridging folds, and may be endoscopically misdiagnosed as adenocarcinoma. Pre-operative diagnosis can be done by endoscopic ultrasound guided fine needle aspiration cytology. 3 However, diagnosis by endoscopic biopsy is rarely reported.4 We report here, two cases of GIST that were diagnosed by endoscopic biopsy and confirmed by examination of the resected mass.

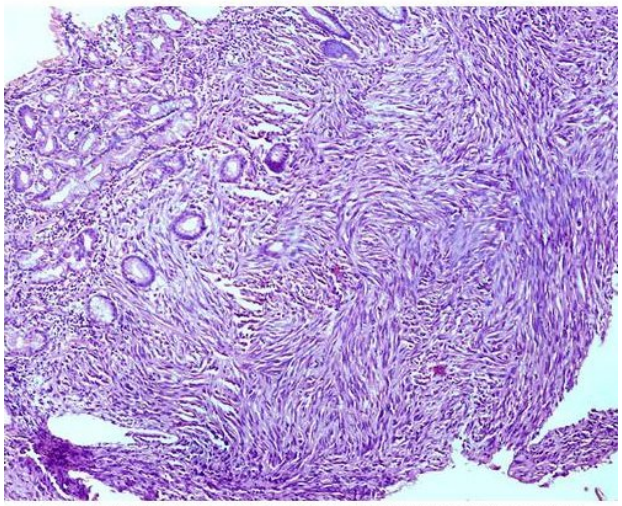
CASE REPORTS

Case 1:

A 48 years old male presented with increasing weakness, pallor and upper G.I.symptoms. Routine haematological and biochemical investigations were within normal limits. Upper gastrointestinal endoscopy was done by an upper G.I. (Olympus GIF-130) endoscope. On endoscopic examination, an irregular growth was found in the fundus, on

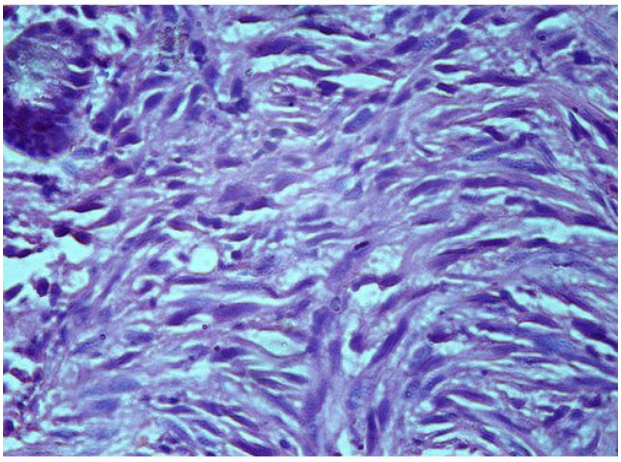
greater curvature. The surface was partly smooth and partly covered with irregular mucosal folds. Multiple endoscopic biopsies were taken by jumbo biopsy forceps and sent for histopathological examination with the differential diagnosis of (i) carcinoma stomach (ii) mesenchymal tumour. Sections from endoscopic biopsies showed gastric mucosa with hyperplasia of the gastric pits, and regenerative changes in the lining epithelial cells in the form of mild pleomorphism, loss of polarity, and prominent nucleoli. In some pieces, proliferation of spindle shaped cells was seen in the deep lamina propria. At places, these cells were seen extending into the superficial lamina propria with ulceration of the lining epithelium. [Table/Fig 1] Cells were arranged in bundles, having a pale eosinophilic cytoplasm with an elongated blunt ended nucleus. Foci of epithelioid cells were also seen in between the spindle shaped cells. Three to four mitotic figures/30 HPF were seen. [Table/Fig 2] A provisional diagnosis of benign mesenchymal tumour - probably GIST, was made, that was further confirmed by CD117 positivity on immunohistochemistry. [Table/Fig 3] The patient was operated, and a mass of 20 x 10 x 6cm was removed after partial gastrectomy. The cut surface showed a central area of necrosis.[Table/Fig 4] Histopathology with immunohistochemistry showed the same picture as in the endoscopic biopsy tissue. The proliferation of spindle cells was confined to the submucosa only. Muscularis propria was not involved.

**Table/fig 1**



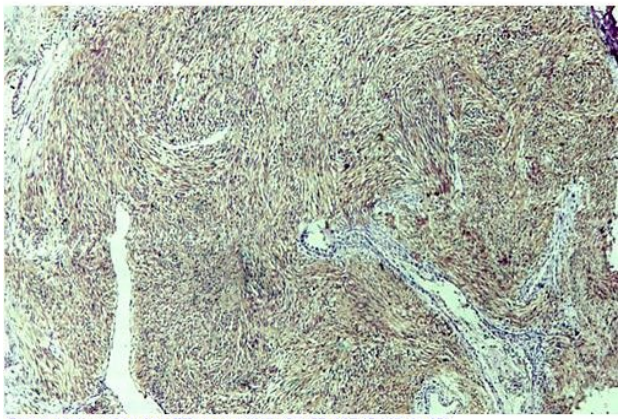
Section from endoscopic biopsy of case 1 showing proliferation of spindle shaped cells in lamina propria with ulceration of lining epithelium.(H&E x 40)

**Table/Fig 2**



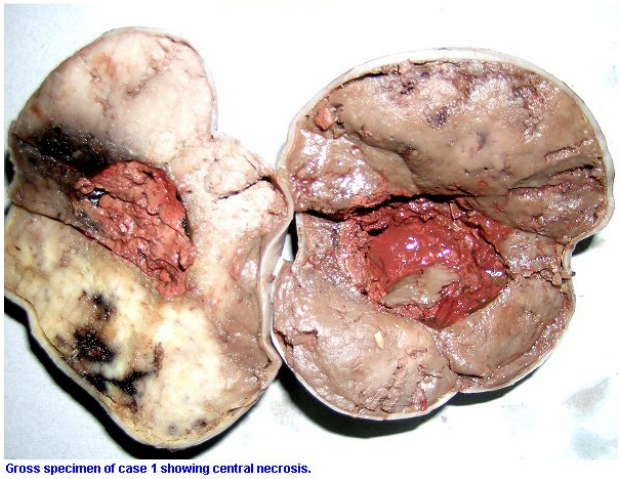
Higher magnification of the same section showing spindle shaped cells arranged in bundles, having pale eosinophilic cytoplasm with elongated blunt ended nucleus. (H&E x 400).

**Table/Fig 3**



Same section showing diffuse positivity for CD 117 (C-kit). (x 40)

**Table/Fig 4**



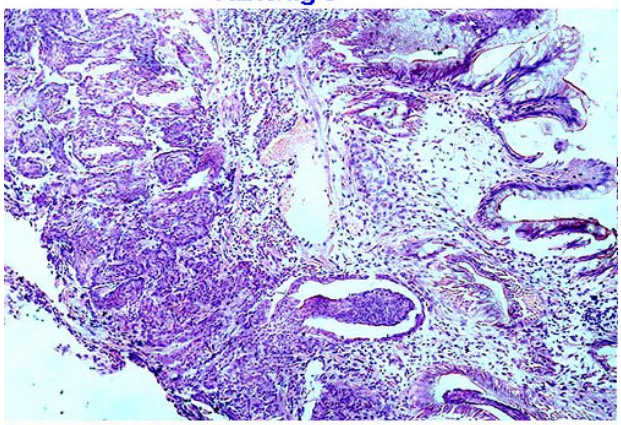
Gross specimen of case 1 showing central necrosis.

Case2:

A 70 years old male presented with increasing weakness and upper GI symptoms. Routine investigations were normal. Endoscopy showed a mass with irregular mucosal folds in the antral area. Multiple endoscopic biopsy specimens taken with the help of jumbo biopsy forceps were sent for histopathology, with a provisional diagnosis of

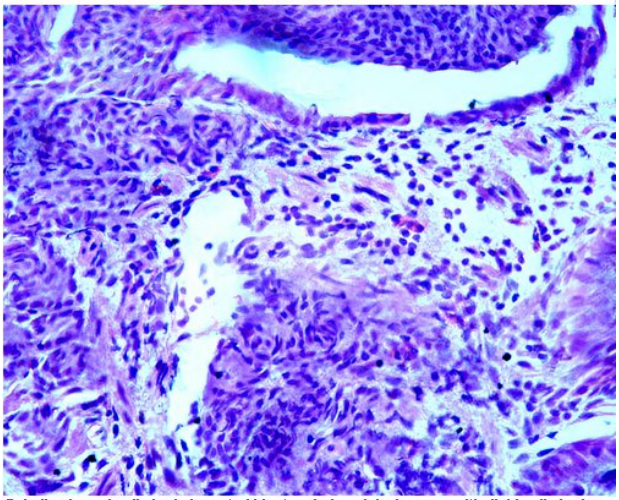
adenocarcinoma. Sections from biopsies showed hyperplastic gastric mucosa with clumps of dark cells in the deeper part of tissue highly suspicious of adenocarcinoma / neuroendocrine tumour. A deeper section showed proliferation of spindle shaped and epithelioid cells in bundles and clumps in the deep lamina propria, at places protruding into the gastric pits. The spindle shaped cells had elongated blunt ended nuclei, whereas the epithelioid cells had abundant eosinophilic cytoplasm with round to ovoid nucleus. Less than two mitotic figures /HPF were seen [Table/fig 5] and [Table/Fig 6]. Positivity for CD117 helped in confirming the diagnosis as GIST. The patient was operated. Pre-operatively, a mass of 15 x 10 x 5cm was removed, and diagnosis of GIST was confirmed by histopathology and immunohistochemistry. Proliferation of spindle cells was mainly localized in the submucosa, with evidence of infiltration of muscularis mucosa, mucosa, and muscularis propria at places.

**Table/fig 5**



Deeper section from 2nd case showing proliferation of spindle shaped and epithelioid cells in bundles and clumps in deep lamina propria, at places protruding in the gastric pits.(H&E x40)

**Table/Fig 6**



Spindle shaped cells had elongated blunt ended nuclei whereas epithelioid cells had abundant eosinophilic cytoplasm with round to ovoid nucleus.(H&E x 100)

## DISCUSSION

GISTs are rare neoplasms with an incidence of 0.1-1% of all GI malignancies, with unique histological, immunophenotypic and molecular features. The age onset ranges between the 4th and 6th decade, with no sex predilection. Most GISTs are symptomatic, and may present with vague GI symptoms as was seen in the above two cases. Epidemiological data regarding the incidence and prevalence of these tumours is not well documented due to lack of well defined pathological criteria for diagnosis and grading of these tumours, over the past few decades. Most of these tumours were either labeled as benign or stromal tumours of uncertain malignant potential (STUMP), with increase in the size of the tumour and number of mitosis.5 Though benign GIST outnumbers malignant GIST by the ratio of 10:1,the malignant potential of benign tumours ranges from 3%-38%.1 Hence, early diagnosis and close follow up becomes mandatory.

Extensive Medline search shows that pre-operative diagnosis of GIST is difficult, and the most accurate technique till date, has been endoscopic ultrasound guided FNAC 3, that could not be done in the above cases due to non-availability of the equipment. Only one report describing the preoperative diagnosis by endoscopic biopsy has been documented.4 Accurate diagnoses of sub mucosal lesions by endoscopic biopsies is usually difficult. Many methods like use of jumbo biopsy forceps and 'bite-on bite technique' are used for obtaining larger pieces and sampling of deeper areas. Advent of submucosal resection technique, further helped in diagnosis and treatment of submucosal lesions.6 In a recent study, Cantor et al compared the yield of forceps biopsy by using jumbo biopsy forceps and Bite-on bite technique with endoscopic submucosal resection, and found a significant difference ($P < 0.0001$) in the yield of correct diagnosis of sub epithelial lesions.[7] In the above cases, a preoperative diagnosis could be done by endoscopic biopsies, only because mucosa was infiltrated in both the cases. Reports of endoscopic removal of small submucosal tumours and treatment with the drug Imatinib mesylate, further stresses the need of correct preoperative diagnosis.[6-9]

In both cases, the sub mucosal GIST was mimicking adenocarcinoma endoscopically, due to the presence of irregular mucosal proliferation over the tumour mass. However, in the biopsy specimen, the mesenchymal proliferation at a deeper level, with spindle shaped cells and epithelioid cells in bundles and clumps, helped us to reach a

provisional diagnosis of GIST, that was further confirmed by immunohistochemistry(CD 117+ve). Based on our diagnosis, tumours were surgically resected in both the cases, and the diagnosis was further confirmed. Only drawback of preoperative diagnosis by endoscopic biopsy is that, it is insufficient for grading and predicting the behavior of the tumour. However, infiltration of lamina propria, number of mitosis, and a correlation of histological features with good radiological assessment regarding size, may help. Campbell et al have observed that a clear cut invasion of lamina propria, if observed histologically, is highly suggestive of malignancy.[1] In the present study, both cases had invasion of lamina propria, and their tumour size was > 10 cm, that indicated a poor prognosis despite absence of pleomorphic changes and number of mitoses being in the range of borderline (case1) and benign (case2) according to Campbell et al.1 Newman et al proposed grading of GISTs on the basis of cell type, nuclear pleomorphism and mitotic figures.[10]

From the above case reports and discussion, it is obvious that a proper endoscopy with larger biopsies that include deeper proliferative elements, may be helpful in the preoperative diagnosis of sub mucosal GISTs. Mesenchymal proliferation in deeper areas of endoscopic biopsy should be evaluated properly, to avoid the misdiagnosis of GIST as adenocarcinoma due to regenerative changes of overlying mucosa, as GIST and adenocarcinoma have different management and prognosis. Furthermore, in smaller submucosal lesions, treatment by endoscopic removal/Imatinib may even prevent the patient from undergoing surgery.

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