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Case Report

GIST: Institutional Experience at SRMS–IMS, India

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Abstract

Gastro-Intestinal Stromal Tumors (GIST) is a malignant, non-epithelial, mesenchymal tumor of the digestive tract that is not uncommon in clinical practice nowadays; diagnosis being based upon immuno-histo-chemical analysis of the resected or biopsied (FNAC) specimen. Abdominal lump with or without intra-luminal bleed is a common mode of presentation. Early diagnosis and appropriate management with surgery and/or Imatinib therapy improves recurrence free survival and may impact overall survival. We present here our institutional experience of four patients, admitted in Onco-Surgery Dept., with pain abdomen and upper/lower gastro-intestinal bleed, which, on subsequent workup were diagnosed to be cases of GIST, were appropriately managed according to their disease stage and show recurrence–free survival on follow–up.

Keywords

GIST, CD-117, melena, Imatinib.

Introduction

GIST (Gastro-Intestinal Stromal Tumors), although rare, found mostly in stomach (~60%) and small intestine (~25%), are the most common mesenchymal tumors of the gastro-intestinal tract (~80%) . Other less common locations include colon and rectum, mesentery and omentum, esophagus (4–6); rarer still are those found in the duodenal ampulla, appendix, gall bladder, genito-urinary tract and “extra intestinal–GISTs” (eGIST) (7,8). Incidence of GIST in India is unknown, but might parallel the world–wide increasing trend, mainly due to increased recognition or screening, or true increased incidence of GIST (9).

Based on their histologic features (long fascicles of spindle cells ± epithelioid cells) and immuno-histo-chemical properties (CD–117 staining, which is tyrosine kinase receptor KIT, in ~85%), GISTs are postulated to arise from the interstitial cells of Cajal (ICC) or their stem cell precursors, components of intestinal autonomic nervous system, serving as intestinal pacemakers. In KIT–negative tumors (PDGFRA in ~5–15%, WT <5%) (10–13), diagnosis rests on histologic features alone. First described by Mazur and Clark in 1983, as non-epithelial mesenchymal tumors, extensive studies have been undertaken since regarding its molecular biology (3,14). Until the last decade, such lesions were frequently misclassified as leiomyoma/sarcoma due to lack of definitive objective criterio (5,15).

A patient of GIST is usually between 40 and 80 years age, either sex (M/F = ~1), with no racial or ethnic predilection (2,16) ; rarely a child, with a familial syndrome or part of Carney’s triad, with typically different clinical presentation and probability of lymph node metastases (17,18). Symptomatic GISTs (~69%), influenced by size and tumor location, can present with life–threatening bleed (intra-luminally in bowel, as melena or intra—peritoneally), or intestinal obstruction leading to perforation. GISTs >6cm diameter may be palpable and produce symptoms of pressure or pain (3,19); smaller tumors present with symptoms of chronic anemia and associated fatigue or remain asymptomatic (16) ; or occur as an incidental finding at another surgery (~21%) (2,13,16).

Approximately 25% of gastric and 50% of small intestinal GISTs are clinically malignant, with metastases to liver, peritoneum and omentum, etc. at diagnosis; lymph nodes and extra—abdominal sites being rarely involved (<5%) (20–22).

Diagnosis is initially by imaging study (ultrasonography (USG) or computed tomography (CT) or magnetic resonance imaging (MRI) scan of the abdomen and pelvis, in a patient with above symptoms. Primary GISTs typically present as well–circumscribed masses within the walls of hollow viscera. On endoscopy of the upper/lower GI tract, primary GISTs may appear as submucosal lesions, with/ without ulceration. Endoscopic Ultra Sound (EUS) guided
fine-needle aspiration (FNA) is not consistently diagnostic; and pre-operative biopsy may rupture a suspected GIST. Immunohistochemical staining with CD117/KIT, CD34 Protein Kinase C Theta, DOG–1 (Discovered on GIST – 1), are useful in diagnosis (3–5,23,24).

Of the three established prognostic factors (Fletcher’s criteria: tumor size, mitotic index and tumor site of origin), “mitotic count” is the most important (6,8); additional factors of lesser significance are indicated in other studies (later also, modified NIH, AFIP and TNM) (25,26). The ideal margin of resection is not known; R0 resection has better prognosis, but, no data to confirm longer survival (5). Wedge resection with clear margins suffices for localized lesions; malignancy (invasion of adjacent structures) demands en-bloc resection of involved surrounding organs (27). Regular six-monthly and annual surveillance is advised after resection. Recurrence is common (~50%) around a median of 24 months post-op, despite patients undergoing a macroscopically complete resection (1,2,28).

Imatinib mesylate (first-line tyrosine kinase inhibitor) therapy in neoadjuvant / adjuvant setting increases two-year recurrence–free survival rate; optimal duration of treatment is yet to be determined. Sunitinib (a second-line TKI) is used in Imatinib resistant / intolerant cases. In spite of no evidence of superior overall outcomes, cyto-reductive surgery for resectable advanced or

<table>
<thead>
<tr>
<th>Pt. SNo.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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</thead>
<tbody>
<tr>
<td>Pt. Particulars (Age/Sex)</td>
<td>50y/M</td>
<td>70y/M</td>
<td>50y/M</td>
<td>40y/M</td>
</tr>
<tr>
<td>Presentation / Primary Symptom</td>
<td>Gastric Outlet Obstruction</td>
<td>Massive Hematemesis</td>
<td>Epigastric Pain &amp; Generalized Weakness</td>
<td>Epigastric Pain &amp; Melena</td>
</tr>
<tr>
<td>Mode of Diagnosis / Evaluation</td>
<td>UGIE</td>
<td>Gastric outlet obstruction, biopsy-inconclusive</td>
<td>Cardia to lesser curvature growth with extensive bleeding, biopsy-not taken in view of bleeding</td>
<td>Growth in distal body and antrum, biopsy-GIST</td>
</tr>
<tr>
<td>CECT Abdomen</td>
<td>Pyloro-antric thickening, no regional nodes, no metastasis</td>
<td>Fundus, cardia to lesser curvature growth, no regional nodes enlarged, no metastasis</td>
<td>Body to antrum of stomach thickening present, multiple bilobar liver metastasis</td>
<td>Periampullary region bulge present with ulceration in duodenum, biopsy-GIST</td>
</tr>
<tr>
<td>Location of GIST</td>
<td>Pyloro-antral region</td>
<td>Proximal stomach</td>
<td>Body of stomach</td>
<td>Pancreatic Head</td>
</tr>
<tr>
<td>Size</td>
<td>&gt;5cm</td>
<td>&gt;10cm</td>
<td>&gt;10cm</td>
<td>5–10cm</td>
</tr>
<tr>
<td>Primary treatment</td>
<td>Distal gastrectomy</td>
<td>Total gastrectomy</td>
<td>Imatinib</td>
<td>Imatinib</td>
</tr>
<tr>
<td>Histopathology, Immunohistochemistry /Grade</td>
<td>CD117 +, low</td>
<td>CD117 +, high</td>
<td>CD117 +</td>
<td>CD117 +</td>
</tr>
<tr>
<td>Adjuvant treatment (Imatinib)</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Follow up/ recurrence</td>
<td>10 months, No</td>
<td>9 months, No</td>
<td>9 months</td>
<td>1 month</td>
</tr>
</tbody>
</table>

Table 1: GISTS at Onco—Surgery Dept., SRMS–IMS (Sep 2014 – Jun 2015)
metastatic disease for disseminated solid tumors may be attempted\(^\text{24-29,30}\).

**Our Experience**

In the backdrop of this information, we would like to present these four cases that we have managed in this institution in the recent past 10 months (September 2014 – June 2015).

**Observation and Discussion**

All patients in our experience (Table 1) were middle aged (40 to 70 years) males, presenting with the most common symptom, i.e. upper gastro-intestinal bleed (hematemesis and/or melena). Stomach was the most common site as in other studies, with one rare case of pancreatic head mass. Metastases were most commonly to liver with none having lymph node involvement (CECT view as in Figure 1). No family history could be elicited in any of the patients. All of the GISTs were morphologically spindle cell tumors with CD117 positivity and size >5cm. Potentially resectable GISTs were treated surgically (excised specimen in Figure 2), followed by adjuvant Imatinib in view of high risk (size >5cm); whereas, metastatic ones were primarily treated with Imatinib. As of date, the above two operated patients are recurrence-free and metastatic ones are symptom free.

**Conclusion**

In today’s era, GIST is not an uncommon entity; a high index of suspicion and sound clinical judgment is required to make a diagnosis in patients presenting with pain / bleeding from the gastro-intestinal tract. Diagnosis should be confirmed with appropriate immuno–histrochemistry tests of tissue obtained during FNAC/biopsy/excision, as outlined above and treatment streamlined to improve outcome. Timely diagnosis can help improve symptom-free survival in patients.

**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>~</td>
<td>Approximately</td>
</tr>
<tr>
<td>CD (117)/(34)</td>
<td>Cluster of Differentiation</td>
</tr>
<tr>
<td>(CE)CT</td>
<td>Contrast Enhanced Computed Tomography</td>
</tr>
<tr>
<td>FNAC</td>
<td>Fine Needle Aspiration Cytology</td>
</tr>
<tr>
<td>GIST</td>
<td>Gastro Intestinal Stromal Tumor(s)</td>
</tr>
<tr>
<td>GIT</td>
<td>Gastro Intestinal Tract</td>
</tr>
<tr>
<td>ICC</td>
<td>Interstitial Cells of Cajal</td>
</tr>
<tr>
<td>KIT/c–KIT</td>
<td>Transmembrane Tyrosine Kinase</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>PDGFRA</td>
<td>Platelet–Derived Growth Factor Receptor Alpha</td>
</tr>
<tr>
<td>TKI</td>
<td>Tyrosine Kinase Inhibitor</td>
</tr>
<tr>
<td>UGIE</td>
<td>Upper Gastro–Intestinal Endoscopy</td>
</tr>
<tr>
<td>USG</td>
<td>Ultra Sono Graphy</td>
</tr>
<tr>
<td>WT</td>
<td>Wild Type</td>
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</table>
References


