Case Report
Primary gastrointestinal stromal tumor of the liver: a case report with review of literature

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Abstract: We present a rare case of primary gastrointestinal stromal tumor (GIST) in the left liver of an 84-year-old woman. The patient underwent left lateral liver sectionectomy and transverse colon resection. Histologically, the tumor was composed of sheets of epithelioid and spindle cells with high mitotic activity. Immunohistochemically, tumor cells were positive for CD117, DOG-1, CD34, and negative for desmin, SMA, S-100 protein, HepPar1, Pan-cytokeratin. Therefore, a diagnosis of gastrointestinal stromal tumor of the liver was made. After the operation, the patient was admitted to the intensive care unit (ICU) with respiratory distress, and died of multiple organ dysfunction syndrome 13 days after surgery.

Keywords: Gastrointestinal stromal tumor, liver, primary

Introduction
Gastrointestinal stromal tumors (GISTs) are common mesenchymal tumors primarily located in the alimentary tract. GISTs frequently contain activating mutations of the KIT or PDGFRA genes [1]. GISTs occur mainly in the stomach (50-60%) and small intestine (30-35%), and less frequently in the colon and rectum (5%) and esophagus (<1%) [2]. A few cases of GISTS occurring outside the gastrointestinal tract, such as the mesentery, omentum, retroperitoneum, pancreas, uterus, gallbladder and liver, have been reported [3-6] and are referred to as “extra-gastrointestinal stromal tumors (EGISTs)”. EGISTS have a higher malignant potential and risk of recurrence after surgery than GISTs in the alimentary tract [2]. We report a rare case of primary GIST of the liver in an adult female.

Case report
An 84-year-old woman was admitted to the Department of Surgery for a palpable abdominal mass with dyspepsia and constipation for four months. The patient had undergone total gastrectomy 12 years ago for advanced gastric cancer with no history of recurrence by esophagogastroduodenoscopy and biopsy. Tumor marker levels were elevated for carcinoembryonic antigen (7.9 ng/ml; normal range, <5.0 ng/ml) and CA125 (47.9 U/ml; normal range, <35.0 U/ml) and within normal limits for CA19-9 (2 U/ml; normal range, <37.0 U/ml) and alpha-fetoprotein (1.7 ng/ml; normal range, <20.0 ng/ml). Enhanced abdominal bone computed tomography (CT) scan revealed a 20 × 15 cm heterogeneously enhancing exophytic mass in the left hepatic lobe (Figure 1). No other abdominal neoplasm was detected, and there were no signs of recurrence of the previous malignancy.

The mass was excised in December 2016. Focal invasion of the hepatic mass into the transverse colon was detected during surgery, and the patient underwent left lateral liver sectionectomy and transverse colon resection. On gross examination, the hepatic mass was attached to the muscularis propria of the colon (Figure 2A). Microscopically, the tumor was composed of sheets of epithelioid cells mixed with spindle cells. High mitotic activity of 48/50 high power fields (HPF) and areas of necrosis were observed (Figure 2B). Immunohistoc...
After the operation, the patient was admitted to the intensive care unit (ICU) with respiratory distress, and died of multiple organ dysfunction syndrome 13 days after surgery.

**Discussion**

GISTs are specific mesenchymal tumors found in the gastrointestinal tract, including the stomach, small intestine, colorectum, and esophagus. GISTs originate from interstitial cells of Cajal (ICC) located in the gastrointestinal mesenchyme. However, in recent years, the number of case reports involving GISTs outside the gastrointestinal tract has increased [3-6].

The presence of ICCs outside the gastrointestinal tract has reported extensively. A specific type of interstitial cells named interstitial Cajal-like cells (ICLCs) were recently reported in the upper and lower urinary tracts, blood vessels, pancreas, and other sites, and ICLCs are often referred to as telocytes (TCs) [7]. Fu et al. reported the presence of TCs in the liver, which were diminished in liver fibrosis [8]. An immunohistochemistry study in human specimens detected intrahepatic ICCs in the portal space, portal septa, and periphery of the hepatic lobules [9], indicating that primary GISTs may develop in the liver.

In cases of hepatic GISTs, metastatic GISTs from other sites and other primary hepatic tumors must be excluded. In the present case, the tumor was identified as a primary hepatic GIST based on intra-operative inspection and
# Primary gastrointestinal stromal tumor of the liver

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Maximum diameter (cm)</th>
<th>Cell type</th>
<th>Mitotic count (50 HPF)</th>
<th>NIH risk category</th>
<th>Treatment</th>
<th>Recurrence (months)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luo et al., 2009 [12]</td>
<td>17</td>
<td>M</td>
<td>No symptoms</td>
<td>Anterior segment</td>
<td>5.1</td>
<td>Spindle</td>
<td>0</td>
<td>High</td>
<td>RFA</td>
<td>No</td>
<td>Alive (3)</td>
</tr>
<tr>
<td>Ochiai et al., 2009 [13]</td>
<td>30</td>
<td>M</td>
<td>Abdominal fullness</td>
<td>Bilateral lobe</td>
<td>27</td>
<td>Mixed</td>
<td>75</td>
<td>High</td>
<td>- Lt. trisegmentectomy (initial)</td>
<td>Residual liver (24) - Residual liver and thoracic operative scar (60)</td>
<td>Alive (&gt;66)</td>
</tr>
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<td>Luo et al., 2009 [12]</td>
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<td>Spindle</td>
<td>0</td>
<td>High</td>
<td>RFA</td>
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<td>Residual liver (24) - Residual liver and thoracic operative scar (60)</td>
<td>Alive (&gt;66)</td>
</tr>
</tbody>
</table>

**Table 1. Clinical and pathological characteristics of hepatic GISTs**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Location</th>
<th>Maximum diameter (cm)</th>
<th>Cell type</th>
<th>Mitotic count (50 HPF)</th>
<th>NIH risk category</th>
<th>Treatment</th>
<th>Recurrence (months)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamamoto et al., 2010 [14]</td>
<td>70</td>
<td>M</td>
<td>Loss of appetite</td>
<td>Left lobe</td>
<td>20</td>
<td>Epithelioid</td>
<td>1</td>
<td>High</td>
<td>Lt. HTX</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Louis et al., 2014 [16]</td>
<td>55</td>
<td>F</td>
<td>Hypochondriac pain</td>
<td>Segment 3/2/6/8</td>
<td>18/6/6/6/6</td>
<td>Spindle</td>
<td>10</td>
<td>High</td>
<td>Segmentectomy and partial resection + IM</td>
<td>No</td>
<td>Alive (6)</td>
</tr>
<tr>
<td>Kim et al., 2014 [17]</td>
<td>71</td>
<td>M</td>
<td>No symptoms</td>
<td>Lateral segment</td>
<td>6.8</td>
<td>Spindle</td>
<td>30</td>
<td>High</td>
<td>Lateral segmentectomy and tumor resection + IM</td>
<td>No</td>
<td>Dead (19)</td>
</tr>
<tr>
<td>Mao et al., 2015 [18]</td>
<td>60</td>
<td>F</td>
<td>No symptoms</td>
<td>Right lobe</td>
<td>19</td>
<td>Spindle</td>
<td>10</td>
<td>High</td>
<td>Hepatic resection and auto-transplantation + IM</td>
<td>No</td>
<td>Alive (12)</td>
</tr>
<tr>
<td>Lin et al., 2015 [19]</td>
<td>67</td>
<td>F</td>
<td>Fatigue</td>
<td>Right lobe</td>
<td>7.4</td>
<td>Mixed</td>
<td>8</td>
<td>High</td>
<td>- Surgery + IM (initial)</td>
<td>Residual liver (25) - Multiple bone metastaeses (50)</td>
<td>Alive (50)</td>
</tr>
<tr>
<td>Su et al., 2015 [20]</td>
<td>65</td>
<td>M</td>
<td>Malaise, loss of appetite, and epigastric pain</td>
<td>Left lobe</td>
<td>12</td>
<td>Spindle</td>
<td>5</td>
<td>High</td>
<td>IM + chemotherapy + sunitinib</td>
<td>No</td>
<td>Dead (13)</td>
</tr>
<tr>
<td>Nagai et al., 2016 [21]</td>
<td>70</td>
<td>F</td>
<td>No symptoms</td>
<td>Lateral segment</td>
<td>6.8</td>
<td>Spindle</td>
<td>35</td>
<td>High</td>
<td>Lateral segmentectomy</td>
<td>No</td>
<td>Alive (6)</td>
</tr>
<tr>
<td>Wang et al., 2016 [22]</td>
<td>61</td>
<td>M</td>
<td>No symptoms</td>
<td>Caudate lobe</td>
<td>7.3</td>
<td>Spindle</td>
<td>NA</td>
<td>High</td>
<td>Caudate lobe resection</td>
<td>No</td>
<td>Alive (&gt;12)</td>
</tr>
<tr>
<td>Cheng et al., 2016 [23]</td>
<td>63</td>
<td>M</td>
<td>No symptoms</td>
<td>Right lobe</td>
<td>15</td>
<td>Spindle</td>
<td>&gt;5</td>
<td>High</td>
<td>Hepatic resection + IM</td>
<td>No</td>
<td>Alive (60)</td>
</tr>
<tr>
<td>Present case</td>
<td>84</td>
<td>F</td>
<td>Palpable abdominal mass with dyspepsia and constipation</td>
<td>Left lobe</td>
<td>20</td>
<td>Mixed</td>
<td>48</td>
<td>High</td>
<td>Lt. lateral sectionectomy with segmental colon resection</td>
<td>No</td>
<td>Dead (0.43)</td>
</tr>
</tbody>
</table>

**Notes:**
- HPF, high-power field; HTX, hepatectomy; IM, imatinib; Lt., left; NA, not available; RFA, radio-frequency ablation; Rt., right.
imaging examinations. Despite the direct invasion of the hepatic tumor into the transverse colon, the invasive focus was limited to one section of the colon, and the center of the tumor was located in the hepatic parenchyma. On CT scan, a positive beak sign was observed at the tumor margin, and the vascular supply of the tumor was derived from the hepatic artery, suggesting that the tumor originated from the liver. Additionally, histopathological features detected by immunohistochemical staining strongly supported a GIST diagnosis. Negative staining for pan-cytokeratin, HepPar1, desmin, SMA, and S-100 excluded the possibility of recurrent gastric carcinoma or other types of sarcoma.

Since the first report by Hu et al. [6] in 2003, 15 cases (including the present case) diagnosed as primary liver GIST have been reported. The clinicopathological features and treatment outcomes of the reported cases are detailed in Table 1. Our reviews exhibited a slight male predominance (60.0%) with an age range of 17 to 84 years (median, 63 years). Clinical manifestations of the patients were nonspecific. The majority of the tumors were larger than 10 cm in greatest dimension with a median diameter of 15 cm (range 5.1-27 cm).

Microscopically, 11 of the 15 cases showed spindle cell type, one was of an epithelioid cell type, and three had mixed spindle and epithelioid cell types. Excepting one case with no available data, the median mitotic count was 15/50 HPF (range, 0-75/50 HPF). According to the modified 2008 National Institute of Health (NIH) risk classification [10], all 15 cases categorized as high-risk tumors, including the present case.

Of 15 patients, 13 patients underwent complete surgical resection; one patient received radiofrequency ablation; one patient was treated with chemotherapy alone. Two patients had received imatinib chemotherapy at time of recurrence and effectively treated. Five patients underwent adjuvant imatinib therapy and only one of them died of the disease. Of the 14 patients with available prognostic data, the median recurrence-free survival was 19 months (95% confidence interval, 9.6-28.4 months; range, 0.4-60.0 months).

Consistent with the previous reports, our case showed a large tumor size with high mitotic activity and a high risk of tumor metastasis by NIH consensus criteria. Treatment with imatinib mesylate was indicated; however, the patient died of multiorgan failure 13 days after surgery. The present case represents a rare occurrence of primary GIST of the liver. Preoperative diagnosis of primary hepatic GISTs is difficult because of lack of special features on CT and MRI scans. Hepatic GISTs must be distinguished from metastatic lesions from the gastrointestinal tract or other liver neoplasms. Primary hepatic GISTs should be considered as highly aggressive tumors.

Disclosure of conflict of interest

None.

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References

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