Abstract:
A case of perforated gastrointestinal stromal tumour (GIST) of small intestine causing acute abdomen is described, with a brief review of the literature. A male patient presented with symptoms of acute abdomen. After evaluation, a laparotomy was performed, where perforation of a tumour in the jejunum was found. The perforated part along with the tumour was resected and the cytopathological examination showed that the tumour was GIST. Postoperatively, the patient received treatment, using imatinib. Gastrointestinal stromal tumours are relatively rare and often present with vague symptoms. Their first clinical manifestation as acute abdomen due to their perforation is extremely rare. In emergency laparotomy, a R0 resection is required and adjuvant therapy with imatinib must be considered.

Keyword: Acute abdomen, perforation, GIST, imatinib.

A 25 year-old male patient presented with diffuse abdominal pain lasting for 10 hours, vomiting, abdominal distention. Patient was dehydrated, tachycardia was present and there was diffuse rigidity of all the quadrants of abdomen. Acute abdomen was diagnosed and he was admitted to the Surgical Department. Routine blood investigations were normal except for elevated white blood cell (WBC) count. Serum amylase and lipase were normal. Upright chest and abdominal radiograph showed no abnormalities. Plain CT abdomen was performed urgently which showed soft tissue lesion seen adjacent to small intestinal loops in the left iliac fossa measuring 5 * 3 cms (Fig 1).

FIG 1 : PLAIN CT ABDOMEN SHOWING THE SOFT TISSUE MASS 5 * 3 CM ADJACENT TO SMALL INTESTINAL LOOPS
An emergency laparotomy was done immediately for peritonitis, which revealed diffuse peritonitis caused by a perforated small intestinal tumour of size 5 * 4 cm seen in the jejunum about 20 cm from the DJ flexure with mesenteric nodes (Fig 2). The tumour with 5cm margin on either side excised and regional lymph nodal biopsy done and end to end anastomosis of the jejunum was performed. A search of the entire gastrointestinal tract and the peritoneal cavity did not reveal other abnormalities. The patient had a postoperative course without complications and was discharged from the hospital on the 12th postoperative day.

Cytopathological examination of the tumour revealed a solid greyish white neoplastic mass sized 5 * 4 cm and the microscopic examination of the tumour showed spindle cells with elongated nuclei and few polygonal cells with moderate nuclear pleomorphism, with 3-4 mitotic counts / 50 HPF. The resected lymph node showed reactive hyperplasia. Further examination, using immunohistochemical techniques, was positive for the surface antigen CD 117 / C-KIT, thus suggesting the diagnosis of GIST of the small intestine. Postoperatively, the patient was treated by oral administration of 400 mg once a day of imatinib and the patient is on regular follow up.

FIG 2 : JEJUNAL MASS 5 * 4 CMS SHOWING PERFORATION, MASS SEEN 20 CMS FROM DJ FLEXURE
GISTs typically occur in patients around the sixth decade of life and can be found in any site of the gastrointestinal tract (1,3,5,6). Small-sized tumors (<2 cm) are usually asymptomatic, and are discovered incidentally, while larger lesions present as large abdominal masses, with or without clinical manifestations. The symptoms and signs are not disease-specific (1,3,7) and as a consequence about 50% of GISTs have already metastases at the time of diagnosis, usually to the liver or the peritoneum (1,8,9). Although the diagnostic procedure includes several examinations, such as barium examination of the gastrointestinal tract (10), computer tomography (6) and angiography (11), none of them can establish the correct diagnosis with 100% certainty. The preoperative percutaneous fine needle aspiration of the tumor for diagnostic purpose is not indicated because of the danger for potential intraperitoneal migration or tumor rupture (1). Recently, several studies pointed out the significance of endoscopic ultrasound-guided fine-needle aspiration for the diagnosis of GIST with a reported accuracy of 89% (12). On the other hand, positron-emission tomography (PET) with 18F-fluoro-2-deoxy-D-glucose is a very useful tool for the postoperative follow-up of patients receiving imatinib (13). GISTs can be categorized as low or high-risk tumours by taking into account the possibility of metastasis or recurrence (4,14). However, the main prognostic factor is the mitotic count. A prognostic classification was defined by Fletcher et al and is widely accepted and used today.

Table I: GISTs classification by Fletcher et al (15)

<table>
<thead>
<tr>
<th>Risk of malignancy</th>
<th>Size of tumour (cm)</th>
<th>Mitotic counts (80HPF)</th>
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<tbody>
<tr>
<td>Very low</td>
<td>&lt; 2</td>
<td>&lt; 5 / 50</td>
</tr>
<tr>
<td>Low</td>
<td>2 – 5</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&lt; 5 – 10</td>
<td>6 – 10 &lt; 5</td>
</tr>
<tr>
<td>High</td>
<td>&gt; 5 &gt; 10 Any size</td>
<td>&gt; 5 Any counts &gt; 10</td>
</tr>
</tbody>
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Immunohistochemical examination of GISTs is always positive for KIT protein (CD117 antigen), while the positivity regarding other markers varies (Table II) (1,3,4,16,17). Table II: Proportion of GISTs positivity for various immunohistochemical markers

<table>
<thead>
<tr>
<th>Marker</th>
<th>Positivity</th>
</tr>
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<tbody>
<tr>
<td>C-KIT</td>
<td>90-95%</td>
</tr>
<tr>
<td>CD34</td>
<td>70%</td>
</tr>
<tr>
<td>SMA</td>
<td>20-30%</td>
</tr>
<tr>
<td>S100</td>
<td>10%</td>
</tr>
<tr>
<td>Desmin</td>
<td>&lt;5%</td>
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</tbody>
</table>

DOG-1 (Discovered on GIST-1) is a new marker for diagnosing GISTS. The treatment of choice for GISTS is the surgical excision of the tumour. All tumours must be completely resected (R0 resection), where possible, including the tissues that are infiltrated, while systemic lymph node dissection is not recommended by many authors (18,19). Complete surgical resection is connected with 48-65% five-year survival. Partial resection must only be performed in case of large tumours, for palliative purposes or for the control of symptoms or complications such as compression of other organs, hemorrhage, or pain (1).

The prognosis is dismal when the tumour presents with symptoms or signs such as perforation, multifocal location or metastatic lesions. Patients with locally advanced tumours have 46% five-year survival. Perforation of the tumour lowers the five-year survival to 24%, probably due to peritoneal dissemination (20). These patients have a similar evolution as patients with incomplete tumour resection, with shorter disease-free survival and mean survival of 17 months (19).

GIST response to conventional chemotherapy is very poor (<10%), while radiotherapy is only used in cases of intraperitoneal hemorrhage, when the precise location of the tumour is known, or for analgesic purposes (1,4,19). Imatinib, was found to act as a powerful selective inhibitor of tyrosinekinases (c-ABL, bcr-ABL), of PDGFR receptor (platelet-derived growth factor receptor) and of c-kit receptor. Imatinib is well tolerated by oral administration, and the suggested efficient dose must be >300 mg per day to achieve curative results (1,21). The first clinical studies demonstrate that imatinib is the first effective treatment for non-resectable or metastatic GISTS, whereas long-term results are still not extracted because of the short time of use (1). Further clinical studies are designed, studying the use of imatinib both preoperatively and postoperatively (1,5).

CONCLUSIONS:

Patients with GISTS have limited treatment options. Complete surgical resection without extensive lymph node sampling is still the primary treatment option, but even this has resulted in poor outcome and recurrence. Patients with complications such as perforated tumours, metastatic tumors and locoregional recurrence have an even worse outcome. Prior to the advent of imatinib, systemic treatments were largely ineffective. Although adjuvant and neoadjuvant therapies with imatinib are still investigational, it has considerable activity in patients with advanced disease such as perforated tumours and should thus be considered as an adjuvant to surgery.
REFERENCES: