Pathological examination showed a tumour (A) measuring 15 cm x 10 cm with a thin outer capsule. The tumour was attached to the bowel wall (A, B arrows). Cut section showed prominent haemorrhagic and cystic degeneration and irregular solid pale nodules of tumour were noted (B). Microscopic examination showed a spindle cell tumour comprising uniform cells arranged as ill-defined fascicles (C). The tumour cells were patchy SMA positive and diffusely CD117 positive (F, brown staining). Mitotic activity was not seen.

WHAT IS THE DIAGNOSIS?

This issue we bring you a case report of an abdominal tumour followed by an overview of the relevant pathological, molecular and prognostic features.

CLINICAL HISTORY
A 53 year old male presents with abdominal pain and distension. A palpable tumour was noted and CT imaging confirmed an intra-abdominal mass. Intra-operatively the mass was attached to the small bowel. Complete excision including removal of a short segment of bowel was undertaken.

Incidence: It is the commonest gastrointestinal mesenchymal tumour with an incidence 10-20 per million people, annually. 90% occur in adults with a median age of 63 years. No geographic, race, ethnic or occupational predilection is known.

Sites: entire gastrointestinal tract ? mouth to anus. Commonest sites: stomach, small intestine. Rarely occurs outside the GIT ? these are referred to extra-intestinal GISTs (eGISTS) ? mesentery, retroperitoneum, omentum.

DIAGNOSIS: GASTROINTESTINAL STROMAL TUMOUR (GIST) ? HIGH RISK

QUICK FACTS:
Definition: GISTs are tumours that arise from the specialised pacemaker cells within the GI tract that control peristalsis ? the interstitial cells of Cajal. Historically this tumour was diagnosed leiomyoma or leiomyosarcoma.
Prognostic features: Systems attempting to predict outcome have been developed. Currently, the most widely accepted system is the NIH Consensus system. The 7th edition of the UICC TNM staging system has been provisionally incorporated into the T-staging. Due to lack of large scale studies, variable tumour size and site-specific dependency, the grading system may be revised - see table for details.

MANAGEMENT

Localised GIST: Complete surgical resection is the gold standard. The aim is removal without tumour rupture.

Advanced GIST (metastatic/recurrent/tumour inaccessibility): Imatinib mesylate - a powerful inhibitor of c-kit and PDGFRA receptors initially used for chronic myeloid leukaemia treatment has been shown to improve survival. It can be used as neo-adjuvant therapy to improve chances of complete resection, post operatively to reduce the risk of recurrence and as palliation in metastatic disease.

Primary resistance to this treatment is rare and is associated with KIT exon 9 mutation or a non-detectable kinase mutation. 50% of patients have been shown to become resistant to treatment after 2 years - usually due an acquired secondary mutation.

Clinical presentation: variable, 70% symptomatic ? related to bleeding or a mass.

Diagnosis: Confirmation requires histology. These tumours show a varied microscopic appearance ranging from spindled to epithelioid. The differential diagnosis is wide and includes smooth muscle tumours, nerve sheath tumours, myofibroblastic proliferations/tumours, mesothelioma and carcinoma.

Special investigations: Immunohistochemical positivity for CD117/c-KIT (95%), CD34 (50-80%) and SMA (30%) is documented. Newer markers include DOG-1 (Discovered on GIST 1) and Protein kinase theca. 5% of tumour cells are CD117 negative which show wild type KIT or PDGRFA mutations.

Molecular features: Most tumours show distinct activating gene mutations of the c-KIT tyrosine trans-membrane receptor. PDGFRA mutations are also described. Detailed mutational analyses of the c-KIT and PDFRA genes have linked mutations within certain exons to prognosis and treatment response e.g. c-KIT mutations comprising in-frame deletions of exon 11 are associated with a poor clinical outcome but missense point mutations of the same exon are associated with a better prognosis.

RISK STRATIFICATION OF GASTROINTESTINAL STROMAL TUMOURS

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>NIH Risk Category</th>
<th>TNM ? T stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour size (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2</td>
<td>Very low</td>
<td>T1</td>
</tr>
<tr>
<td>&gt;2≤5</td>
<td>Low</td>
<td>T2</td>
</tr>
<tr>
<td>&gt;5≤10</td>
<td>Intermediate</td>
<td>T3</td>
</tr>
<tr>
<td>&gt;10</td>
<td>High</td>
<td>T4</td>
</tr>
<tr>
<td>≤2</td>
<td>Intermediate/high</td>
<td>T1</td>
</tr>
<tr>
<td>&gt;2≤5</td>
<td>Intermediate/high</td>
<td>T2</td>
</tr>
<tr>
<td>&gt;5≤10</td>
<td>High</td>
<td>T3</td>
</tr>
<tr>
<td>&gt;10</td>
<td>High</td>
<td>T4</td>
</tr>
</tbody>
</table>

REFERENCES AVAILABLE ON REQUEST.


- Rubin BP et al. Gastrointestinal Tumour Advancements in Diagnosis and Management. Arch Pathol Lab Med 2011;(135), 1298-1310


Headquarters and Main Laboratory
Umuyenzi Plaza | 1st floor
Remera | Kisimenti | Airport Road
Kigali | Rwanda
Tel: +250 784 035 660 | 252 582 901
Website: www.lancet.co.rw

Rubavu Branch Opening Soon!

Follow us on twitter
www.lancet.co.rw @LancetRwanda