INTRODUCTION
The small bowel accounts for 80% of the length and 90% of the mucosal surface of the gastrointestinal tract and yet only 1% of the gastrointestinal (GI) malignancies arise from it. The age-adjusted incidence of small bowel malignancies is 1/100,000 with a prevalence of 0.6%. Compared to other GI tumours, information about small intestinal malignant tumours is rather limited. This is not surprising given that estimated malignant tumours of the small intestine are 40-70 times less common than colonic carcinoma. Small bowel, for example, adenocarcinoma accounts for 2% of GI tumours, and 1% of GI cancer deaths.

The uncommon nature, vague and non-specific manifestations, and the varied tumour types lead to delay not only in diagnosis, but also in the treatment of these tumours. In case of malignant tumours, this extrapolates to an overall poor prognosis.

In the past, the authors have published the surgical outcomes with colon, rectal and duodenal cancers. However, since small bowel tumours are rare, it is imperative that an improved appreciation of their clinical and pathological features be emphasized for better management of these rare neoplasms.

Epidemiology:
The average age at diagnosis of small bowel tumours is 59.5 years, with a range of 14-84 years. Patients harbouring malignant lesions have an average age of 56.8 years compared with mean age of 62.2 years for patients with benign lesions. Although there is no significant gender preference, many investigators, including the Surveillance, Epidemiology and End Results (SEER) program (1973-2000) have reported a slight male predominance for the malignant types. Recently, incidence data from the SEER program were used to analyse the four histologic types of small bowel cancer i.e. adenocarcinomas, carcinoid tumours, lymphomas, and sarcomas/gastrointestinal stromal tumours (GIST). Blacks had almost double the incidence of carcinomas and carcinoid tumours compared to whites (10.6 vs. 5.6 per million people; 9.2 vs. 5.4 per million people, respectively). Furthermore, the geographic correlation between large and small bowel cancer suggested shared aetiologies. Small bowel adenocarcinomas have an increased incidence in developed Western countries. Mediterranean lymphomas are common in Middle East and North Africa occurring in lower socio-economic classes and younger patients.

Classification of small intestinal tumours:
Benign tumours of the small intestine include leiomyomas, adenomas, lipomas, lymphangiomas, haemangiomas, fibromas and others. The four most common malignant neoplasms of the small bowel are adenocarcinomas (33-50%), carcinoids (17-40%), lymphomas (14-19%) and GIST/sarcomas (15-19%). While most studies report that adenocarcinomas constitute the largest number of patients with small bowel tumours, a large series from Di Sario et al. reported that carcinoid had listed carcinoids as the most frequent tumour. Primary gastrointestinal lymphomas have numerous classifications but amongst the most widely used are the Isaacson classification (Table I) and the WHO classification (lymphomas are considered to be of 6 main types, viz. diffuse large cell lymphoma, MALT lymphoma, Burkitt’s lymphoma, peripheral T-cell lymphoma, mantle cell lymphoma, and follicular lymphoma).
Clinical features:
The presentation is very non-specific, with insidious onset and slow progression. Malignant tumours, in general, present with anorexia, weight loss, unexplained anaemia, abdominal pain and symptoms of obstruction. Dorman identified cramping abdominal pain, weight loss and a palpable abdominal mass as a “diagnostic triad of paramount importance”.21

Adenocarcinomas tend to cause cramps (due to partial obstruction), jaundice (in duodenal or periampullary locations), and occasional complete intestinal obstruction. Leiomyosarcomas present more commonly with GI bleeding. As with lymphomas, they present with abdominal masses, or pain caused by pressure from a large mass or occasionally an acute abdomen. Extensive intestinal lymphomas can present with malabsorption and steatorrhoea. Carcinoid tumours can present with mechanical bowel obstruction and rarely, with carcinoid syndrome that is characterized by flushing, diarrhoea, bronchospasm and signs of right-sided heart failure. GISTs present with abdominal pain, bleeding, weight loss and anaemia. Weight loss and a palpable mass usually differentiate a malignant from a benign tumour.

Diagnosis (Algorithm 1):
A gastrointestinal source of pathology cannot be excluded without evaluating the small intestine. The duodenum and proximal jejunum are best investigated by an extended upper GI endoscopy. The distal jejunum and ileum can be studied by enteroclysis, enteroscopy and wireless capsule endoscopy. Double contrast small bowel examination, or enteroclysis is currently the best technique that can be employed for accurate information regarding the status of the small intestine. Barium and methylcellulose are infused in the small bowel under pressure and this produces distension of the small bowel, thereby, enabling the radiologist to follow the infused material throughout its course in the small intestine. Furthermore, this examination offers the advantage of evaluating the mucosa for irregularities and hence this method is easily the best technique that is widely available and relatively inexpensive (Figure 1).

Computerized tomography aided enteroclysis, combining a CT scan with enteroclysis is considered an even better investigational approach in small bowel cancers. Johanssen while comparing wireless capsule endoscopy versus CT enteroclysis for neuroendocrine tumours found that capsule endoscopy had a limited role due to the extraluminal growth of these tumours. It was also found that CT enteroclysis had a high false positive rate.22 In a comparison of enteroclysis and barium meal follow through,23 enteroclysis demonstrated a sensitivity of 95% and detection rate of 90% as opposed to 61% and 33% for barium meal follow through, respectively. Magnetic resonance enteroclysis is very efficient in the diagnosis of small bowel tumours.24 Push enteroscopy enables examination of the jejunum for 40-60 cm distal to the ligament of Treitz with the help of a longer endoscope. CT scan is used to stage the disease. Radiologic appearances of lymphomas include six patterns, viz. aneurysmal form, infiltrative, diffuse or polypoidal nodular type, ulcerative, mesenteric form and sprue form.25 Percutaneous FNAC is not to be attempted as it carries the risk of tumour spillage intra-abdominally. The biopsied tissue obtained should be subjected to immunohistochemistry staining for c-KIT, CD 117, CD34, SMA, desmin and S-100.

Role of capsule endoscopy:
Capsule Endoscopy (CE) has been extensively studied for its role in obscure gastrointestinal bleeding. The number of studies evaluating the use of CE for the diagnosis of small bowel tumours is very limited.26-28

Table I: Classification of primary GI lymphomas (Isaacson).19

<table>
<thead>
<tr>
<th>Classification</th>
<th>B-Cell (&gt;90%)</th>
<th>Mucosa Associated Lymphoid Tissue (MALT) type</th>
<th>Low-Grade</th>
<th>High Grade with/without low-grade component</th>
<th>Immunoproliferative small intestinal disease</th>
<th>Low-grade</th>
<th>High grade with/without low-grade component</th>
<th>Mantle cell (lymphomatous polyposis)</th>
<th>Burkitts – like and Burkitts</th>
<th>Other lymphomas corresponding to lymph node equivalents</th>
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<tbody>
<tr>
<td>T-Cell (&lt;10%)</td>
<td>Enteropathy associated T-Cell lymphoma</td>
<td>Non-enteropathy associated T-Cell Lymphoma</td>
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Figure 1: Diagnostic flow chart for small bowel tumours.
The advantages over the existing diagnostic modalities include its relative non-invasiveness, lack of need for sedation, and non-exposure to ionizing radiation. A recent meta-analysis, as well as a large retrospective analysis have confirmed that while CE does enable diagnosis of small bowel tumours, its routine use should be selective. The criteria for its use should be young patients (< 50 years) with obscure GI bleeding, chronic abdominal pain, and inflammatory bowel disease, all in whom the diagnosis has not been established by the routine investigations mentioned above.

Besides the limitations in the inability to obtain a biopsy, precisely localize lesions, and perform therapeutic interventions, an important problem encountered is the risk of capsule impaction that is more likely to be seen in the presence of bowel strictures present in malignant and inflammatory diseases.

Thus, while some have suggested that CE does have a role in diagnosing specific tumours like lymphomas and neuroendocrine tumours, further studies are required to characterize its overall benefit in terms of outcome and prognosis.

Role of double balloon enteroscopy:
Double Balloon Enteroscopy (DBE), developed in 2001, has also found an application in the diagnosis of small bowel tumours and reports on its safety, efficacy, and indications are now coming in which it will help to decide its final position in the diagnostic algorithm.

The main advantage offered by DBE appears to be its ability to permit a total enteroscopy. This would allow the endoscopist to be able to localize lesions seen on capsule endoscopy, biopsy the lesions, and also perform few therapeutic modalities.

The current applications appear to be diagnosis of tumours including biopsies, and also, therapeutic interventions like polypectomies and stenting of inoperable malignant strictures.

Limitations continue to be the long duration for performing the investigation, the increased exposure to radiation required for fluoroscopic guidance, and the increased risk of loop formation seen during the colonoscopy portion if the study owing to the length of the endoscope, flexibility of the overtube, and the diameter of the system. Important complications encountered are perforations and pancreatitis.

Staging:
The American Joint Committee on Cancer (AJCC) has designated staging by TNM Classification as described in Table II and III.

Treatment:
Benign tumours of the small intestine, whether leiomyomas or haemangiomas, are best treated by segmental resection with clear margins. Adenomas, which usually arise in the duodenum, where they tend to be periampullary, can be treated by ampullectomy if they are definitely benign. High-grade dysplasia in an adenoma is treated by a pancreaticoduodenectomy.

The basic surgical principles for managing small bowel tumours include – wide resection (with clear margins) with lymphovascular clearance down to the mesentery with restoration of bowel continuity by end-to-end stapled or hand-sewn anastomoses.

Adenocarcinomas in the duodenal or ampullary regions are best treated by a pancreaticoduodenectomy. Ileal and jejunal malignancies are treated by radical segmental small bowel resection along with the mesentery and draining involved lymph nodes. Adequate proximal and distal disease-free surgical cut margins must be ensured. Both, hand-sewn and stapler anastomoses, achieve equally good results. Terminal ileal lesions may have to be treated by radical right hemicolectomy.

Small bowel resection, together with resection of the associated mesentry, is the treatment of choice for small bowel carcinoids. These tumours are frequently associated with “buckling” of the intestine as a result of extensive mesenteric fibrosis. Occasionally, mesenteric ischaemia due to either fibrosis or an associated mesenteric angiopathy may occur. Resection is, therefore, undertaken for palliative purposes, even in patients with known metastatic disease.

Liver
metastases may be treated by local ablation or resection to reduce the total tumour burden and to prevent further growth, or to reduce the release of bioactive peptides.\textsuperscript{43} Somatostatin analogues are the first line treatment for carcinoid syndrome and metastatic disease. Reports of use of interferon alpha alone showed a regression in 15% patients.\textsuperscript{44} When used along with somatostatin in tumours that were resistant to somatostatin alone, the results were accompanied by low regression rates and a considerable amount of side effects.\textsuperscript{45} Cytotoxic chemotherapy has limited uses in metastatic carcinoid disease.

Leiomyosarcomas are also best managed by radical surgical resection whenever possible, with surgical bypass being reserved for unresectable primary disease. In metastatic unresectable disease, the benefit provided by chemotherapy and radiotherapy is limited because of the low mitotic activity of the tumour cells and its weak vascularisation. Long-term survival is limited by poor prognosis criteria: high-grade malignancy, size greater than 5 cm, tumour extension, perforation of the tumour, quality of surgical resection and histological type.

Standard treatment of primary GISTs is resection. There is no need for a lymphadenectomy. Imatinib Mesylate is being used for metastatic tumours that express c-KIT.

Prognostic factors for GISTs determine survival.\textsuperscript{46} Poor prognostic factors include: a tumour size > 5 cm, incomplete resection at surgery or tumour rupture at surgery, high tumour grade, presence of metastases, mitotic rate > 5 mitosis per 50 high power films, high cellularity, coagulative tumour necrosis, pleiomorphism, high S phase fraction, and DNA aneuploidy, high Ki-67 score and telomerase activity.

Lymphomas of the small intestine are well-managed by chemotherapy i.e., cyclophosphamide, doxorubicin, vincristine, and prednisolone, except for low-grade lymphomas limited to the submucosa. Resections for lymphomas entail a complete resection with a wedge of mesentery. Surgical resections are indicated for disease localized to the bowel wall and occasionally in patients who receive chemotherapy and radiotherapy and are at risk for perforations. Follicular – anti CD20 Antibody Rituximab is used for indolent mantle cell lymphoma.\textsuperscript{47}

A recent publication has shown that Rituximab can induce and maintain a complete remission following surgery in primary GI lymphomas (NHL).\textsuperscript{48} T-cell lymphomas are generally unresponsive to conventional chemotherapy. The best prognosis for intestinal lymphoma is for B-cell lymphomas of low-grade (75% 5-year survival), while the worst is for T-cell lymphomas (25% 5-year survival).\textsuperscript{49} Radiation therapy is used to decrease recurrence in the tumour bed. Adjuvant therapy has shown to improve survival. Lymphomas that respond faster and better to chemotherapy do tend to have a shorter disease-free survival as compared to the indolent lymphomas or the slow responders. The overall survival of lymphomas of the intestine is better than that of carcinoma for the same site. The most consistent factor in prognosis is the stage of the disease. Better survival is seen in patients with localized disease.\textsuperscript{50}

**CONCLUSION**

Small bowel tumours do have a vague presentation but an alert clinician should suspect such a lesion when a patient presents with bowel symptoms and a normal oesophagogastrocolonoscopy and colonoscopy. A CT-scan is an important first investigation in such situations. Wireless capsule endoscopy and double balloon enteroscopy are evolving as diagnostic modalities. Surgical resection with a wide margin continues to be the best treatment modality available. Adjuvant treatment is dictated by the detected pathology following an exploration.

**REFERENCES**


34. Pennazio M. Capsule endoscopy: where are we after 6 years of clinical use? Dig Liver Dis 2006; 38:867-78.